CASE NO. A163682

IN THE COURT OF APPEAL
OF THE STATE OF CALIFORNIA

FIRST APPELLATE DISTRICT, DIVISION 1

CENTER FOR ENVIRONMENTAL HEALTH,

Plaintiff-Appellant,

v.

PERRIGO COMPANY, et al.,

Defendants-Respondents.

Appeal from a Judgment Based on an Order Sustaining Demurrers Without Leave to Amend

Superior Court of the State of California for the County of Alameda, Case No. RG 20-054985
the Honorable Winifred Y. Smith, Presiding

APPELLANT'S APPENDIX IN LIEU OF CLERK'S TRANSCRIPT

VOLUME 3 (EXHIBITS 35-66)(AA0660-AA1201)

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

Case No. RG 20-054985

ASSIGNED FOR ALL PURPOSES TO:
Hon. Winifred Smith, Department 21

PLAINTIFF'S OMNIBUS OPPOSITION TO DEFENDANTS' DEMURRERS

Date: April 21, 2021
Time: 10:00 a.m.

Reservation Numbers: R-2240281, R-2240282, R-2240283, R-2240276, R-2242157

SAC Filed: January 4, 2021
Trial Date: None Set

[Filed concurrently with Plaintiff's Request for Judicial Notice; Declaration of Mark N. Todzo]

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CEH respectfully submits this brief in response to four separate demurrers filed by (1) Defendants Sanofi-Aventis U.S. LLC and Chattem, Inc. (hereinafter, the "Brand Name Manufacturers"); (2) Defendants Perrigo Company, Granules USA, Inc., Dr. Reddy's Laboratories, Inc., and Dr. Reddy's Laboratories Louisiana, LLC (hereinafter, the "Generic Manufacturers"); (3) Defendant Apotex Corp., another manufacturer of generic drug products (hereinafter, "Apotex"); and (4) Defendants Target Corporation and 7-Eleven, Inc. (hereinafter, the "Private Label Retailers"). Because of the overlapping issues among the demurrers (and in accordance with the Court's order dated February 24, 2021), CEH has elected to file a single omnibus opposition to all four for the convenience of the Court.[1]

I. INTRODUCTION

Defendants' over-the-counter ("OTC") antacid products made with ranitidine as the active ingredient (the "Products") are all contaminated with n-nitrosodimethylamine ("NDMA"), a carcinogen so potent that it is used in laboratory experiments to cause cancer in animals. NDMA is not the active ingredient in the Products. Nor is it an inactive ingredient that is listed on any labeling for any of the Products or any applications for approval to the U.S. Food and Drug Administration ("FDA"). NDMA is, however, so harmful that when the FDA learned that the Products were contaminated with significant amounts thereof, it required Defendants to recall the Products due to the potential for harmful exposure of the public to NDMA. Defendants nevertheless never bothered to reduce or eliminate the NDMA in the Products or even attempt to warn consumers about these exposures until the FDA (tipped off by a third-party laboratory) alerted them of the need to take action. Defendants themselves could and should have uncovered the NDMA contamination through simple testing of their Products. Fixing the contamination problem may be as simple as cleaning the manufacturing facilities and/or storing the Products more carefully. Defendants' utter failure to address the NDMA contamination and resulting exposures to California consumers is unconscionable. This lawsuit seeks to hold Defendants

[1] Pursuant to ¶6 of the Court's order, CEH is permitted to file a single opposition with up to 61 pages. While CEH's brief is long, it is significantly fewer pages than the aggregate number of pages set forth in the demurrers.

accountable for this conduct.

Defendants argue that they were powerless to address the NDMA contamination problem or warn for the resulting exposures because FDA regulations preclude them from taking any such action. Yet, while arguing that it is impossible for them to comply with both California and federal law, Defendants ignore the myriad ways in which they could potentially comply with Proposition 65 without prior FDA approval. Indeed, many of these steps were specifically identified by the U.S. District Court of Florida in the pending federal multi-district litigation ("MDL") involving state law products liability claims as to NDMA in ranitidine. Defendants cite to that court's recent motion to dismiss order, but somehow overlook that the court there found many of the plaintiffs' claims were ***not*** preempted by the impossibility doctrine. That court's ruling is unsurprising, since, in order for a party to successfully demonstrate impossibility preemption, it must demonstrate that ***all*** possible means of compliance with state law conflict with federal law. Defendants have made no such showing here.

The exposure provision of Proposition 65 prohibits a business from exposing individuals to listed chemicals without first providing a warning. Health and Safety Code §25249.6. Thus, there are two principal means of compliance: (1) eliminating the exposure; or (2) providing a warning for the exposure. Defendants argue that they cannot possibly comply with Proposition 65 without running afoul of FDA regulations while essentially ignoring the first means of compliance with Proposition 65's exposure provision. Defendants excuse this failure by offering an interpretation of Proposition 65 that no court has ever adopted: that the statute's provision exempting preempted claims – Health and Safety Code §25249.10(a) – actually operates more broadly than Constitutional preemption principles so as to preclude enforcement whenever federal law governs warnings, even where compliance with Proposition 65 through alternate means (such as reformulation) is eminently possible. The preemption exemption does no such thing. That provision states that Proposition 65's exposure provision shall not apply where "federal law governs warning in a manner that preempts state authority." Thus, unless Defendants can show that ***all*** methods of compliance with Proposition 65 are impossible – including the reduction or elimination of the exposure such that no warning is required – the exemption does not apply.

Moreover, Defendants have not demonstrated that they were incapable of providing warnings for the exposures. For example, all Defendants could have provided warnings by means of public advertising, which is not even regulated by the FDA. Additionally, the Brand Name Manufacturers acknowledge that they were able to add warning statements to their Products via the FDA's Changes-Being-Effected ("CBE") regulation. Although they never bothered to attempt using the CBE regulation to inform users of the dangerous NDMA exposures resulting from the use of their Products, they nevertheless argue that the CBE regulation would not have permitted such a change because the harm associated with NDMA exposure is not significant enough to warrant addition of a warning under that regulation. However, the FDA determined that such exposure posed such a significant risk of illness or injury to initiate a nationwide recall.

The Generic Manufacturers and the Private Label Retailers argue that they could not possibly comply with Proposition 65 because the FDA imposes a "duty of sameness" on them such that they must have identical labeling and ingredients as the Brand Name Manufacturers. But these Defendants fail to demonstrate that this duty of sameness extends to unintended contaminants such as the NDMA in the Products. Indeed, the FDA's own testing of the Products demonstrates that this alleged sameness does not extend to the NDMA contamination, as the Products contain drastically differing amounts of NDMA. While the intensely fact-based determinations of precisely how the NDMA is formed in the Products and what Defendants should have done to avoid it remain to be proven, a preliminary review discloses that simple changes such as different storage techniques and cleaner manufacturing processes could have significantly reduced or eliminated such contamination. That Defendants failed to take such simple actions is appalling.

Nevertheless, Defendant Apotex goes so far as to make two additional arguments – advanced by no other Defendants – that (1) the FDA's regulatory action specifically as to NDMA in ranitidine should lead this Court to find CEH's claims precluded on a "field preemption" theory, and (2) CEH's requests for injunctive relief, civil penalties, and attorneys' fees are now moot. Apotex's novel "field" preemption argument should be rejected as contrary to an express (and unique) Congressional enactment carving out Proposition 65 from the federal "uniformity"

requirements governing OTC drugs. Apotex's argument would also effectively lead to "field" preemption any time a federal agency took deliberate action in any given regulatory case. As for mootness, Apotex overlooks that a demurrer on ***remedies*** – as opposed to ***claims*** – is improper. Moreover, the determination of whether CEH's request for injunctive relief is viable should be made at the conclusion of the case upon a full record of the likelihood that Apotex's abhorrent conduct may continue. Likewise, CEH's entitlement to attorneys' fees will depend on the ultimate resolution of the case. Under no circumstance, however, could CEH's request for civil penalties be mooted. Rather, the imposition of civil penalties here will send the necessary message to Defendants that they cannot use shoddy manufacturing and storage techniques while at the same time failing to test their products for contaminants and then attempt to hide behind federal law as a shield to their liability.

II. PLEADING AND DEMURRER STANDARDS

Under California law, the complaint need only contain "[a] statement of the facts constituting the cause of action, in ordinary and concise language." C.C.P. §425.10(a)(1); *see also Ferrick v. Santa Clara Univ.* (2014) 231 Cal.App.4th 1337, 1341 (role of court is to "determine whether the complaint states facts sufficient to constitute a cause of action"). Thus, "a plaintiff is required only to set forth the essential facts of his case with reasonable precision and with particularity sufficient to acquaint a defendant with the nature, source and extent of his cause of action." *Doheny Park Terrace Homeowners Ass'n, Inc. v. Truck Ins. Exch.* (2005) 132 Cal.App.4th 1076, 1099 (citation omitted) (noting that "modern discovery procedures necessarily affect the amount of detail that should be required in a pleading"). Less particularity is required where, as here, the defendant possesses equal or superior knowledge of the facts at issue. *See id.*; *Doe v. City of Los Angeles* (2007) 42 Cal.4th 531, 549-50. Furthermore, a plaintiff is not required to anticipate and "plead around" a defendant's affirmative defenses. *See Stowe v. Fritzie Hotels, Inc.* (1955) 44 Cal.2d 416, 422; *Gomez v. Toledo* (1980) 446 U.S. 635, 640.

At the demurrer stage, the allegations in CEH's pleadings must be accepted as true. *See Del E. Webb Corp. v. Structural Materials Co.* (1981) 123 Cal.App.3d 593, 604; *Stevens v. Sup. Ct.* (1986) 180 Cal.App.3d 605, 609-10. ("Whether the plaintiff will be able to prove the pleaded

facts is irrelevant to ruling upon the demurrer.") "[A] court reviewing a demurrer must also accept as true those facts that may be implied or inferred from those expressly alleged," while "draw[ing] inferences favorable to the plaintiff, not the defendant." *Perez v. Golden Empire Transit Dist.* (2012) 209 Cal.App.4th 1228, 1239 (citation omitted) (pleading allegations are "liberally construed").[2] In the event a court believes that additional pleading is nonetheless required, leave to amend is granted with "liberality." *Angie M. v. Sup Ct.* (1995) 37 Cal.App.4th 1217, 1227.

III. RELEVANT ALLEGATIONS IN THE COMPLAINT

The operative Second Amended Complaint ("SAC"), filed on January 4, 2021, contains factual allegations sufficient to establish all elements of CEH's Proposition 65 claim. *See generally* Health & Safety Code §25249.6. Specifically, the SAC states that:

- Each Defendant is a "person in the course of doing business" that "manufactures, distributes, and/or sells the Products for sale or use in California," and that each "introduce[s] Products containing significant quantities of NDMA into the California marketplace" (SAC ¶¶2, 5-14, *see also id.* ¶41);
- "Individuals in California are exposed to NDMA when they use the Products" (*id.* ¶1; *see also id.* ¶¶2-3, 25);
- Defendants both know and intend that individuals will use the Products, thus exposing such individuals to NDMA (*id.* ¶32; *see also id.* ¶¶34-36 (explaining various ways by which Defendants knew or should have known about the NDMA issue);
- NDMA is listed under Proposition 65 as a chemical known to the State of California to cause cancer (*id.* ¶¶1, 22; *see also id.* ¶23 (NDMA is so carcinogenic that it is "used in laboratory research to induce tumors in experimental animals"); and
- Defendants have provided no warnings as to the NDMA exposures caused by the use of their Products (*id.* ¶¶3, 37, 44-45).

[2] Defendants claim that a court need not accept "mere contentions or assertions contradicted by judicially noticeable facts" (Apotex Demurrer at 3), but offer no examples of the same from CEH's operative complaint. Also, the supposition that "facts not alleged are presumed not to exist" (*id.*) clearly only applies to material facts a plaintiff needs to allege – otherwise, contrary to C.C.P. §425.10(a)(1), every complaint would contain verbose recitations on uncontroversial facts.

To remedy these wrongs, the SAC seeks injunctive relief, an award of civil penalties, and an assessment of attorneys' fees. *Id.* at 8-9 (Prayer for Relief ¶¶1-5).

In addition to pleading the elements of its Proposition 65 claim, CEH, based on the FDA's root cause analysis to determine the sources of NDMA and other nitrosamines in ranitidine, alleges that "Defendants can reduce or eliminate NDMA from the Products by using cleaner ingredients and manufacturing processes and more careful storage techniques." SAC ¶24.

IV. LEGAL BACKGROUND

A. Proposition 65.

The California Safe Drinking Water and Toxic Enforcement Act of 1986, Health & Safety Code §25249.5 *et seq.* – commonly known as Proposition 65 – was passed in a 1986 referendum by nearly two-thirds of California's voters to protect themselves from toxic chemicals. *See* Plaintiff's Request for Judicial Notice (submitted concurrently) ("CEH RJN"), Exh. 1. As its formal name implies, the law governs two activities: (1) discharges of toxicants to drinking water, and (2) exposures of individuals to toxicants. Although Defendants attempt to characterize Proposition 65 as "fundamentally a statute about warnings" (Generic Manufacturers Demurrer at 4), its purpose is considerably broader than this. Finding that "hazardous chemicals pose a serious potential threat to their health and well-being," the voters of California expressly "declare[d] their rights … to protect themselves and the water they drink against chemicals that cause cancer, birth defects, and other reproductive harm." CEH RJN, Exh. 1, at 53 (Proposed Proposition 65, §1). Preventing exposures to toxic chemicals is the driving concern here – indeed, Proposition 65's drinking water discharge restrictions do not mention warnings at all. *Compare* Health & Safety Code §25249.5, *with id.* §25249.6; *see also* CEH RJN, Exh. 1, at 52 (Proposition 65, Analysis by the Legislative Analyst, Background) (statute was intended to improve "state … programs designed to protect people against possible exposures to harmful chemicals").

Outside of the drinking water context, Proposition 65 requires any person in the course of doing business to provide clear and reasonable warnings regarding exposures that they cause to chemicals known to cause cancer, birth defects, or other reproductive harm. Health and Safety Code §25249.6. However, Proposition 65 only requires a warning where the exposure to listed

chemicals from a given product is above certain risk thresholds. *Id.* §25249.10(c). The Section 10(c) exemption allows a defendant to:

> show that the exposure poses no significant risk assuming lifetime exposure at the level in question for substances known to the state to cause cancer, and that the exposure will have no observable effect assuming exposure at one thousand (1000) times the level in question for substances known to the state to cause reproductive toxicity, based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for the listing[.]

Id.[3] For carcinogens such as NDMA, this is known as the "No Significant Risk Level" ("NSRL"). 27 Cal. Code. Regs ("C.C.R.") §25721(a), (b). To reduce burdens on regulated entities, the Office of Environmental Health Hazard Assessment ("OEHHA") – the California agency in charge of administering Proposition 65 – has established by regulation a presumptively valid "safe harbor" NSRL for NDMA of 0.04 micrograms ("µg") per day, which may be used in exposure analyses to determine if a warning is necessary. 27 C.C.R. §25705(c)(2). Thus, a defendant may avoid Proposition 65 liability for consumer product exposures either by (a) taking any number of steps to eliminate or reduce the levels of the listed chemical to below the level requiring a warning, or (2) providing a clear and reasonable warning. *Cf.* 11 C.C.R. §3201(b)(1)-(2) ("public benefit" conferred by Proposition 65 settlements is presumptively established either by "[r]eformulation of a product … or other changes in the defendant's practices that reduce or eliminate the exposure to a listed chemical," or "the giving of a clear and reasonable warning"). Far from being "forced into a Hobson's choice," as Defendants put it (Brand Name Manufacturers Demurrer at 5), this scheme provides regulated entities the proper incentives either to commit to reformulation (and thus avoid having to market their products with a cancer warning – a clear "win-win") or to provide a

[3] Defendants misleadingly claim that "[p]rivate enforcers need not make any showing on [the] applicability [of Section 10(c)] before filing suit." Brand Name Manufacturers Demurrer at 15 (citation omitted). However, prior to filing suit, a private Proposition 65 enforcer must submit information to the California Attorney General and other public enforcers attesting that the plaintiff has consulted with experts and that based on such consultation the plaintiff "believes that there is a reasonable and meritorious case for a citizen enforcement action." Health & Safety Code §25249.7(d); *see also* SAC ¶30 (CEH did so here). As required by 11 C.C.R. §3101(a), such private enforcers also "must certify that the information relied upon does not prove that any affirmative defense has merit," including any Section 10(c) defense.

warning so that California citizens can protect themselves accordingly.[4]

Where warnings are the chosen method of Proposition 65 compliance, the statute provides that:

> 'Warning' … need not be provided separately to each exposed individual and may be provided by general methods such as labels on consumer products, … posting of notices, placing notices in public news media, and the like, provided that the warning accomplished is clear and reasonable.

Id. §25249.11(f); *see also Dowhal v. SmithKline Beecham Consumer Healthcare* (2004) 32 Cal.4th 910, 918 ("The warning may be communicated through product labeling, point-of-sale signs, or public advertising."). There are extensive regulations that elaborate on Proposition 65's clear and reasonable warning requirement and provide examples of "safe harbor" warnings – exemplary warnings already deemed to be "clear and reasonable." 27 C.C.R. §25600 *et seq.* These warnings are not mandatory, *i.e.*, an entity is free to provide other warnings so long as they satisfy Proposition 65. *See Dowhal*, 32 Cal.4th at 918 (safe harbor warnings are "optional").[5] The regulations provide safe harbor warnings for consumer products generally that include warnings provided on signs, shelf tags, shelf signs, and via any electronic device or process. 27 C.C.R. §25602. In any event, a regulated entity "does not have to use the best warning method to comply with Proposition 65." *People ex rel. Lungren v. Cotter & Co.* (1997) 53 Cal.App.4th 1373, 1380 (rejecting contention that Proposition 65 is "a de facto labeling statute").

Proposition 65 provides for two additional statutory "exemptions from [the] warning requirement": one for exposures that occur less than twelve months after the chemical is listed, and another for "[a]n exposure for which federal law governs warning in a manner that preempts

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[4] Proactive companies can avail themselves of a regulatory "safe use determination" by OEHHA to confirm that their products will cause no exposure requiring a Proposition 65 warning. *See* 27 C.C.R. §25204. Alternatively (or in addition), companies can eliminate the offending chemical (or reduce it to undetectable levels) and then seek protection under 27 C.C.R. §25900, which allows an affirmative defense for defendants that have recent testing data showing "that the chemical in question was not detected."

[5] Although certain Defendants dispute this proposition (*see* Brand Name Manufacturers Demurrer at 15), cases cited by other Defendants show it to be entirely valid. *See, e.g.*, *Envt'l Law Found. v. Wykle Rsch., Inc.* (2005) 134 Cal.App.4th 60, 66-67 (cited in Generic Manufacturers Demurrer at 4).

state authority." Health & Safety Code §25249.10(a)-(b). As explained further in Section V.A.4. below, the parties disagree on the meaning of the latter provision and how it affects the federal preemption analysis.

B. OTC Drug Regulation.

Consistent with Proposition 65's protective purpose, the Food, Drug, and Cosmetic Act's ("FDCA") primary objective is "to protect consumers from dangerous products." *U.S. v. Sullivan* (1948) 332 U.S. 689, 696. To do so, the FDCA prohibits the sale of unapproved drugs. *See* 21 U.S.C. §355(a).

There are two methods by which the FDA approves OTC drugs: (1) the OTC drug monograph process, and (2) a new drug application ("NDA"). *See* 21 U.S.C. §355, §355h. All of the Products at issue in this case were approved under the NDA process or its derivative equivalent for generic drugs – an abbreviated new drug application ("ANDA") – applicable to ranitidine specifically. *See id.* §355(a) & (j). An NDA requires the submission of information on the proposed drug's ingredients and labeling, but does not address the issue of undisclosed contaminants that may be present in the drug. *See id.* §355(b)(1)(A). An ANDA is essentially a tag-along to a pre-existing NDA under which a generic drug manufacturer "can gain FDA approval simply by showing equivalence to a reference listed drug that has already been approved by the FDA." *PLIVA, Inc. v. Mensing* (2011) 564 U.S. 604, 612-13 (explaining that "[t]his allows manufacturers to develop generic drugs inexpensively, without duplicating the clinical trials already performed on the equivalent brand-name drug"). In particular, the proposed generic drug and its approved brand-name counterpart must (1) "have the same active ingredient …, route of administration, dosage form, and strength"; (2) "have the same rate and extent of absorption"; and (3) contain the same "labeling." *Mutual Pharm. Co. v. Bartlett* (2013) 570 U.S. 472, 477 (internal quotations and brackets removed). In order to be deemed "safe and effective" under the FDCA, all OTC drugs must be "manufactured in compliance with current good manufacturing practices, as established by [21 C.F.R.] Parts 210 and 211 [.]" 21 C.F.R. §330.1(a).

Once a drug has been approved for sale by the FDA, changes to the NDA or ANDA can only be made in accordance with FDA regulations. *See* 21 C.F.R. §§314.70, 314.97. Whether

FDA approval is required for such changes depends on whether the manufacturer seeks to make a "major," "moderate," or "minor" change, which are defined as whether a given change in "the drug substance, drug product, production process, quality controls, equipment, or facilities" has a "substantial," "moderate," or "minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product." *Id.* §314.70(b)(1), (c)(1), (d)(1). "Major" changes require FDA approval prior to implementation; "moderate" and "minor" changes do not. *Id.* §314.70(b)(3), (c)(3), (d)(3). Specifically included as "moderate" changes that can be made without FDA approval – known as "Changes-Being-Effected" or "CBE" – are "changes in the methods or controls to provide increased assurance that the drug substance or drug product will have the characteristics of identity, strength, quality, purity, or potency that it purports or is represented to possess" and changes "in the labeling to reflect newly acquired information." *Id.* §314.70(c)(3), (c)(6)(i) & (iii). However, for operational changes that were never part of the NDA or ANDA to begin with, such as those to address undisclosed contaminants in a drug product, 21 C.F.R. §§314.70 and 314.97 are facially inapplicable.

C. General Principles Governing Federal Preemption Analyses.

"The party who claims that a state statute is preempted by federal law bears the burden of demonstrating preemption." *Bronco Wine Co. v. Jolly* (2004) 33 Cal.4th 943, 956. Because "the purpose of Congress is the ultimate touchstone in every preemption case" (*Wyeth v. Levine* (2009) 555 U.S. 555, 565), Defendants here must show a congressional intent to preempt state law. *Bronco*, 33 Cal.4th at 955-57. There are two general classes of preemption: express and implied. Implied preemption is subdivided into three types: (1) field ("when it is clear that Congress intended, by comprehensive legislation, to occupy the entire field of regulation, leaving no room for the states to supplement federal law"); (2) obstacle ("when state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress"); and (3) impossibility ("when compliance with both federal and state regulations is an impossibility"). *Bronco*, 33 Cal.4th at 955 (citations omitted). All of the Defendants here argue that Proposition 65 is impliedly preempted under the "impossibility" prong. Defendant Apotex alone argues that Proposition 65 is further impliedly preempted under the "field" prong.

In assessing claims of implied preemption, the Court's task is guided by a "presumption against preemption" of state law – one that is especially strong where "federal law touches a field that has been traditionally occupied by the States." *Solus Indus. Innovs., LLC v. Sup. Ct.* (2018) 4 Cal.5th 316, 332; *see also Hillsborough Cty. v. Automated Med. Lab., Inc.* (1985) 471 U.S. 707, 715 ("[W]e start with the assumption that the historic police powers of the States were not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress."). Proposition 65 has been held to be precisely such an exercise of traditional police power, and thus a stronger presumption against preemption applies. *E.g.*, *Chemical Specialties Mfrs. Ass'n, Inc. v. Allenby* (9th Cir. 1992) 958 F.2d 941, 943. The presumption extends to both the existence of preemption as well as the scope of any preemptive effect. *See Solus*, 4 Cal.5th at 332. Moreover, where a defendant seeks to assert implied preemption, it must prove this defense by a higher "clear evidence" standard. *Levine*, 555 U.S. at 571.[6]

An even further presumption against preemption applies when a state law is carved out from coverage by the express terms of a federal statute purporting to exclude state regulation. This is true for two reasons: first, because "it evidences an intent to allow state and federal regulation to coexist," and second, because such express language "'implies' – *i.e.*, supports a reasonable inference – that Congress did not intend to pre-empt other matters." *Farm Raised Salmon Cases* (2008) 42 Cal.4th 1077, 1091-92 (citing *Freightliner Corp. v. Myrick* (1995) 514 U.S. 280, 298). In 1997, Congress amended the FDCA's provision on "National Uniformity for Nonprescription Drugs" – which had previously disallowed states from "establish[ing] or continu[ing] in effect any requirement … that is different from or in addition to, or that is otherwise not identical with, a requirement under this Act" – to expressly exclude "a State

[6] In the *Mensing* case cited by Defendants, four members of the U.S. Supreme Court suggested that "courts should not strain to find ways to reconcile federal law with seemingly conflicting state law." 564 U.S. at 622. However, this statement was not part of the Court's formal holding. *See id.* at 608 ("Justice Thomas delivered the opinion of the Court, except as to Part III-B-2."). Subsequent case law confirms that the presumption against preemption remains the law of the land. *See, e.g., Tohono O'Odham Nation v. City of Glendale* (D. Ariz. June 30, 2011) 2011 U.S. Dist. LEXIS 71432, at *12-*14 (crediting the U.S. Supreme Court's non-plurality holding in *Levine* that "the presumption applies in 'all' cases" and the fact that the subject matter at issue implicated "an area of law historically subject to state regulation").

requirement adopted by a State public initiative or referendum enacted prior to September 1, 1997." 21 U.S.C. §379r(a) & (d)(2). Notably, "Proposition 65 is the *only* state enactment that falls within the savings clause." *Dowhal*, 32 Cal.4th at 919 (emphasis added). As U.S. Senator Barbara Boxer noted during the passage of this provision, "Proposition 65 has successfully reduced toxic contaminants in a number of consumer products sold in California and it has even led the FDA to adopt more stringent standards for some consumer products." *Id.* at 926 n.6 (quoting 143 Cong. Rec. S9811, S9843 (Sept. 24, 1997)).[7] In light of this express manifestation of Congressional intent, courts should be loath to imply that Congress nonetheless wanted federal law to displace Proposition 65.[8]

As noted above, Defendants assert only two types of implied preemption here: impossibility preemption and field preemption. In order to find impossibility preemption, ***all*** manners of compliance with state law effectively must be forbidden by federal law. *See Florida Lime & Avocado Growers, Inc. v. Paul* (1963) 373 U.S. 132, 142-43 ("compliance with both federal and state regulations" must be "a physical impossibility"). "[A] hypothetical or potential conflict is insufficient to warrant the pre-emption of the state statute." *Rice v. Norman Williams Co.* (1982) 458 U.S. 654, 659.[9] The fact that different sovereigns impose different requirements does not support a finding of a conflict, since state law can always require stricter standards than those required by federal law. *See Bronco*, 33 Cal.4th at 956 (defendant "can comply with the stricter state law and simultaneously comply with federal law"). For these reasons, the U.S.

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[7] As the *Dowhal* court noted, "[s]uch statements … can provide evidence of Congress' intent." 32 Cal.4th at 926 n.6 (citing *Brock v. Pierce County* (1986) 476 U.S. 253, 263). Senator Boxer's statement further confirms that (1) the primary function of Proposition 65 is to reduce toxic exposures, and (2) Congress believed that Proposition 65 improves, not impedes, federal regulation in the OTC drug context.

[8] Defendants cite cases in which implied preemption was found notwithstanding the existence of express savings provisions (*see* Generic Manufacturers Demurrer at 16-18; Private Label Retailers Demurrer at 10), but these cases merely say that such provisions do not categorically rule out implied preemption. One of the U.S. Supreme Court cases cited specifically applied a presumption against preemption. *See Sprietsma v. Mercury Marine* (2002) 537 U.S. 51, 64 (finding that express savings clause in federal statute allowed state tort claims); *id.* at 69 (rejecting field preemption because "our conclusion that the Act's express pre-emption clause does not cover common-law claims suggests the opposite intent").

[9] The *Mensing* and *Bartlett* cases on which Defendants principally rely are in accord. *See Mensing*, 564 U.S. at 617-18; *Bartlett*, 570 U.S. at 480.

Supreme Court has stated that "[i]mpossibility pre-emption is a demanding defense." *Levine*, 555 U.S. at 573.

In the Proposition 65 context, courts have recognized that the "proper approach" to impossibility preemption is to "reconcile the operation of both statutory schemes with one another rather than holding that one has been completely ousted." *Allenby*, 958 F.2d at 949 (citation and internal brackets omitted). Where clear and reasonable warnings are at issue, "[t]o find that Proposition 65 is preempted [by a federal law], we must determine that ***all*** possible consumer product warnings that would satisfy Proposition 65 conflict with provisions of [that law]." *Committee of Dental Amalgam Mfrs. & Distribs. v. Stratton* (9th Cir. 1996) 92 F.3d 807, 810 (emphasis in original). Defendants have cited to no cases where impossibility preemption specifically was held to preclude Proposition 65 claims, and CEH has found none.

In order to find field preemption, a court must find that the state law "regulates conduct in a field that Congress intended the Federal Government to occupy exclusively." *English v. General Elec. Co.* (1990) 496 U.S. 72, 78. However, "federal regulation of a field of commerce should not be deemed preemptive of state regulatory power in the absence of persuasive reasons – either that the nature of the regulated subject matter permits no other conclusion, or that the Congress has unmistakably so ordained." *Florida Lime*, 373 U.S. at 142. Importantly, courts should not infer field preemption "whenever an agency deals with a problem comprehensively," because such an inference would be inconsistent with "the federal-state balance embodied in [the U.S. Supreme Court's] Supremacy Clause jurisprudence." *Hillsborough*, 471 U.S. at 717-18 (crediting "the presumption that state and local regulation related to matters of health and safety can normally coexist with federal regulations").

The *Dowhal* case provides a helpful illustration of how these preemption principles play out in the Proposition 65 context, and of how difficult it truly is to find implied federal preemption of Proposition 65. There, the FDA had expressly held (in formal response to a citizen petition) that a reproductive warning for nicotine – a Proposition 65-listed reproductive toxicant – on smoking-cessation patches would conflict with the federal policy of discouraging smoking. 32 Cal.4th at 919-22. According to highly specific guidance provided by the FDA, there was no way

to provide a reproductive warning that complied with Proposition 65 but would not encourage smoking by making women believe that nicotine patches were essentially as dangerous. *See id.* at 929. Moreover, since nicotine was the active ingredient in these products (and since smokers need this chemical to satisfy their addiction), there no way to reformulate the products to not contain nicotine. Thus, the case presented a "lesser of two evils" situation: exposure to toxicants would occur either via smoking or by a nicotine patch designed to assist in smoking cessation – the FDA determined that the latter was preferable to the former. *See id.* at 922. In ruling that the plaintiff's claims were "obstacle" preempted, the California Supreme Court observed that "this is an unusual case; in most cases FDA warnings and Proposition 65 warnings would serve the same purpose – informing the consumer of the risks involved in use of the product – and differences in wording would not call for federal preemption." *Id.* at 934. *Dowhal* is very much an outlier among Proposition 65 preemption cases, as it involved direct agency statements confirming the unavoidable conflict between state and federal law. There is nothing like that here.

V. ARGUMENT

A. CEH's Proposition 65 Claim Is Not Preempted Under the Doctrine of Impossibility Preemption.

The primary argument raised in each of the demurrers is that CEH's claim is barred on the basis of impossibility preemption. In order to establish its applicability, Defendants must demonstrate that compliance with both federal law and Proposition 65 is "a physical impossibility." To do so here, Defendants must prove that ***all*** possible means of compliance with Proposition 65 are precluded by federal law and thus impossible. *See Florida Lime,* 373 U.S. at 142-43. Defendants cannot meet the strictures of this "demanding defense."

1. There Are Many Steps Each Defendant Can Take to Reduce or Eliminate NDMA in Their Products Without FDA Approval.

Defendants contend that they are unable to comply with Proposition 65 because any possible alteration they could make to the Products to control NDMA contamination requires prior FDA approval, thus creating an impenetrable blockade to such compliance. This is simply untrue. There are a number of measures Defendants could take without FDA intervention that appear

likely to reduce or eliminate the NDMA exposures caused by the Products, thereby bringing them into compliance with Proposition 65.

a. CEH's Complaint and the Motion to Dismiss Orders in the Ranitidine MDL Identify Several Such Steps.

As alleged in the SAC, Defendants "can reduce or eliminate NDMA from the Products by using cleaner ingredients and manufacturing processes and more careful storage techniques." SAC ¶24. These and other actions that could reduce or eliminate the formation of NDMA are outside the scope of the FDA's authority. Indeed, this was the holding of the Southern District of Florida in the pending MDL as to NDMA in ranitidine in its recent motion to dismiss orders, on which Defendants place primary reliance.[10] The court there did ***not*** dismiss all of the plaintiffs' claims with prejudice, as Defendants demand of CEH's claims here. Rather, after carefully reviewing all applicable FDA regulations, the MDL court determined that the plaintiffs' state law tort claims alleging that the defendants had failed to (1) use proper storage temperatures; (2) adequately test the ingredients and/or Products; (3) shorten the expiration dates on the Products' labels; and (4) employ better manufacturing practices were ***not*** federally preempted as a matter of law. *See Zantac II,* 2020 U.S. Dist. LEXIS 245302, at *63-*64, *71, *76-77, *85 (allowing plaintiffs to replead claims relating to each of these measures against generic ranitidine manufacturers); *Zantac III,* 2020 U.S. Dist. LEXIS 245299, at *70-*75 (allowing plaintiffs to replead claims as to storage temperatures against ranitidine retailers). Despite bearing the burden of proving that all means of reducing or eliminating the NDMA exposures underlying CEH's claims are preempted, Defendants here fail to even acknowledge the MDL court's findings regarding these alternative means of potential compliance.[11]

[10] The MDL court issued three motion to dismiss orders of relevance here: one pertaining to a set of brand name ranitidine manufacturers (including Defendants Sanofi-Aventis U.S. LLC and Chattem, Inc.), *see In re Zantac (Ranitidine) Prods. Liab. Litig.* (S.D. Fla. Jan. 8, 2021) 2021 U.S. Dist. LEXIS 4006 ("*Zantac I*"); one pertaining to a set of generic ranitidine manufacturers (including Defendants Dr. Reddy's Laboratories, Inc. and Apotex), *see In re Zantac (Ranitidine) Prods. Liab. Litig.* (S.D. Fla. Dec. 31, 2020) 2020 U.S. Dist. LEXIS 245302 ("*Zantac II*"); and one pertaining to a set of ranitidine retailers, *see In re Zantac (Ranitidine) Prods. Liab. Litig.* (S.D. Fla. Dec. 31, 2020) 2020 U.S. Dist. LEXIS 245299 ("*Zantac III*"). None of these cases included any claim under Proposition 65.

[11] Given Defendants' failure to acknowledge this portion of the MDL orders despite over 60 combined pages of briefing on their demurrers, CEH will not detail the MDL court's specific

This failure is fatal, as any one of these actions – if taken by Defendants – could reduce or eliminate the NDMA exposures alleged in the SAC.[12] For example, proper storage of the Products may well solve the NDMA contamination problem. The FDA has stated that NDMA is a "contaminant" that "increases … when stored at higher than room temperatures," which "may result in consumer exposures to unacceptable levels of this impurity." Apotex RJN, Exh. 8, at 1; *see also id.* at 2 ("NDMA has been found to increase significantly" under these conditions, which includes "temperatures the product may be exposed to during distribution"). The FDA-approved labels of the Products presently specify a temperature range that essentially approximates room temperature. *See* Brand Name Manufacturers RJN, Exh. J, L.[13] Here, it is possible that any of the Defendants (including the Private Label Retailers) were earlier storing their ranitidine at temperatures higher than the range specified on the label (*e.g.*, in the back of a hot truck). In such instances, compliance with Proposition 65 could have been achieved earlier (and could readily be achieved in the future upon reintroduction of the Products) by taking steps to ensure that these Products are stored at the low end of the temperature range already approved by the FDA, thereby reducing NDMA levels in the Products. This clearly could be accomplished without any FDA approval. Nor would this conflict with FDA regulations, which require strict compliance with good manufacturing practices relating to "[s]torage of drug products under appropriate conditions of temperature, humidity, and light so that the identity, strength, quality, and purity of the drug products are not affected." 21 C.F.R. §211.142(b).

The other measures suggested above could help reduce or remove NDMA from the Products as well, all without FDA approval. Any of the Defendants could simply test the Products

findings why each of these methods of reducing or eliminating NDMA contamination is not preempted. However, should Defendants address it on reply, CEH reserves its right to file a surreply to rebut any points Defendants may raise.

[12] There is no apparent reason the Brand Name Manufacturers here could not likewise take any of these steps to comply with Proposition 65. *See, e.g.*, *Zantac* I, 2021 U.S. Dist. LEXIS 4006, at *54, *62 (non-preempted claims include those involving product "storage" and "expiration"). Remarkably, these entities do not claim to the contrary in their moving papers here (although it was their burden to do so), focusing instead exclusively on the labeling issues discussed in Section V.A.2., *infra*. *See* Brand Name Manufacturers Demurrer at 16-22.

[13] The FDA has apparently also found that NDMA levels may increase even when held at room temperature, albeit to a much lesser degree. *See* Apotex RJN, Exh. 8, at 2.

(or specific constituents in Products) for NDMA, and then not sell those Products or use those constituents if high levels of NDMA are found.[14] *See* CEH RJN, Exh. 2, at 3. The fact that a third-party laboratory was able to discover the NDMA contamination issue through basic testing shows that Defendants could have done so on their own as well. *See* SAC ¶36. As a further compliance step, either the Brand Name Manufacturers or the Generic Manufacturers could reduce the amount of time specified as an expiration date on the Products' labels, thereby leading to lower levels of NDMA in those Products at the relevant time that they are ingested by consumers. *See* Apotex RJN, Exh. 8, at 2 (reporting the FDA's observation that NDMA in ranitidine products increases over time); *see also id.*, Exh. 9, at 1 (same). As the MDL court found, this can be accomplished without FDA approval as a "moderate" change under the CBE process, especially since generic manufacturers have no duty under federal regulations to use the same expiration date on their drugs as the brand name equivalent. *See Zantac II*, 2020 U.S. Dist. LEXIS 245302, at *33, *63-*64 (citing 21 C.F.R. §314.94(a)(8)(iv) and FDA guidance).

Lastly, the Brand Name Manufacturers or the Generic Manufacturers could adopt better manufacturing practices designed to reduce NDMA contamination. This does not conflict with FDA regulations, which already require OTC drug manufacturers to comply with good manufacturing practices; a failure to do so may subject the manufacturer to FDA enforcement for marketing an adulterated or misbranded drug. *See* 21 C.F.R. §§210.1(b), 330.1(a). Even non-manufacturers such as the Private Label Retailers (especially given that the Products are being sold under their name) could take steps to ensure that upstream entities are complying with these FDA standards, such as issuing specifications to and requiring certifications from such entities.[15]

[14] CEH is not advocating that Defendants must stop selling the Products altogether, but rather that they perform testing for NDMA on a batch level before the Products are sold to consumers and, sensibly enough, refrain from selling Products or using ingredients that contain high levels of NDMA. Defendants themselves concede that "[t]he FDA did not observe unacceptable levels of NDMA in many of the samples … tested" (Brand Name Manufacturers Demurrer at 13 (citation omitted); *see also* Apotex RJN, Exh. 8 (same)), so it appears that employing such a screening mechanism would not lead to a total cessation in all sales. Thus, this option would not run afoul of *Bartlett*'s holding that impossibility preemption cannot be circumvented by suggesting that a drug company could simply "cease acting altogether in order to avoid liability." 570 U.S. at 488-90. And, as CEH alleges, the FDA wants Defendants to perform additional testing for NDMA (SAC ¶36), so this in no way contravenes the agency's goals.

[15] Under Proposition 65's implementing regulations, private label retailers are essentially treated

b. The Authorities Cited by Defendants Do Not Compel a Different Result.

Defendants rely almost exclusively on *Bartlett* to support their contention that any potential reformulation of the Products is preempted by FDA rules. *E.g.*, Generic Manufacturers Demurrer at 9-10, Apotex Demurrer at 14-16; Private Label Retailers Demurrer at 5. *Bartlett* is distinguishable. *Bartlett* was focused exclusively on a design defect claim brought under New Hampshire law as to the generic drug sulindac, a prescription drug. *See* 570 U.S. at 475, 478. Since New Hampshire law specified that the design defect could be resolved "either by changing a drug's design or by changing its labeling," the court examined both options. *Id.* at 482. As to the design, the court recognized that "the FDCA requires a generic drug to have the same active ingredients, route of administration, dosage form, strength, and labeling as the brand-name drug on which it is based." *Id.* at 483-84 (citing 21 U.S.C. §355(j)(2)(A)(ii)-(v) & (8)(B), 21 C.F.R. §320.1(c)). Since sulindac was a "one-molecule drug," it was "chemically incapable of being redesigned." *Id.* at 484. Here, however, NDMA is not the active ingredient or an ingredient at all in the Products. Eliminating NDMA contamination could be as simple as cleaning the production facility more frequently or storing the Products at the proper temperature. These steps are not product reformulation as envisioned by *Bartlett*. Indeed, the Florida MDL court discussed and applied *Bartlett* throughout each of its decisions, yet nonetheless found that various methods of compliance are not federally preempted as a matter of law.

Ignoring the MDL court's findings, Apotex alone argues that FDA regulations require prior FDA approval for any action that would affect a drug's "impurity profile." Apotex Demurrer at 18 (citing 21 C.F.R. §314.70(b)). That regulation addresses "changes in the synthesis or manufacture of the drug that may affect the impurity profile." *Id*. On its face, this regulation does not apply to product storage or testing, both of which the MDL court found were not preempted. Moreover, it is entirely unclear whether "impurity profile" encompasses undisclosed contaminants. While Apotex bears the burden of proving that it does, it cites no case or FDA

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as "upstream" entities when it comes to compliance with the statute. *See* 27 C.C.R. §25600.2(e)(1).

regulation that says so.[16] Moreover, the FDA has published guidelines on "impurities in drug substances" in the NDA/ANDA context, but notes that "[e]xcluded from this document are … extraneous contaminants, which should not occur in drug substances and are more appropriately addressed as good manufacturing practice issues." CEH RJN, Exh. 3, at 3; *see also id.*, Exh. 4, at 3 (same). Thus, the FDA appears to agree that steps to address contamination issues (especially those that were undisclosed at the time of the FDA's initial drug approval) do not have to be part of a request to change an NDA or ANDA.

Defendants do not cite a single case that holds or even mentions a situation where a state law claim regarding an undisclosed contaminant in an OTC drug product was preempted by the FDA approval process. There could be any number of reasons that a perfectly designed ranitidine product could nonetheless contain high levels of NDMA, such as the use of contaminated materials received from a given vendor, the employment of sloppy manufacturing process leading to the generation of nitrates or amines at various steps, or perhaps something as simple as a failure to ensure clean facilities. *See* SAC ¶¶24-25. Rectifying these problems could be as simple as switching vendors, undertaking a process audit, or sweeping the floor more regularly, none of which Defendants have argued require FDA approval. Thus, impossibility preemption does not bar CEH's claims.

2. There Are Various Methods by Which Each Defendant Can Provide Clear and Reasonable Warnings Regarding NDMA in Their Products Without FDA Approval.

Defendants argue that their demurrers should be granted because *Mensing*, *Bartlett*, and their progeny broadly hold all claims to be preempted based on ***any*** "failure to communicate"

[16] Apotex cites *Gustavsen v. Alcon Labs., Inc.* (1st Cir. 2018) 903 F.3d 1, 9-10, for the proposition that any change that affects this "impurity profile" – including, apparently, ones that have a ***positive*** effect on drug purity – are "major" changes requiring FDA approval under 21 C.F.R. §314.70(b). Apotex Demurrer at 18. But *Gustavsen* did not involve contaminants; rather, the plaintiffs there sought to sue drug manufacturers for "deliberately" designing the containers for their eye drop medications so as to emit too much fluid in each drop, thereby forcing patients to waste medication (and buy more eye drops). 903 F.3d at 4-5. In finding these claims to be preempted, the court relied on an FDA regulation explicitly defining any "[c]hanges in a drug product container closure system that controls the drug product delivered to a patient" as a *per se* "major" change. *Id.* at 11-12 (citing 21 C.F.R. §314.70(b)(2)(vi)). Thus, the court did not address the "impurity profile" issue. *Id.* at 11-13.

known dangers about a drug product in essentially ***any*** form. *E.g.*, Generic Manufacturers Demurrer at 10-14. Defendants base their argument that Proposition 65 warnings are preempted on the false premise that their "only real option is to use a pre-approved 'safe harbor' warning," which would "need to … be on the outer container of the packaging." Brand Name Manufacturers Demurrer at 15-16, 19 (citing 27 C.C.R. §§25601(c) & 25603). This is simply untrue. As noted in Section IV.A., *supra*, the statute, its implementing regulations, and governing case law all indicate that a defendant can comply with Proposition 65 using ***any*** content and via ***any*** method that is "clear and reasonable."[17] Defendants attempt to obscure this point because, although label warnings regarding NDMA and cancer may be subject to certain provisions of the FDCA, other means of warning decidedly are not.

a. The FDA's OTC Drug Labeling Regulations Do Not Preclude Proposition 65 Cancer Warnings.

Defendants argue that an FDA regulation governing the "format and content" of "OTC drug labeling," prohibits the sort of cancer warnings contemplated by Proposition 65 as to NDMA. Brand Name Manufacturers Demurrer at 17 (citing 21 C.F.R. §201.66).[18] However, the regulation on which Defendants rely, 21 C.F.R. §201.66(c)(5), only applies to "[t]he outside container or wrapper of the retail package, or the immediate container label if there is no outside container or wrapper." By its own terms, these formatting restrictions do not regulate the content of off-label representations that could provide a cancer warning prior to the purchase or use of the product, such as a "posted sign" or "shelf tags" in a physical retail location where the product is sold, or "a clearly marked hyperlink … on the product display page" for internet sales. 27 C.C.R. §25602(a)(1), (b). Moreover, there is nothing inconsistent with the FDCA or the FDA's

[17] In support, Defendants cite *National Ass'n of Wheat Growers v. Becerra*, 468 F.Supp.3d 1247, 1261 (E.D. Cal. 2020) (Brand Manufacturers Demurrer at 15), but the holding there was entirely limited to its facts. In that case, the California Attorney General could identify no warning that would, in fact, comply with Proposition 65 as to glyphosate. *See id.* at 1261-63. This was true only because the Court also found significant scientific doubt as to whether glyphosate, in fact, causes cancer – a doubt wholly absent from the present dispute as to NDMA.

[18] Defendants also cite to certain provisions relating to the content and format of labeling for ***prescription*** drug products (21 C.F.R. §201.57), which are not at issue in this suit. Brand Manufacturers Demurrer at 18.

regulatory goals about providing such a cancer warning for NDMA.[19] Thus, the OTC drug labeling regulation does not avail Defendants.

b. Any of the Defendants Could Provide Proposition 65 Warnings by Means of Public Advertising.

There are numerous methods by which a company exposing California consumers to toxic chemicals may comply with Proposition 65's warning requirement, including by means of public advertising. *See Dowhal*, 32 Cal.4th at 918.[20] Defendants claim that the FDCA's broad definition of "labeling" also extends to "advertising and promotional materials," such that any attempt to provide a Proposition 65 warning by wider means would likewise be preempted. Generic Manufacturers Demurrer at 13-14 (citing *Strayhorn v. Wyeth Pharm., Inc.* (6th Cir. 2013) 737 F.3d 378, 394); Brand Manufacturers Demurrer at 11-12 (same); Private Label Retailers Demurrer at 6-7 (same). This argument fails for a straightforward reason: ***the FDCA does not regulate the advertising of OTC drugs at all***. As stated on the FDA public website's "Questions and Answers" page on "Prescription Drug Advertising":

> Does the FDA control advertisements for all drugs?
>
> No. The FDA ***does not*** oversee the advertising of over-the-counter (OTC) drugs. The Federal Trade Commission (FTC) is responsible for regulating OTC drug ads. The FDA regulates advertising only for prescription drugs.

CEH RJN, Exh. 5, at 2 (emphasis in original). *See also* Brand Name Manufacturers RJN, Exh. F, at 13 n.25 (confirming that "[t]he Federal Trade Commission (FTC) has primary responsibility for

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[19] Defendants argue that safety warnings on OTC drug labels are qualitatively different from Proposition 65 warnings because of the "FDA's focus on balancing product safety with treatment and prevention of disease." Brand Manufacturers Demurrer at 18. This is an odd thing to point out here, where there is no such balancing. Unlike in cases like *Dowhal* (where there were competing policy objectives), the FDA has determined that the Products at issue should not be ingested by consumers so long as they continue to contain high levels of NDMA. Defendants' further suggestion that "[21 C.F.R.] §201.66(g) … supersedes Proposition 65 under the Supremacy Clause" (*id.* at 18) is specious. That provision only states that OTC drug products are "subject to regulatory action" if not in compliance with the on-label content requirements, not that other methods of warning are impermissible. Also, this agency regulation could not possibly override the express Congressional directive in 21 U.S.C. §379r(d)(2), which excludes Proposition 65 from all national uniformity requirements as to OTC drugs.

[20] Indeed, public advertising was previously considered a "safe harbor" method of compliance. While no longer an explicit safe harbor method, public advertising remains a viable method for providing a statutorily compliant warning. *See* Health & Safety Code §25249.11(f).

regulating the advertising of nonprescription drug products"); 21 U.S.C. §352(n) (setting forth restrictions on "prescription drug advertising," but not OTC drugs); 21 C.F.R. §202.1 (same).[21] Thus, there is no federal impediment to ***any*** of the Defendants providing warnings by means of public advertising, nor has there been any such obstacles at any time. Indeed, the lone case cited by Defendants on this point involved prescription, not OTC, drugs. *See Strayhorn*, 737 F.3d at 383-84.

Defendants' own conduct following the third-party NDMA findings reveals that they can and did undertake remedial advertising without running afoul of FDA regulations. Apotex crows about its "voluntary" recall without FDA urging or approval, yet overlooks that the press release it published in September 2019 could have contained a valid Proposition 65 warning. For instance, that release states that NDMA is a "probable human carcinogen" and that this chemical has been found in its ranitidine (Apotex RJN, Exh. 4), both of which are predicates to a "clear and reasonable" Proposition 65 warning.[22] *See also* CEH RJN, Exh. 7 (press release on NDMA-related recall was likewise published by Brand Name Manufacturers). Defendants' issuance of press releases regarding NDMA in the Products without prior FDA approval demonstrates that Defendants were capable of providing clear and reasonable warnings via press release or other similar method regarding that hazard at any time.

c. Any of the Defendants Could Provide Proposition 65 Warnings by Means of Shelf Signs or Internet Warnings.

Shelf-signs and other point of sale warnings are and have always been safe-harbor methods for providing Proposition 65 warnings. *See Dowhal*, 32 Cal.4th at 918. Defendants contend that the FDCA's broad definition of "labeling" in 21 U.S.C. §321(m) – which includes label text and graphics as well as materials "accompanying" such labels – compels the conclusion that off-label warnings such as shelf signs or internet warnings can only be altered with prior FDA approval.

[21] Defendants claim that "[a]dvertising of an NDA-approved medication must stay consistent with the labeling," but the provision they cite – 21 U.S.C. §352(f)(1) – says no such thing. Brand Name Manufacturers Demurrer at 12.

[22] This is not to say that these representations satisfied Proposition 65 (which is doubtful, given the cagey language employed by Apotex in an effort to downplay the risks), but it does show that Product vendors can widely publicize this issue without hazarding FDA enforcement.

Generic Manufacturers Demurrer at 13-14; Private Label Retailer Demurrer at 6-7. Oddly, Defendants fail to cite any of the three Proposition 65 preemption cases involving the permissibility of warnings on "labeling" and "accompanying" materials. *See Allenby*, 958 F.2d at 945-46; *Cotter*, 53 Cal.App.4th at 1378-79; *American Meat Inst. ("AMI") v. Leeman* (2009) 180 Cal.App.4th 728, 750. These cases all addressed the precise question of whether Proposition 65 point of sale warnings are precluded by federal statutes with the same broad definition of labeling as the FDCA. Two of the three cases held that point of sale signs are not labeling and therefore found no preemption. *See Allenby*, 958 F.2d at 946-47; *Cotter*, 53 Cal.App.4th at 1384-93. The dissenting *AMI* case found otherwise. *See* 180 Cal.App.4th at 760-61. This Court should follow the weight of authority in holding that Proposition 65 point of sale signs are not labeling under the FDCA and therefore not preempted.[23] The reasoning in *Allenby* and *Cotter* applies as readily to Proposition 65 warnings provided over the internet where the sale is made online, and Defendants have cited no cases holding that such warnings are preempted "labeling" under the FDCA.

d. The Brand Name Manufacturers Could Change the Label Itself Under the FDA's CBE Regulation.

As a general matter, it is "a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times." *Levine*, 555 U.S. at 570-71. Thus, the Florida MDL court held that "[b]ecause the CBE process enables brand-name drug manufacturers to strengthen warnings on labeling without waiting for FDA approval, a labeling claim against a brand-name drug manufacturer is not necessarily pre-empted." *Zantac I*, 2021 U.S. Dist. LEXIS 4006, at *61 (allowing the plaintiffs to replead this as a design defect claim). Appellate courts have likewise recognized that, because the CBE regulation permits such changes, "a drug manufacturer will not ordinarily be able to show that there is an actual conflict between state and federal law such that it was impossible to comply with both." *Risperdal & Invega Cases* (2020) 49 Cal.App.5th 942, 956 (citing *Merck Sharp & Dohme Corp. v. Albrecht* (2019) __ U.S. __, 139

[23] None of the "failure to warn" cases cited by Defendants even address point of sale signs. *See, e.g., Johnson v. Teva Pharm. USA, Inc.* (5th Cir. 2014) 758 F.3d 605, 611 (rejecting suggestion that warnings could be provided to prescribing physicians via "Dear Doctor" letters); *In re Darvocet, Darvon, and Propoxyphene Prods. Liab. Litig.* (6th Cir 2014) 756 F.3d 917, 932-33 (same); *Strayhorn*, 737 F.3d at 391 (same). As such, those cases are of no value here.

S. Ct. 1668, 1679).[24] Importantly, the burden is on the brand name manufacturer to provide "clear evidence" that the FDA would not have approved the requested label change. *Zantac I*, 2021 U.S. Dist. LEXIS 4006, at *61-*62 (citing *Levine*, 555 U.S. at 571). Brand Name Manufacturers cannot establish this here.

Brand Name Manufacturers argue that the CBE provision only allows a labeling change for strengthening warnings for a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug. Brand Name Manufacturers Demurrer at 9-10, 20 (citing 21 C.F.R. §§314.70, 201.57). These Defendants further contend that the carcinogenicity of NDMA does not rise to this standard, citing to prescription (not OTC) drug regulations suggesting that "warnings and precautions" are limited to "clinically significant adverse reactions" and "other potential safety hazards." *Id*. at 18 (citing 21 C.F.R. §201.57(c)(6)).[25] In the first place, cancer ***is*** a clinically significant risk, and (as CEH's pleadings allege) NDMA is a potent carcinogen. *See* SAC ¶¶22-23.[26] More glaringly, Brand Name Manufacturers ignore that the FDA has banned the sale of the Products ***because*** of this cancer risk. *See id.* ¶36; Apotex RJN, Exh. 8. The FDA's action was taken pursuant to 21 C.F.R. §7.45(a)(3), which requires the agency to make a finding that the recall "is necessary to protect the public health and welfare." Defendants fail to explain how this risk can be serious enough to require a recall, but ***not*** serious enough to require a warning. At the very least, there is no "clear evidence" here that the FDA would have rejected a good faith attempt by Brand Name Manufacturers to petition to change the label of the Products under the CBE provision. As such, this preemption argument fails.

[24] Several of the cases cited by Defendants actually rejected impossibility preemption on this ground, noting again that the defense is "demanding." *Batoh v. McNeil-PPC, Inc.* (D. Conn. 2016) 167 F.Supp.3d 296, 316; *Reckis v. Johnson & Johnson* (Mass. 2015) 28 N.E.3d 445, 460.

[25] Defendants fault CEH for not adhering to the same pleading standard on this point as a state law tort claim (Brand Name Manufacturers Demurrer at 20-21 (citing *Gibbons v. Bristol-Myers Squibb Co.* (2d Cir. 2019) 919 F.3d 699, 708)), but this ignores California pleading norms as to affirmative defenses. *See Stowe*, 44 Cal.2d at 422.

[26] Defendants note that Proposition 65 plaintiffs such as CEH need not allege actual harm to have standing to sue (Brand Name Manufacturers Demurrer at 22), but this does not (and cannot) controvert the specific cancer allegations in the SAC, which must be accepted as true at this stage.

3. The Generic Manufacturers' Construction of the Duty of Sameness Is Overbroad and Clearly Wrong.

Defendants argue that the "duty of sameness" applicable to drug labels and active ingredients applies to undisclosed contaminants. Generic Manufacturers Demurrer at 3, 5-7, 9, 14, 17; Apotex Demurrer at 15. Defendants fail to cite a single case in which any court held that reducing or eliminating undisclosed contaminants in a drug product conflicts with either FDA rules or the "duty of sameness." Rather, the cases relied on by Defendants almost universally address failure to warn regarding alleged side effects of the active ingredient of a drug product. *See, e.g.*, *Brinkley v. Pfizer, Inc.* (8th Cir. 2014) 772 F.3d 1133 (metoclopramide); *Greager v. McNeil-PPC, Inc.* (N.D. Ill. 2019) 414 F.Supp.3d 1137 (ibuprofen); *Ko v. Mutual Pharm Co., Inc.* (N.D. Cal. Oct. 18, 2013) 2013 U.S. Dist. LEXIS 151112 (sulindac). In those cases, the FDA had carefully examined the data regarding the side effects associated with the product at issue and the specific labeling proposed for each product. The courts analyzing the allegations that the generic manufacturer should have added or strengthened a warning thus have held that a generic manufacturer may not change the labeling of the product where the brand name equivalent has not done so. This is not the case here. The NDMA in the Products is not the active ingredient; in fact, it is not an ingredient at all. Rather, the NDMA is an undisclosed contaminant, one that was not publicly acknowledged by Defendants until an independent laboratory happened to test the Products and discovered the NDMA contamination.

Defendants' contention that there is a duty of sameness for contaminants is further contradicted by the fact that NDMA contaminant levels vary significantly between different Products. The FDA's testing, which was performed on prescription and OTC ranitidine made by roughly twelve different vendors (including several Defendants in this action), show that NDMA levels are highly variable across different Products as well as different vendors. *See* CEH RJN, Exh. 6. For instance, the FDA found NDMA levels as low as 0.02 parts per million ("ppm") (for vendor Strides Shasun Ltd.) and as high as 2.85 ppm (for vendor Novitium). *Id.* at 2. Prescription ranitidine made by Defendant Dr. Reddy's Laboratories, Inc. tested at 0.68 ppm NDMA – this is 34 times higher than the lowest result. *Id.* OTC ranitidine made by Defendant Sanofi-Aventis

U.S. LLC tested in the range of 0.07-2.38 ppm for its 150 mg tablets and in the range of 0.08-2.17 for its 300 mg tablets, but at a lower range of 0.1-0.55 ppm for its 75 mg tablets. *Id.* at 2-3.

This great variability in NDMA levels even as to the same FDA-approved Products reflects that ***the amount of NDMA in a particular Product is related to something outside the four corners of the FDA-approved NDA or ANDA***. Not only does this demonstrate that the NDMA problem is not an inherent feature of the ranitidine molecule, but it also suggests that some manufacturers may already be taking some of the remedial steps (evidently, without obtaining FDA approval) that CEH believes all of the Product manufacturers should be taking. It also shows that, to the extent there is a duty of sameness with which the Generic Manufacturers must comply, it does not extend to contaminants.

Defendants' contention as to the duty of sameness for contaminants would also lead to absurd consequences. For example, if Zantac, the name brand, were contaminated with rodent droppings, the generic brands would, under their construction, have to ensure that their products were likewise contaminated. Then, given Defendants' argument that cleaning up contaminants constitutes a major change requiring FDA approval, Defendants would need prior FDA approval to clean the droppings from their respective facilities. This cannot possibly be the law.

Likewise, Defendants varied response to the FDA's guidance regarding NDMA in ranitidine products in the fall of 2019 belie the broad reach of the duty of sameness as applied to remedial steps and communications regarding NDMA. Apotex boasts that it issued a precautionary voluntary recall of the Products on September 25, 2019, which is nearly a month prior to a similar voluntary recall issued by the brand-name manufacturers. *Compare* Apotex Demurrer at 1-2, *with* Brand Name Manufacturers Demurrer at 13. Thus, it appears that the generic manufacturer was permitted to send out a press release and issue recall notices independent of the brand name manufacturer's actions. It is also noteworthy that Apotex's press release is not identical to the press release issued by the Brand Name Manufacturers. *Compare* Apotex RJN, Exh. 4, *with* CEH RJN, Exh. 7.[27] If any written proclamation was "labeling"

[27] For instance, while Apotex admits that its recalled Products "contain a nitrosamine impurity called [NDMA]," Brand Name Manufacturers hedge on whether their Products actually contain NDMA in light of "inconsistencies in preliminary test results." *Compare* Apotex RJN, Exh. 4, at

triggering a duty of sameness (as Defendants contend), then both should have been entirely identical.

4. The Exemption in Proposition 65 for Preempted Claims Does Not Operate More Broadly than the Federal Constitution.

As explained above, Health & Safety Code §25249.10(a) provides that the exposure prohibition in Health & Safety Code §25249.6 "shall not apply to … [an] exposure for which federal law governs warning in a manner that preempts state authority." Defendants interpret this provision to mean that any time a federal warning requirement precludes a warning relating to a given exposure, Proposition 65 is wholly preempted, even where the violations could be rectified by means other than a warning (such as reformulation). *See* Brand Name Manufacturers Demurrer at 16-17; Generic Manufacturers Demurrer at 6; Private Label Retailers Demurrer at 3-4. Thus, Defendants' position is that to the extent federal law preempts ***some*** state authority, it preempts ***all*** state authority. But that is not what the provision says. Nor does it make sense that the voters who enacted Proposition 65 to be more protective than existing laws intended for federal law to have a ***greater*** preclusive effect on their state rights than the floor set by the Supremacy Clause (which, again, requires "a physical impossibility" of compliance with the two regimes). *See Bartlett*, 570 U.S. at 501. This surprising argument should be rejected.

The California appellate courts have issued several instructive opinions on how to read Proposition 65 specifically. First and foremost, Proposition 65 should be "construe[d] … broadly to accomplish [its] protective purpose." *People ex rel. Lungren v. Sup. Ct.* ("*Lungren II*") (1996) 14 Cal.4th 298, 314. The intent of the electorate in this regard is paramount to this analysis. *See Styrene Info. & Rsch. Ctr. v. OEHHA* (2012) 210 Cal.App.4th 1082, 1098 (noting that "the spirit of the act" should guide competing interpretations as to its "literal construction"). Moreover, "in construing voter-approved measures, words must be understood, not as the words of the civil service commission, or the city council, or the mayor, or the city attorney, but as the words of the voters who adopted the amendment." *People ex rel. Lungren v. Sup. Ct.* ("*Lungren I*") (1995) 48 Cal.App.4th 1452, 1460 (citation omitted) (disavowing "technical" readings of Proposition 65 in

1, *with* CEH RJN, Exh. 7, at 2.

favor of "common popular" ones),[28] *rev'd on other grounds by Lungren II* (1996) 14 Cal.4th 298. "When the enactment follows voter approval, the ballot summary and arguments and analysis presented to the electorate in connection with a particular measure may be helpful in determining the probable meaning of uncertain language." *Styrene*, 210 Cal.App.4th at 1098 (citation omitted). Finally, "[a]ny interpretation that would lead to absurd consequences is to be avoided." *DiPirro v. Bondo Corp.* (2007) 153 Cal.App.4th 150, 191.

Health & Safety Code §25249.10(a) simply recognizes that where the state's authority under Proposition 65 is preempted as to a particular exposure, Proposition 65 does not apply to that exposure. This provision was likely included because the drafters of Proposition 65 wanted to make sure that the statute as a whole would survive against a preemption challenge if any part of it was found to conflict with federal law. Predictably, there were several facial challenges to Proposition 65 on federal preemption grounds – all unsuccessful – in the years directly following the law's enactment. *See, e.g.*, *Allenby*, 958 F.2d at 943; *Cotter*, 53 Cal.App.4th at 1379. There is no indication or authority for Defendants' contention that, under Section 10(a), all means of Proposition 65 compliance are preempted where the provision of a state-imposed label warning is preempted. Defendants might have a point if Section 10(a) ended right after "governs warning" or concluded with "state authority ***to require warnings***," but it does not.

To the extent there is any ambiguity regarding Section 10(a), the ballot materials on which two-thirds of Californians relied in enacting Proposition 65 demonstrate the implausibility of Defendants' interpretation. As stated in those materials, the voters proclaimed that their objective was to "protect themselves" from toxic chemicals by reducing reliance on government agencies. CEH RJN, Exh. 1, at 53 (Proposed Proposition 65, §1(a)). As the California Supreme Court noted in *Lungren II*, "Proposition 65 purported to partially supersede existing environmental laws, which the proponents of the initiative argued were not 'tough enough.'" 14 Cal.4th at 311 n.7. The stated intent of Proposition 65 is to "secure strict enforcement of the laws controlling hazardous

[28] Against this backdrop, Defendants' statement that "the framers of Proposition 65 recognized that some products are closely governed by federal law in a manner that precludes manufacturers and sellers from altering federally required warnings or from issuing new warnings not permitted under federal law" (Generic Manufacturers Demurrer at 5) strikes as pedantic.

chemicals" and to "deter actions that threaten public health and safety." CEH RJN, Exh. 1, at 53 (Proposed Proposition 65, §1(c)). Why would these same voters want federal preemption to extend even ***further*** than already allowed by the U.S. Constitution, especially when federal law is less "tough" than state law (as it appears to be with respect to NDMA exposures)?

Defendants have not cited a single case adopting their position – and indeed there are none.[29] Rather, the published cases that discuss Section 10(a) all perform the usual constitutional preemption analysis, without once indicating that Proposition 65 itself has in any way altered that analysis. *See, e.g.*, *PCRM*, 187 Cal.App.4th at 565 (holding, consistent with CEH's view, that "[c]onflict preemption of [Proposition 65] by federal law does not automatically and necessarily result in the complete displacement of state law by federal law in its entirety," but "only insofar … as there is conflict") (citation omitted). Since Defendants' position leads to a less protective statute (*e.g.*, one that allows a federal warning to take precedence over not having the chemical in the product at all), while denying California's citizens their self-enacted right to enforce more stringent California toxics standards, it should be rejected.

B. Congress Did Not Intend to Preempt the "Field" of Ranitidine Regulation as to NDMA.

Apotex alone, in an overreaching argument that none of the other Defendants make, asserts that the "FDA's robust oversight and management of potential NDMA in ranitidine products supports a finding of field preemption." Apotex Demurrer at 20. This argument is absurd.

Field preemption occurs where the "scheme of federal regulation [is] so pervasive as to make reasonable the inference that Congress left no room for the States to supplement it, or where an Act of Congress touches a field in which the federal interest is so dominant that the federal system will be assumed to preclude enforcement of state laws on the same subject." *English*, 496 U.S. at 79 (citation omitted). Here, the federal statute that provides the authority for any

[29] Defendants claim that their interpretation of Section 10(a) is supported by *Committee of Dental Amalgam Alloy Mfrs. v. Henry* (S.D. Cal. 1994) 871 F.Supp. 1278. *See* General Manufacturers Demurrer at 5. It is not. First, that case involved a straightforward express preemption analysis under the Medical Device Amendments to the FDCA, 21 U.S.C. §360k, which contain no saving provision for Proposition 65. *Id.* at 1282. Second, the lower court's opinion finding preemption was ***overturned by the Ninth Circuit*** in the *Stratton* decision. *See* 92 F.3d at 813-14.

preemption of the field expressly preserves state authority in a number of circumstances. *See*, *e.g.*, 21 U.S.C. §379r(d)(2) (preserving non-identical Proposition 65 requirements). Given this (and other) express reservations of state authority in the arena of OTC drug regulation (*see also id.* §379r(b), (e), (f)), it is clear that Congress neither left no room for states to regulate nor sought to preclude state regulation on this subject.

To address this glaring problem with its argument, Apotex seeks to narrow the "field" to NDMA in ranitidine rather than OTC drugs. Apotex Demurrer at 20. Of course, there is no authority for field preemption of such a narrow category. Indeed, Congress itself has never regulated in the area of NDMA in ranitidine, so divining its intent for that field is impossible. Moreover, the mere fact that the FDA has taken action with regard to NDMA in ranitidine products does not speak to field preemption. Had the FDA intended to preempt the field, it would be expected to say so. *See Hillsborough*, 471 U.S. at 718 (finding it probative where "an agency does not speak to the question of preemption"). Here, the FDA has made no concrete statements that it believes the states have no role to play in the regulation of ranitidine, either now or in the future. This contrasts starkly with *Dowhal* and the lone case Apotex cites – the Supreme Court of New Jersey's decision in *R.F. v. Abbott Labs.* (N.J. 2000) 745 A.2d 1174 – both of which involved specific, affirmative statements by the FDA that state regulation would necessarily conflict with the agency's own findings about how best to balance competing policy concerns. *See Dowhal*, 32 Cal.4th at 919-22, *Abbott*, 745 A.2d at 1177-84. Such concerns are absent here, since both the FDA and CEH agree that there should be no or less NDMA in ranitidine.[30] Moreover, courts do not find field preemption just because the FDA has taken significant action as to a specific drug –

[30] Apotex claims that field preemption should be found in light of the FDA's "exhaustive" oversight on issues relating to NDMA in ranitidine. Apotex Demurrer at 22. But if this is true, the California Supreme Court in *Dowhal* would have found field preemption as to nicotine patches, about which the FDA made far more exacting statements regarding the conflict with federal law. The *Abbott* case (which, as Apotex concedes, is not even clearly a field preemption case (Apotex Demurrer at 21 n.10)) is readily distinguishable. The court there, stressing on several occasions that the facts were "unique," found a conflict because the FDA had been intimately involved in the development of the specific blood test at issue, and had made affirmative statements confirming that it did not want the several states to impose different requirements. *See* 745 A.2d at 1188-92, 1197-98. Tellingly, the *Dowhal* case discussed *Abbott* at length (*see* 32 Cal.4th at 932), but did not find field preemption.

even where that action is requiring a recall. *See, e.g., Stengel v. Medtronic Inc.* (9th Cir. 2013) (*en banc*) 704 F.3d 1224, 1227, 1230-33. Thus, Apotex's sweeping assertion that the FDA has "elbowed out" state authority here is plainly misguided.

C. CEH's Claim Is Not Moot.

Apotex – again, alone among the Defendants – further argues that its "voluntary" decision to pull its Products from the market renders the remedies CEH seeks in this action "moot." Apotex Demurrer at 5.[31] For various reasons, Apotex is wrong.

1. A Demurrer Is Not Apposite to Resolve Alleged Deficiencies in CEH's Prayer for Relief.

As an initial matter, Apotex's argument is procedurally defective because demurrers are meant to determine whether the complaint states "a cause of action" (C.C.P. §430.10(e)) – which the SAC plainly does – not whether one or more of the specific remedies it seeks will ultimately be found appropriate to award at trial. Here, CEH's allegations as to injunctive relief, civil penalties, and attorneys' fees only arise in the context of the SAC's "Prayer for Relief." SAC at 8-9 (¶¶1-4). It is black-letter law that "a demurrer tests the sufficiency of the factual allegations of the complaint rather than the relief suggested in the prayer of the complaint." *Venice Town Council, Inc. v. City of Los Angeles* (1996) 47 Cal.App.4th 1547, 1562; *see also Grieves v. Sup. Ct.* (1984) 157 Cal.App.3d 159, 166 n.9 ("a prayer is not subject to a demurrer"); *Kong v. City of Hawaiian Gardens Redev. Agency* (2002) 108 Cal.App.4th 1028, 1047 ("a demurrer cannot rightfully be sustained to part of a cause of action or to a particular type of damage or remedy"). Thus, if CEH can show that any aspect of the case is not moot, the entire case goes forward.

2. CEH's Prayer for Civil Penalties Is Not Moot.

The determination of penalties under Proposition 65 is an intensely fact-based exercise that

[31] Apotex also raises a "special" demurrer on CEH's allegations being "uncertain, ambiguous, and unintelligible" (Apotex Notice of Demurrer at 2), but its accompanying Memorandum of Points and Authorities does not explain how CEH's allegations are impermissibly vague. If Apotex means that CEH has to specify ***how*** the company can comply with federal law, CEH does not have such an obligation but did suggest several such means. *See* SAC ¶24. Further, a complaint can be vague to some extent because discovery can be "used to clarify the contentions of the parties [as] an adjunct to the pleadings" and "should be used liberally for the purpose of clarifying and narrowing the issues made by the pleadings." *Jacobs v. Coldwell Banker Residential Brokerage Co.* (2017) 14 Cal.App.5th 438, 445 (citation omitted).

requires the court to consider seven factors. *See* Health and Safety Code §25249.7(b)(2). Apotex requests judicial notice of a single fact: its recall of the Products following an independent laboratory's exposé of NDMA in ranitidine products and the FDA's initial alert regarding NDMA in ranitidine products. *See* Apotex RJN, Exh. 4; Brand Name Manufacturers RJN, Exh G. This fact, however, does not begin to address most of the penalty factors. For example, it does not the address "[t]he nature and extent of the violations." Health and Safety Code §25249.7(b)(2)(A). Nor does it address "[t]he deterrent effect that the imposition of the penalty would have" on Apotex "and the regulated community as a whole" or any of the other factors, with the possible exception of "[w]hether the violator took good faith measures to comply." *Id.* §25249.7(b)(2)(F)(D). Thus, this lone fact cannot possibly moot CEH's request for penalties.

Potential "deterrent effects" is why courts almost invariably reject mootness claims regarding civil penalties. As the U.S. Supreme Court has noted, civil penalties "do more than promote immediate compliance by limiting the defendant's economic incentive to delay its attainment of [applicable legal] limits; they also deter future violations." *Friends of the Earth, Inc. v. Laidlaw Envtl. Servs. (TOC), Inc.* (2000) 528 U.S. 167, 185; *accord DiPirro*, 153 Cal.App.4th at 183 ("[a]n award of civil penalties under [Proposition 65] is … designed to deter misconduct and harm").

The necessity of deterrence appears to be particularly strong here. Although Apotex could likely have remedied the NDMA contamination issue much sooner by cleaning its production facilities, properly storing the Products, or simply testing its Products, it failed to do so until its hand was forced. While Apotex self-servingly claims that a penalty "will have no deterrent effect" given its "own voluntary compliance measures" (Apotex Demurrer at 11), this ignores that penalties will (1) incentivize Apotex to take proactive remedial steps in the future to ensure the safety of its ranitidine (should it decide to re-enter the market) or its various other drug products (which Apotex continues to sell), and (2) send a message to Apotex and other Product manufacturers and retailers that dangerous contaminants in drug products will not be tolerated. *See generally Student Pub. Int. Rsch. Gp., Inc. v. AT&T Bell Labs.* (D.N.J. 1985) 617 F.Supp. 1190, 1200-02 (applying the concepts of "specific deterrence" and "general deterrence" in the

similar context of civil penalties under the federal Clean Water Act).[32]

Application of the other penalty factors to the present state of the record also reveals that an award of civil penalties may well be appropriate here. There are likely to have been thousand, if not millions, of unwarned exposures to NDMA in California prior to Apotex's cessation of Product sales, and there may be many more upon reintroduction. *See* Health & Safety Code §25249.7(b)(2)(A)-(B) (going to the "extent" and "number" of the violations). The violations were serious enough to warrant an FDA-mandated nationwide recall, as well as subsequent testing and remedial steps to ensure that NDMA levels will be reduced. *See id.* (going to the "nature" and "severity" of the violations). Although Apotex claims that the violations were not "willful" under Health & Safety Code §25249.7(b)(2)(E), it appears that the company could have and should have learned of problem much earlier, which goes both to willfulness and to "the time [good faith] measures [to comply] were taken." *Id.* §25249.7(b)(2)(D). *See also* SAC ¶37 (alleging that "Defendants continued to expose individuals to NDMA without prior clear and reasonable warnings regarding the carcinogenic hazards of NDMA even after the publicity and recalls").

At heart, Apotex appears to believe that a company can ignore California law and other evidence of NDMA contamination for years and then escape all liability with a belated *mea culpa*. Plainly, this is a company that has not remotely learned its lesson, thus demonstrating the need for deterrence that civil penalties provide. *See Laidlaw*, 528 U.S. at 186 ("[A] defendant once hit in its pocketbook will surely think twice before [violating the law] again."). At any rate, it is plain that there is no way Apotex can categorically rule out at the pleading stage the possibility that civil penalties will be deemed necessary at the trial stage.

3. Neither CEH's Prayer for Injunctive Relief Nor its Prayer for Attorneys' Fees and Costs Are Moot.

Apotex's voluntary cessation of the illegal conduct alleged in the complaint does not moot

[32] Apotex's argument that this would have the "perverse effect" of deterring early recall efforts makes no sense. Apotex Demurrer at 11-12. By ceasing sales, Apotex limited the number of NDMA exposures for which it can be liable, which will yield a smaller penalty under Health & Safety Code §25249.7(b)(2)(A)-(B). Also, Apotex is not being "whipsawed" by a request for penalties (Apotex Demurrer at 12) – CEH is not seeking to punish the company for recalling its Products, but for what Apotex failed to do prior to the recall (*e.g.*, test its Products for NDMA) and for what it may fail to do later upon reintroduction (*e.g.*, continue to violate California law).

CEH's requests for injunctive relief or attorneys' fees and costs. *See Marin County Bd. of Realtors, Inc. v. Palsson* (1976) 16 Cal.3d 920, 930-31 (injunctive relief); *California Common Cause v. Duffy* (1987) 200 Cal.App.3d 730, 742 (attorneys' fees and costs). These rules make sense because the alleged violator may restart the illegal conduct at any time.

As an initial matter, Apotex fails to note that CEH has alleged a "continuing failure" to warn about NDMA (SAC ¶1), that unwarned exposures "continue to occur … through the use" of Apotex's Products (*id.* ¶¶25-26), and that Apotex "continue[s] to fail" to provide warnings (*id.* ¶44); consequently, in the Prayer, CEH asks the Court not only to enjoin Apotex from offering Products for sale without warnings, but also to "take action to stop ongoing unwarned exposures to NDMA resulting from use of Products" (*id.* at 9 (Prayer ¶2)). *See also id.* ¶39 (noting that "[a]ny person 'violating or threatening to violate' Proposition 65 may be enjoined") (quoting Health & Safety Code §§25249.7 & 25249.11(e)). These allegations, which are to be taken as true at the demurrer stage, wholly defeat Apotex's mootness challenge. Notably, there could be ongoing unwarned exposures to NDMA occurring even ***today*** for any Product purchasers that did not learn of the recall or the NDMA contamination issues through Apotex's single press release on the issue.

Moreover, it is somewhat rich for Apotex to pat itself on the back for taking certain steps starting in late September 2019 to notify customers and consumers of the NDMA issue and to remove its Products from the market. As alleged in CEH's operative complaint (*see* SAC ¶36), the recall happened because a third-party laboratory figured out a contamination issue that manufacturers such as Apotex should have themselves discovered years earlier. Apotex also fails to note that its own recall was prompted by a prior FDA statement on September 13, 2019 reporting these third-party findings, and suggesting that consumers instead use any of the other readily-available OTC acid reduction medications that do not contain ranitidine (or NDMA). *See* Brand Name Manufacturers RJN, Exh G, at 2.[33] Apotex is also wrong to fault CEH for not suing it earlier (Apotex Demurrer at 1-2) given that the ranitidine it makes are private label products that

[33] Perhaps Apotex saw the writing on the wall at this point, or perhaps it had belatedly performed its own tests indicating that the NDMA levels in its Products were dangerously high.

do not reveal the identity of the ultimate manufacturer. CEH only learned of Apotex's involvement in the supply chain for the Products at issue at a later stage, during discussions with its private label retailer. This raises no inference that CEH was dilatory here, especially given the "discovery rule" applicable in Proposition 65 cases. *See Shamsian v. Atl. Richfield Co.* (2003) 107 Cal.App.4th 967, 979-80.

In any event, Apotex is in no position to say ***now*** what it may do in the future as to ranitidine, and thus what injunctive relief may be appropriate at a later stage in the case.[34] Even if Apotex has "discontinued both of its OTC formulations of ranitidine" at present (Apotex Demurrer at 5), nothing precludes it from changing its mind at some point prior to trial in this action. Should Apotex later reenter the market, the Court will be able to award any number of injunctive measures, such as measures to reduce NDMA or to warn California consumers.[35]

As with injunctive relief, the determination of whether attorneys' fees are appropriate is inchoate at present. If CEH can prove entitlement to any other remedies later, or that its pre-suit notice was the catalyst for any change in Apotex's conduct leading to compliance with Proposition 65, then it may be entitled to reimbursement of its attorneys' fees. Surely, the earlier recall was not the full extent of possible relief – as explained above, CEH could establish at trial that remedial steps should be taken to reduce NDMA levels or provide warnings, or that civil penalties should be awarded for past, present, or future violations.[36] It is simply not true that "CEH's

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[34] Apotex's argument here is in tension with its argument on field preemption. At the same time that Apotex claims this Court should decline CEH's request for injunctive relief based on "unsubstantiated conjecture" that "the FDA may or may not take certain action in the future" (Apotex Demurrrer at 6-7), the company asserts that the Court should find CEH's claims preempted based essentially on what the FDA might do in the future. *See id.* at 5 (noting that the FDA "will continue to work with drug manufacturers to ensure safe, effective, and high-quality drugs for the American public").

[35] Other cases cited by Apotex – *Consumer Cause, Inc. v. Johnson & Johnson* (2005) 132 Cal.App. 4th 1175, 1186 and *Pacific Legal Found. v. Cal. Coastal Comm.* (1983) 33 Cal.3d 158, 170 – are ***ripeness*** cases, not mootness cases, and therefore are inapplicable here. In general, both cases stand for the undisputed proposition that the appropriateness of an injunction depends on the state of facts at the time the remedy is adjudicated, not that prayers for injunctive relief should be rejected at the pleading stage.

[36] The California Attorney General's Settlement Guideline do not assist Apotex. Apotex protests that that there must be "evidence of an exposure for which a warning plausibly is required" (Apotex Demurrer at 9) (citing 11 C.C.R. §3201(b)(1)), but here there undeniably ***were*** such NDMA exposures (and may be again). The Guidelines also specify that a "significant benefit on the public" can be conferred either by the provision of a clear and reasonable warning or product

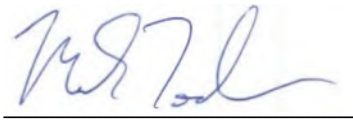
proposed enforcement action does not (and cannot) confer a greater public benefit than the FDA's threshold for drug manufacturers to reenter the ranitidine market" (Apotex Demurrer at 10), since California NDMA standards upon reintroduction may be more stringent than what federal law requires. In sum, this is not a defect in CEH's pleadings; it is an issue of entitlement to remedies that will have to await resolution at a later stage in the case.

VI. CONCLUSION

Because Defendants have failed to carry their burden of demonstrating federal preemption or mootness, their demurrers should be overruled. However, should the Court nonetheless be inclined to grant the demurrers, the resultant dismissal should be without prejudice so that CEH may conduct discovery in furtherance of amending its allegations.[37]

DATED: March 29, 2021

LEXINGTON LAW GROUP



Mark N. Todzo
Joseph Mann
Attorneys for Plaintiff
Center for Environmental Health

reformulation in lieu of such warning. 11 C.C.R. §3201(b)(1)-(2). Either of these remedies will be available at trial.

[37] Discovery will illuminate the exact cause (or causes) of NDMA in ranitidine as well as the different steps Defendants could have taken to remedy the contamination. It is for this reason that California appellate courts agree that even where a demurrer raises federal preemption as a "pure question of law," a dismissal with prejudice is improper on manufacturing defect claims because "without discovery, it would be impossible to meet a pleading standard requiring [the plaintiffs] to identify a specific federal requirement" that the defendants violated. *Coleman v. Medtronic, Inc.* (2014) 223 Cal.App.4th 413, 422, 436.

Exhibit 36

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CENTER FOR ENVIRONMENTAL HEALTH

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

Case No. RG 20-054985

ASSIGNED FOR ALL PURPOSES TO:
Hon. Winifred Smith, Department 21

DECLARATION OF MARK N. TODZO IN SUPPORT OF PLAINTIFF'S OMNIBUS OPPOSITION TO DEFENDANTS' DEMURRERS

Date: April 21, 2021
Time: 10:00 a.m.

Reservation Numbers: R-2240281, R-2240282, R-2240283, R-2240276, R-2242157

SAC Filed: January 4, 2021
Trial Date: None Set

[Filed concurrently with Plaintiff's Omnibus Opposition to Defendants' Demurrers; Request for Judicial Notice]

I, Mark N. Todzo, declare as follows:

1. I am a partner with the Lexington Law Group ("LLG") and I represent Plaintiff Center for Environmental Health ("CEH") in this action. I have personal knowledge of the matters set forth below and, if called upon, I could and would competently testify thereto.

2. Attached hereto as Exhibit 1 is a true and correct copy of the Proposition 65 Ballot Pamphlet, which was obtained from the California Office of Environmental Health Hazard Assessment's public website at https://oehha.ca.gov/media/downloads/proposition-65/general-info/prop65ballot1986.pdf on or about March 25, 2021.

3. Attached hereto as Exhibit 2 is a true and correct copy of the U.S. Food and Drug Administration's ("FDA") publicly available webpage on "Questions and Answers: NDMA impurities in ranitidine (commonly known as Zantac)" (https://www.fda.gov/drugs/drug-safety-and-availability/questions-and-answers-ndma-impurities-ranitidine-commonly-known-zantac), visited on or about March 24, 2021.

4. Attached hereto as Exhibit 3 is a true and correct copy of the FDA's "Guidance for Industry – Q3A Impurities in New Drug Substances," dated June 2008, which was obtained from the FDA's public website at https://www.fda.gov/media/71727/download on or about March 18, 2021.

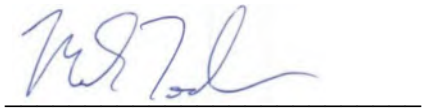
5. Attached hereto as Exhibit 4 is a true and correct copy of the FDA's "Guidance for Industry – ANDAs: Impurities in Drug Substances," dated November 1999, which was obtained from the FDA's public website at https://www.fda.gov/files/drugs/published/ANDA's--Impurities-in-Drug-Substances.pdf on or about March 18, 2021.

6. Attached hereto as Exhibit 5 is a true and correct copy of the FDA's publicly available webpage on "Prescription Drug Advertising – Questions and Answers" (https://www.fda.gov/drugs/prescription-drug-advertising/prescription-drug-advertising-questions-and-answers), visited on or about March 21, 2021.

7. Attached hereto as Exhibit 6 is a true and correct copy of the FDA's publicly available webpage on "Laboratory Tests – Ranitidine" (https://www.fda.gov/drugs/drug-safety-and-availability/laboratory-tests-ranitidine), visited on or about March 24, 2021.

8. Attached hereto as Exhibit 7 is a true and correct copy of Defendant Sanofi-Aventis U.S. LLC's "Company Announcement – Sanofi Provides Update on Precautionary Voluntary Recall of Zantac OTC in U.S.," as posted to FDA's publicly available website at https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/sanofi-provides-update-precautionary-voluntary-recall-zantac-otc-us, visited on or about March 24, 2021.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct. Executed on March 29, 2021 in Hillsborough, California.



Mark N. Todzo

Exhibit 1

65 Restrictions on Toxic Discharges into Drinking Water; Requirement of Notice of Persons' Exposure to Toxics. Initiative Statute

Official Title and Summary Prepared by the Attorney General

RESTRICTIONS ON TOXIC DISCHARGES INTO DRINKING WATER; REQUIREMENT OF NOTICE OF PERSONS' EXPOSURE TO TOXICS. INITIATIVE STATUTE. Provides persons doing business shall neither expose individuals to chemicals known to cause cancer or reproductive toxicity without first giving clear and reasonable warning, nor discharge such chemicals into drinking water. Allows exceptions. Requires Governor publish lists of such chemicals. Authorizes Attorney General and, under specified conditions, district or city attorneys and other persons to seek injunctions and civil penalties. Requires designated government employees obtaining information of illegal discharge of hazardous waste disclose this information to local board of supervisors and health officer. Summary of Legislative Analyst's estimate of net state and local government fiscal impact: Costs of enforcement of the measure by state and local agencies are estimated at $500,000 in 1987 and thereafter would depend on many factors, but could exceed $1,000,000 annually. These costs would be partially offset by fines collected under the measure.

Analysis by the Legislative Analyst

Background

Currently, the state has a number of programs designed to protect people against possible exposures to harmful chemicals. The major programs involve the regulation of:

- **Waste Discharges.** The State Water Resources Control Board and the regional water quality control boards regulate the discharge of wastes into state waters, including rivers, streams, and groundwater that may be used as sources of drinking water. The Department of Health Services regulates the disposal and cleanup of hazardous waste, including hazardous waste that may contaminate drinking water.
- **Drinking Water.** Current law prohibits local water agencies from supplying drinking water to the public that contains dangerous levels of certain harmful chemicals. Local water agencies must inform customers when the level of these chemicals exceeds certain limits. The Department of Health Services enforces these limits.
- **Workplace Hazards.** The Department of Industrial Relations regulates exposure to cancer causing materials and other harmful substances in the workplace. Current law also requires employers to inform workers of possible exposure to dangerous substances.
- **Pesticides.** The Department of Food and Agriculture regulates the use of pesticides in agriculture and in other business applications, such as maintenance of landscaping and golf courses.

These regulatory agencies must make judgments about the amounts of harmful chemicals that can be released into the environment. In doing so, they try to balance what it costs to prevent the release of chemicals against the risks the chemicals pose to public health and safety. As the level of allowable exposure goes down, the cost of prevention typically goes up. The risk that some substances pose to health is not always known. Often, scientists cannot determine precisely the health impact of low-level exposures that occur over 20 or 30 years.

Proposal

This measure proposes two additional requirements for businesses employing 10 or more people. First, it generally would prohibit those businesses from knowingly releasing into any source of drinking water any chemical in an amount that is known to cause cancer or in an amount that exceeds 1/1000th of the amount necessary for an observable effect on "reproductive toxicity." The term "reproductive toxicity" is not defined. Second, the measure generally would require those businesses to warn people before knowingly and intentionally exposing them to chemicals that cause cancer or reproductive toxicity. The measure would require the state to issue lists of substances that cause cancer or reproductive toxicity.

Because these new requirements would result in more stringent standards, the practical effect of the requirements would be to impose new conditions for the issuance of permits for discharges into sources of drinking water. In order to implement the new requirements, state agencies that are responsible for issuing permits would be required to alter state regulations and develop new standards for the amount of chemicals that may be discharged into sources of drinking water.

The measure also would impose civil penalties and increase existing fines for toxic discharges. In addition, the measure would allow state or local governments, or any person acting in the public interest, to sue a business that violates these rules.

Fiscal Effect

It is estimated that the administrative actions resulting from the enactment of this measure would cost around $500,000 in 1987. Starting in 1988, the costs of these actions are unknown and would depend on many factors, but these costs could exceed $1 million annually.

In addition, the measure would result in unknown costs to state and local law enforcement agencies. A portion of these costs could be offset by increased civil penalties and fines collected under the measure.

Beyond these direct effects of the measure, state and local governments may strengthen enforcement activities to ensure compliance with the new requirements. The costs of any additional enforcement could be significant.

Text of Proposed Law

This initiative measure is submitted to the people in accordance with the provisions of Article II, Section 8 of the Constitution.

This initiative measure amends and adds sections to the Health and Safety Code; therefore, existing provisions proposed to be deleted are printed in ~~strikeout type~~ and new provisions proposed to be added are printed in *italic type* to indicate that they are new.

PROPOSED LAW

SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986

SECTION 1. The people of California find that hazardous chemicals pose a serious potential threat to their health and well-being, that state government agencies have failed to provide them with adequate protection, and that these failures have been serious enough to lead to investigations by federal agencies of the administration of California's toxic protection programs. The people therefore declare their rights:

(a) To protect themselves and the water they drink against chemicals that cause cancer, birth defects, or other reproductive harm.

(b) To be informed about exposures to chemicals that cause cancer, birth defects, or other reproductive harm.

(c) To secure strict enforcement of the laws controlling hazardous chemicals and deter actions that threaten public health and safety.

(d) To shift the cost of hazardous waste cleanups more onto offenders and less onto law-abiding taxpayers.

The people hereby enact the provisions of this initiative in furtherance of these rights.

SECTION 2. Chapter 6.6 (commencing with Section 25249.5) is added to Division 20 of the Health and Safety Code, to read:

CHAPTER 6.6.

SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986

25249.5. Prohibition On Contaminating Drinking Water With Chemicals Known to Cause Cancer or Reproductive Toxicity. No person in the course of doing business shall knowingly discharge or release a chemical known to the state to cause cancer or reproductive toxicity into water or onto or into land where such chemical passes or probably will pass into any source of drinking water, not withstanding any other provision or authorization of Law except as provided in Section 25249.9.

25249.6. Required Warning Before Exposure · To Chemicals Known to Cause Cancer Or Reproductive Toxicity. No person in the course of doing business shall knowingly and intentionally expose any individual to a chemical known to the state to cause cancer or reproductive toxicity without first giving clear and reasonable warning to such individual, except as provided in Section 25249.10.

25249.7. Enforcement.

(a) Any person violating or threatening to violate Section 25249.5 or Section 25249.6 may be enjoined in any court of competent Jurisdiction.

(b) Any person who has violated Section 25249.5 or Section 25249.6 shall be liable for a civil penalty not to exceed $2500 per day for each such violation in addition to any other penalty established by law. Such civil penalty may be assessed and recovered in a civil action brought in any court of competent jurisdiction.

(c) Actions pursuant to this section may be brought by the Attorney General in the name of the people of the State of California or by any district attorney or by any city attorney of a city having a population in excess of 750,000 or with the consent of the district attorney by a city prosecutor in any city or city and county having a full-time city prosecutor, or as provided in subdivision (d).

(d) Actions pursuant to this section may be brought by any person in the public interest if (1) the action is commenced more than sixty days after the person has given notice of the violation which is the subject of the action to the Attorney General and the district attorney and any city attorney in whose jurisdiction the violation is alleged to occur and to the alleged violator, and (2) neither the Attorney General nor any district attorney nor any city attorney or prosecutor has commenced and is diligently prosecuting an action against such violation.

25249.8 List Of Chemicals Known to Cause Cancer Or Reproductive Toxicity.

(a) On or before March 1, 1987, the Governor shall cause to be published a list of those chemicals known to the state to cause cancer or reproductive toxicity within the meaning of this chapter, and he shall cause such list to be revised and republished in light of additional knowledge at least once per year thereafter. Such list shall include at a minimum those substances identified by reference in Labor Code Section 6382(b)(1) and those substances identified additionally by reference in Labor Code Section 6382(d).

(b) A chemical is known to the state to cause cancer or reproductive toxicity within the meaning of this chapter if in the opinion of the state's qualified experts it has been clearly shown through scientifically valid testing according to generally accepted principles to cause cancer or reproductive toxicity, or if a body considered to be authoritative by such experts has formally identified it as causing cancer or reproductive toxicity, or if an agency of the state or federal government has formally required it to be labeled or identified as causing cancer or reproductive toxicity.

(c) On or before January 1, 1989, and at least once per year thereafter, the Governor shall cause to be published a separate list of those chemicals that at the time of publication are required by state or federal law to have been tested for potential to cause cancer or reproductive toxicity but that the states qualified experts have not found to have been adequately tested as required.

(d) The Governor shall identify and consult with the state's qualified experts as necessary to carry out his duties under this section.

(e) In carrying out the duties of the Governor under this section, the Governor and his designates shall not be considered to be adopting or *amending a regulation within the meaning of the Administrative Procedure Act as defined in Government Code Section 11370.*

25249.9 Exemptions from Discharge Prohibition.

(a) Section 25249.5 shall not apply to any discharge or release that takes place less than twenty months subsequent to the listing of the chemical in question on the list required to be published under subdivision (a) of Section 25249.8.

(b) Section 25249.5 shall not apply to any discharge or release that meets both of the following criteria:

(1) The discharge or release will not cause any significant amount of the discharged or released chemical to

Continued on page 62

Proposition 65 Text of Proposed Law

Continued from page 53

enter any source of drinking water.

(2) The discharge or release is in conformity with all other laws and with every applicable regulation, permit, requirement, and order.

In any action brought to enforce Section 25249.5, the burden of showing that a discharge or release meets the criteria of this subdivision shall be on the defendant.

25249.10 Exemptions from Warning Requirement.

Section 25249.6 shall not apply to any of the following:

(a) An exposure for which federal law governs warning in a manner that preempts state authority.

(b) An exposure that takes place less than twelve months subsequent to the listing of the chemical in question on the list required to be published under subdivision (a) of Section (a) of Section 25249.8.

(c) An exposure for which the person responsible can show that the exposure poses no significant risk assuming lifetime exposure at the level in question for substances known to the state to cause cancer, and that the exposure will have no observable effect assuming exposure at one thousand (1,000) times the level in question substances known to the state to cause reproductive toxicity, based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for the listing of such chemical pursuant to subdivision (a) of Section 25249.8. In any action brought to enforce Section 25249.6, the burden of showing that an exposure meets the criteria of this subdivision shall be on defendant.

25249.11 Definitions.

For purposes of this chapter:

(a) "Person" means an individual, trust, firm, joint stock company, corporation, company, partnership, and association.

(b) "Person in the course of doing business" does not include any person employing fewer than ten employees in his business; any city, county, or district or any department or agency thereof or the state or any department or agency thereof or the federal government or any department or agency thereof; or any entity in its operation of a public water system as defined in Section 4010.1.

(c) "Significant amount" means any detectable amount except an amount which would meet the exemption test in subdivision (c) of Section 25249.10 if an individual were exposed to such an amount in drinking water.

(d) "Source of drinking water" means either a present source of drinking water or water which is identified or designated in a water quality control plan adopted by a regional board as being suitable for domestic or municipal uses.

(e) "Threaten to violate" means to create a condition in which there is a substantial probability that a violation will occur.

(f) "Warning" within the meaning of Section 25249.6 need not be provided separately to each exposed individual and may be provided by general methods such as labels on consumer products, inclusion of notices in mailings to water customers, posting of notices, placing notices in public news media, and the like, provided that the warning accomplished is clear and reasonable. In order to minimize the burden on retail sellers of consumer products including foods, regulations implementing Section 25249.6 shall to the extent practicable place the obligation to provide any warning materials such as labels on the producer or packager rather than on the retail seller, except where the retail seller itself is responsible for introducing a chemical known to the state to cause cancer or reproductive

toxicity into the consumer product in question. 25249.12 Implementation. The Governor shall designate a lead agency and such other agencies as may be required to implement the provisions of this chapter including this section. Each agency so designated may adopt and modify regulations, standards, and permits as necessary to conform with and implement the provisions of this chapter and to further its purposes.

25249.13 Preservation Of Existing Rights, Obligations, and Penalties. Nothing in this chapter shall alter or diminish any legal obligation otherwise required in common law or by statute or regulation, and nothing in this chapter shall create or enlarge any defense in any action to enforce such legal obligation. Penalties and sanctions imposed under this chapter shall be in addition to any penalties or sanctions otherwise prescribed by Law.

SECTION 3. Subdivision (d) of Section 25189.5 of the Health and Safety Code is amended to read:

(d) The court shall also impose upon a person convicted of violating subdivision (b) or (c) a fine of not less than five thousand dollars ($5,000) or more than ~~fifty~~ *one hundred* thousand dollars ~~($50,000)~~ *($100,000)* for each day of violation *except as further provided in this subdivision. If the act which violated subdivision (b) or (c) caused great bodily injury or caused a substantial probability that death could result, the person convicted of violating subdivision (b) or (c) may be punished by imprisonment in the state prison for up to 36 months, in addition to the term specified in subdivision (b) or (c), and may be fined up to two hundred fifty thousand dollars ($250,000) for each day of violation.*

SECTION 4. Section 25180.7 is hereby added to the Health and Safety Code as follows:

(a) Within the meaning of this section, a "designated government employee" is any person defined as a "designated employee" by Government Code Section 82019, as amended.

(b) Any designated government employee who obtains information in the course of his official duties revealing the illegal discharge or threatened illegal discharge of a hazardous waste within the geographical area of his jurisdiction and who knows that such discharge or threatened discharge is likely to cause substantial injury to the public health or safety must, within seventy-two hours, disclose such information to the local Board of Supervisors and to the local health officer. No disclosure of information is required under this subdivision when otherwise prohibited by law, or when law enforcement personnel have determined that such disclosure would adversely affect an ongoing criminal investigation, or when the information is already general public knowledge within the locality affected by the discharge or threatened discharge.

(c) Any designated government employee who knowingly and intentionally fails to disclose information required to be disclosed under subdivision (b) shall, upon conviction, be punished by imprisonment in the county jail for not more than one year or by imprisonment in state prison for not more than three years. The court may also impose upon the person a fine of not less than five thousand dollars ($5000) or more than twenty-five thousand dollars ($25,000). The felony conviction for violation of this section shall require forfeiture of government employment within thirty days of conviction.

(d) Any local health officer who receives information pursuant to subdivision (b) shall take appropriate action to notify local news media and shall make such information available to the public without delay.

SECTION 5. Section 25192 of the Health and Safety Code is amended to read:

25192. (a) All civil and criminal penalties collected pursuant to this chapter *or Chapter 6.6 (commencing with Section 25249.5)* shall be apportioned in the following manner:

(1) Fifty percent shall be deposited in the ~~Hazardous Waste Control Account~~ *Hazardous Substance Account* in the General Fund.

(2) Twenty-five percent shall be paid to the office of the city attorney, *city prosecutor,* district attorney, or Attorney General, which ever office brought the action, *or in the case of an action brought by a person under subdivision (d) of Section 25249.7 to such person.*

(3) Twenty-five percent shall be paid to the department and used to fund the activity of the local health ~~officers~~ *officer* to enforce the provisions of this chapter pursuant to Section 25180. *If investigation by the local police department or sheriffs office or California Highway Patrol led to the bringing of the action, the local health officer shall pay a total of forty percent of his portion under this subdivision to said investigating agency or agencies to be used for the same purpose: If more than one agency is eligible for payment under this provision, division of payment among the eligible agencies shall be in the discretion of the local health officer.*

(b) If a reward is paid to a person pursuant to Section 25191.7, the amount of the reward shall be deducted from the amount of the civil penalty before the amount is apportioned pursuant to subdivision (a).

(c) Any amounts deposited in the Hazardous Substance Account pursuant to this section shall be included in the computation of the state account rebate specified in Section 25347.2.

SECTION 6. If any provision of this initiative or the application there of is held invalid, that invalidity shall not affect other provisions or applications of the initiative which can be given effect without the invalid provision or application, and to this end the provisions of this initiative are severable.

SECTION 7. To further its purposes this initiative may be amended by statute, passed in each house by a two-thirds vote.

SECTION 8. This initiative shall take effect on January 1, 1987.

65 Restrictions on Toxic Discharges into Drinking Water; Requirement of Notice of Persons' Exposure to Toxics. Initiative Statute

Argument in Favor of Proposition 65

Nearly every week sees a new toxic catastrophe. Children in Fullerton, Riverside, McFarland, Sacramento, and San Jose have already been exposed to chemicals that may make them sterile or give them cancer.

There are certain chemicals that are scientifically known not merely suspected, but known to cause cancer and birth defects. Proposition 65 would:

- Keep these chemicals out of our drinking water.
- Warn *us* before we're exposed to any of these dangerous chemicals.
- Give private citizens the right to enforce these laws in court
- Make government officials tell the public when an illegal discharge of hazardous waste could cause serious harm.

The cost to taxpayers will be negligible, according to the Attorney General's official estimate.

Our present toxic laws aren't tough enough. Despite them, polluters contaminate our drinking water and expose us to extremely toxic chemicals without our knowing it. The health of innocent people is jeopardized. And the public must pay massive costs for cleanup.

The Governor's Toxics Task Force found:

- Toxic chemicals can cause cancer, birth defects, and genetic damage.
- Much of our drinking water is polluted by toxic chemicals.
- Exposure to toxics costs Californians more than $1.3 *billion* per year in medical care, lost income, and deaths.

Proposition 65 turns that report into action, with requirements that are clear, simple, and straightforward.

Proposition 65 gets tough on toxics.

SAFE DRINKING WATER

Proposition 65 singles out chemicals that are scientifically known to cause; cancer or reproductive disorders (such as birth defects). Effectively, it tells businesses: Don't put these chemicals into our drinking water supplies.

WARNING BEFORE EXPOSURE

Proposition *65* also tells businesses: Don't expose us to any of these same chemicals without first giving us a clear warning. We each have a right to know, and to make our own choices about being exposed to these chemicals.

TOUGHER ENFORCEMENT

Both public prosecutors and ordinary citizens can enforce these health protections directly in court.

Proposition 65 also toughens enforcement for criminal laws already on the books. Fines and jail terms are doubled for toxic crimes like midnight dumping. Police and prosecutors are given extra rewards for enforcing toxics laws.

Proposition 65's new civil offenses focus only on chemicals that are *known to the state* to cause cancer or reproductive disorders. Chemicals that are only suspect are not included. The Governor must list these chemicals, after full consultation with the state's qualified experts. At a minimum, the Governor must include the chemicals already listed as known carcinogens by two organizations of the most highly regarded national and international scientists: the U.S.'s National Toxicology Program and the U.N.'s International Agency for Research on Cancer.

These new laws will not take anyone by surprise. They apply only to businesses that *know* they are putting one of the chemicals out into the environment, and that *know* the chemical is actually on the Governor's list.

Proposition 65 will give California the clearest, most effective toxic control laws in the nation.

VOTE *YES* ON PROPOSITION 65.

IRA **REINER**
District Attorney, Los Angeles County

ART TORRES
State Senator, 24th District
Chair, Senate Toxics and Public Safety Management Committee

PENNY NEWMAN
Chair, Concerned Neighbors in Action (Stringfellow Acid Pits)

Rebuttal to Argument in Favor of Proposition 65

WE JOIN SCIENTISTS, HEALTH PROFESSIONALS AND FARMERS IN URGING A "NO" VOTE ON PROPOSITION 65.

Everybody wants safe drinking water. Proposition 65 simply won't give it to us.

PROPOSITION 65 WILL NOT PRODUCE SAFE DRINKING WATER.

FACT: Proposition 65 EXEMPTS the biggest water polluters in the state.

FACT: Proposition 65 *limits* funds available to district attorneys to enforce the law.

FACT: IT UNDERMINES CALIFORNIA TOXICS LAW-THE TOUGHEST IN THE COUNTRY.

PROPOSITION 65 WONT PRODUCE USEFUL WARNINGS.

It requires "warnings" on millions of ordinary and safe items. We won't know what products are really dangerous anymore. THE WARNINGS WE REALLY NEED WILL GET LOST IN LOTS OF WARNINGS WE DON'T NEED.

PROPOSITION 65 IS THE WRONG APPROACH.

A leading spokesman for the proponents recently said, "We have plenty of laws on the books already ... you can't clean up anything by loading on more legislation."

We couldn't agree more.

FACT: Toxics enforcement personnel has *increased* 48% in the last four years.

FACT: The toxics cleanup budget has *increased* nearly 150% in the last four years.

FACT: Several million dollars in fines have *already* been collected, used for cleanup and future enforcement.

Proposition 65 will take environmental regulation out of the hands of lawmakers and prosecutors and create a system of vigilante justice with bounty hunters seeking rewards.

PROPOSITION 65 IS FILLED WITH EXCEPTIONS, HURTS FARMERS, AND WILL NOT GIVE US SAFE DRINKING WATER.

VOTE NO on the Toxics Initiative.
VOTE NO on Proposition 65.

EDWARD R. JAGELS
District Attorney, Kern County

MICHELE BEIGEL CORASH
Former General Counsel
U.S. Environmental Protection Agency

CATHIE WRIGHT
Member of the Assembly, 37th District
Member, Assembly Committee on Environmental Safety and Toxic Materials

Restrictions on Toxic Discharges into Drinking Water; Requirement of Notice of Persons' Exposure to Toxics. Initiative Statute

65

Argument Against Proposition 65

TOXIC POLLUTION IS A SERIOUS MATTER REQUIRING SERIOUS ATTENTION. Proposition 65 is a *simplistic response* to a *complex problem.*

As scientists, health professionals, and farmers, we are on *solid ground* when we say that *Proposition 65* is *faulty* from a scientific point of view, is so *full of exemptions* as to be meaningless from, a health point of view, and is *unfair* and *devastating to farmers.*

FACT: UNDER PROPOSITION 65 THE GOVERNMENT AND MANY BUSINESSES ARE EXEMPT.

- Publicly owned nuclear power plants *ARE EXEMPT!*
- Cities which dump raw sewage into freshwater streams *ARE EXEMPT!*
- Public water systems *ARE EXEMPT!*
- Military bases which contaminate residential drinking water *ARE EXEMPT!*
- County landfills *ARE EXEMPT!*
- Thousands of businesses *WOULD BE EXEMPT.*
- A GOOD LAW APPLIES EVENLY AND EQUALLY TO EVERYONE.
- This is a bad law made worse because it is *loaded with exemptions.*

FACT: PROPOSITION 65 UNFAIRLY TARGETS CALIFORNIA FARMERS.

Normally, manufacturers-not users-must prove the safety of their product. But Proposition 65 *puts that burden on farmers.*

Many common fertilizers, weed and pest control materials perfectly safe when properly *used-would be effectively banned for most farmers but* allowed for many nonfarmers.

FARMERS MAY EVEN HAVE TO STOP IRRIGATING.

Farmers are having a tough time as it is providing quality food, in adequate supply, at the lowest possible price. Proposition 65 would add to their burden and may be the final straw to break the back of many.

FACT: PROPOSITION 65's BOUNTY HUNTER PROVISION IS A BONANZA FOR PRIVATE LAWYERS.

Proposition 65 creates a lawyer's paradise: anyone can sue; almost anyone can be sued. People who sue will get a reward from penalties collected. *Thus, environmental regulation is taken from the hands of government regulators and prosecutors and handed to private lawyers and judges.*

WE HAVE THE LAWS; WE NEED BETTER ENFORCEMENT.

We have many thoughtful laws relating to toxic pollution on the books. They include:

- Porter-Cologne Water Quality Act.
- Toxic Air Contaminants Program.
- Water Supply Testing Program.
- Pesticide Contamination Prevention Act.
- Birth Defect Prevention Act.
- Toxics Pit Clean-up Act.

Over 50 new laws have been passed in the last two years to *control* chemicals and toxics.

We *need to build* on the system we have, *not* abandon it in favor of extreme "solutions."

The simple *scientific fact* of the matter is that manmade carcinogens represent only a tiny fraction of the total carcinogens we are exposed to most of which are natural substances such as tobacco, alcohol, and chemicals in green plants, Significant amounts of manmade carcinogens are highly regulated in California under the most stringent laws in the United States. This initiative will result in chasing after trivial amounts of manmade carcinogens at *enormous cost* with minimal benefit to our health. We're *concerned about safer, cleaner drinking water.* And we're *concerned* that we get there in an *intelligent, rational* and *fair* manner.

Proposition 65 just won't do that.

We urge you to VOTE NO ON THE TOXICS INITIATIVE. Vote no on PROPOSITION 65.

DR. BRUCE AMES
Chairman, Department of Biochemistry, University of California, Berkeley

HENRY VOSS
President, California Farm Bureau

ALICE OTTOBONI, Ph.D.
Toxicology Staff Toxicologist, California Department of Health Services, Rtd.

Rebuttal to Argument Against Proposition 65

Who's really against Proposition 65?

The big oil and chemical companies are leading the opposition because they know they would *be* forced to stop dumping extremely dangerous chemicals into your drinking water if Proposition 65 passes. The existing laws don't stop them. Proposition 65 will. That's why they're spending millions of dollars on a misleading media campaign.

DON'T BE FOOLED.

Proposition 65 simply says that businesses shouldn't put chemicals that are scientifically known to cause cancer, or birth defects, into your drinking water. And that they must warn you before they expose you to such a chemical.

- Proposition 65 means tougher law enforcement. It will help prosecutors put polluters in jail. That's why the California District Attorneys Association has endorsed it.
- Proposition 65 applies equally to all businesses in California. except for the smallest businesses (those with fewer than 10 employees).
- Proposition 65 applies to the big businesses that produce more than 90% of all hazardous waste in California (according to official state estimates) .
- Proposition 65 treats farmers exactly the same as everyone else no tougher, no easier. Small family farms, like other small businesses. are exempt.
- Proposition 65 is based strictly on scientific testing, more than any existing toxics law.
- Proposition 65 does not apply to insignificant (safe) amounts of chemicals.
- Proposition 65 will not in *any* way weaken *any* of California's existing protections in toxics law.

DON'T BE FOOLED BY THE BIG POLLUTERS.

Vote YES on Proposition 65!

GET TOUGH ON TOXICS!

ARTHUR C. UPTON, M.D.
Former Director, National Institutes of Health

NORMAN W. FREESTONE, JR.
Farmer; Visalia

ALBERT H. GERSTEN, JR.
Businessman; Member, Little Hoover Commission

Exhibit 2

Questions and Answers: NDMA impurities in ranitidine (commonly known as Zantac)

Answers to questions about NDMA impurities found in ranitidine and FDA's actions to address the issue

Updates on NDMA in ranitidine (/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine)

Important information about NDMA impurities in ranitidine products

- The U.S. Food and Drug Administration has requested a manufacturer's market withdrawal of ranitidine, known commonly by the brand name Zantac. This means ranitidine products will not be available for new or existing prescriptions or over-the-counter (OTC) use in the U.S.
- FDA has found N-nitrosodimethylamine (NDMA) levels in some ranitidine products increase with time and temperature posing a risk to consumers, and therefore the agency has requested the withdrawal of all ranitidine products from the U.S. market.
- Consumers should stop taking any OTC ranitidine they may currently have. Patients taking prescription ranitidine should speak with their health care professional about other treatment options before stopping the medicine. Multiple drugs are approved for the same or similar uses as ranitidine.
- Consumers should dispose of any ranitidine products properly (/drugs/safe-disposal-medicines/disposal-unused-medicines-what-you-should-know), and not buy more of it including compounded ranitidine.
- To date, FDA's testing has not found NDMA in products used for similar treatment like famotidine (Pepcid), cimetidine (Tagamet), esomeprazole (Nexium), lansoprazole (Prevacid) or omeprazole (Prilosec).

Q. Why are ranitidine products being withdrawn from the market?

A. FDA is requesting a market withdrawal of all remaining prescription and OTC ranitidine products on the U.S. market. This means that ranitidine will not be available for use in the U.S. The agency is taking this action because FDA laboratory testing results show that levels of NDMA in ranitidine may increase to unacceptable levels over time. The tests also show NDMA levels increase in some ranitidine products when the drug is exposed to higher than room temperatures. Based on these findings, FDA has determined that many currently marketed ranitidine products could expose consumers to unacceptable health risks. All ranitidine products, including the oral liquid/syrup, will be withdrawn by their manufacturers and will not be available on the U.S. market.

This differs from past actions because this is the first time FDA is requesting market withdrawal of all ranitidine products.

Q. Will ranitidine be available again in the future?

A. If a company can show, through scientific data, that their ranitidine product is stable and the NDMA levels do not increase over time to unsafe levels, FDA may consider allowing that ranitidine product back on the U.S. market.

Q. How should I dispose of my ranitidine?

A. In light of the current COVID-19 pandemic, we recommend patients and consumers not take their medicines to a drug take-back location but follow the specific disposal instructions in the medication guide or package insert (/drugs/drug-safety-and-availability/medication-guides), or follow these steps, which include ways to safely dispose of these medications at home (/drugs/safe-disposal-medicines/disposal-unused-medicines-what-you-should-know).

Q. What will happen to the ranitidine that manufacturers have in storage and not currently on store shelves? Will the manufactures have to dispose of it as well?

A. Any product in storage and not yet distributed would have to be evaluated following FDA guidance to show it would be safe throughout its shelf-life before the manufacturer can put it back on the market.

Q. Are injectable forms of ranitidine impacted?

A. Yes, all formulations of ranitidine are affected by this action.

Q. Are compounded ranitidine drugs impacted? How does this affect compounding of ranitidine products for animal use?

A. Yes, compounded ranitidine products are affected by this action. FDA also has safety concerns over the compounding of ranitidine-containing drugs intended for animal use. Animal owners should consult their veterinarian for alternative treatment options.

Q. Will FDA withdraw approvals of ranitidine new drug applications and abbreviated new drug applications?

A. At this time, FDA is not withdrawing approvals of ranitidine new drug applications and abbreviated new drug applications (NDAs/ANDAs for ranitidine).

Q. What will happen to ranitidine new drug and abbreviated new drug (generic) applications already submitted to FDA? Will the agency still be able to approve them?

A. FDA will contact ANDA applicants as needed regarding pending submissions that are affected by this withdrawal. If a company can show, through scientific data, that their ranitidine product is stable and the NDMA levels do not increase over time to unsafe levels, FDA may consider allowing that ranitidine product on the U.S. market.

Q. How much did NDMA levels increase from increased temperature and time in the FDA's recent laboratory tests?

A. FDA laboratory tests show that temperature and time generally raise the level of NDMA in some ranitidine products above the acceptable daily intake limit of 96 nanograms per day.

Q. What is the risk to me if I have taken ranitidine?

A. FDA does not expect nitrosamines to cause harm when ingested at low levels. Nitrosamine impurities may increase the risk of cancer if people are exposed to them at above acceptable levels and over long periods of time, but a person taking a drug that contains nitrosamines at, or below, the acceptable daily intake limits every day for 70 years is not expected to have an increased risk of cancer.

Q. How long has NDMA been present in ranitidine?

A. FDA does not have scientific evidence to determine how long NDMA has been present in ranitidine products.

Q. What is the source of NDMA in ranitidine?

A. This is an ongoing investigation and the agency is working to fully determine the root cause. NDMA was present in both the finished drug product samples and the active pharmaceutical ingredients (APIs) that the FDA tested. The FDA's simulated gastric fluid and simulated intestinal fluid testing results illustrated that NDMA was not formed in the conditions of the stomach or the intestines. However, the FDA's recent laboratory testing results demonstrate that levels of NDMA in some ranitidine finished drug products increase over time at room

temperature. Increased temperatures also resulted in increased levels of NDMA in some ranitidine finished drug product.

Q. Is the presence of nitrosamines in drugs a new problem? Why have there been so many recent reports of drugs containing nitrosamines?

A. FDA has ongoing assessment, surveillance, compliance and pharmaceutical quality efforts across every product area, and we will continue to work with drug manufacturers to ensure safe, effective and high-quality drugs for the American public. When we identify new and previously unrecognized risks to safety and quality, we react swiftly to resolve the problem, as we have done in responding to the recent findings of nitrosamine in certain medicines.

Today, we have better testing methods than ever before, and we know what to look for in products' chemical structures and manufacturing processes that may increase the risk of forming low levels of nitrosamines. Improved technology enables us to detect even trace amounts of impurities in drug products and may be the reason why more products have been found to have low levels of nitrosamines. The agency has strict standards for safety, effectiveness and quality, and our staff makes every effort to help keep the U.S. drug supply as safe as possible. We also work closely with international drug regulatory agencies so that we leverage resources and testing done outside the U.S. which can help inform testing of the U.S. drug supply. As our investigations and testing continue, along with the investigations done by international drug regulatory agencies, we may find low levels of nitrosamines in additional drugs.

Q. Why didn't FDA catch this impurity when the product was initially approved?

A. Drug manufacturers and FDA continually gain new knowledge about drugs, which is why FDA constantly evaluates quality and safety information over time. As testing methods have become more sophisticated and sensitive, FDA and industry can identify and mitigate previously-unknown risks to patients.

Through extensive investigation and information-sharing with international regulatory agencies and private sector laboratories, the agency is now able to scientifically show that time and increased temperature can cause increased levels of NDMA in some ranitidine products that may pose a health risk.

Q. Does this action affect products that might be used in veterinary medicine?

A. There are no approved new animal drugs containing ranitidine. However, veterinarians can prescribe an approved human drug for extra-label (off label) use in animals under certain conditions. If a veterinarian has prescribed extra-label use of an approved human drug containing ranitidine for use in their animal patients, the drug will no longer be available. One

common extra-label use of approved human drugs containing ranitidine is for treatment or control of gastric ulcers in horses.

Q. What should animal owners use in place of ranitidine?

A. Animal owners should consult their veterinarian for alternative treatment options.

Q. What products are approved to treat gastric ulcers in horses?

A. GastroGard is approved for treatment and prevention of recurrence of gastric ulcers in horses and foals 4 weeks of age and older. UlcerGard is approved for the prevention of gastric ulcers in horses. Animal owners should consult their veterinarian for appropriate treatment options.

Q. Is the agency granting Valisure and Emery Pharma's Citizen Petitions regarding ranitidine?

A. The agency is responding to citizen petitions from Valisure and Emery Pharma related to nitrosamines in ranitidine. When the Commissioner has issued responses to the citizen petitions the decisions will be available at docket numbers FDA-2019-P-4281 (https://www.regulations.gov/searchResults?rpp=25&po=0&s=FDA-2019-P-4281&fp=true&ns=true) , and FDA-2020-P-0042 (https://www.regulations.gov/searchResults?rpp=25&po=0&s=FDA-2020-P-0042&fp=true&ns=true).

Exhibit 3

Guidance for Industry

Q3A Impurities in New Drug Substances

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

June 2008
ICH

Revision 2

Guidance for Industry

Q3A Impurities in New Drug Substances

Additional copies are available from:

Office of Training and Communication
Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave.
Bldg. 51, Room 2201
Silver Spring, MD 20993-0002
(Tel) 301-796-3400
http://www.fda.gov/cder/guidance/index.htm

and/or

Office of Communication, Training and
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Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Rockville, MD 20852-1448
http://www.fda.gov/cber/guidelines.htm.
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(Tel) 800-835-4709 or 301-827-1800

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

June 2008
ICH

Revision 2

TABLE OF CONTENTS

Contains Nonbinding Recommendations

Guidance for Industry[1]
Q3A Impurities in New Drug Substances

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION (1)

This document is intended to provide guidance for registration applications on the content and qualification of impurities in new drug substances produced by chemical syntheses and not previously registered in a region or member state. Impurities in new drug substances are addressed from two perspectives:

- Chemistry aspects include classification and identification of impurities, report generation, listing of impurities in specifications, and a brief discussion of analytical procedures

- Safety aspects include specific guidance for qualifying those impurities that were not present, or were present at substantially lower levels, in batches of a new drug substance used in safety and clinical studies.

This is the second revision of the Q3A guidance, which was published in 1996 and revised in 2003. In revision 2, Attachment 2 is retitled "Illustration of Reporting Impurity Results for Identification and Qualification in an Application" and includes clarifying information and an additional example.

[1] This guidance was developed within the Expert Working Group (Quality) of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and has been subject to consultation by the regulatory parties, in accordance with the ICH process. This document has been endorsed by the ICH Steering Committee at *Step 4* of the ICH process (October 2006). At *Step 4* of the process, the final draft is recommended for adoption to the regulatory bodies of the European Union, Japan, and the United States.

Arabic numbers reflect the organizational breakdown in the document endorsed by the ICH Steering Committee at Step 4 of the ICH process, October 2006.

This guidance is not intended to apply to new drug substances used during the clinical research stage of development. The following types of drug substances are not covered in this guidance:

- biological/biotechnological
- peptide
- oligonucleotide
- radiopharmaceutical
- fermentation products and semisynthetic products derived therefrom
- herbal products
- crude products of animal or plant origin

II. CLASSIFICATION OF IMPURITIES (2)

Impurities can be classified into the following categories:

- Organic impurities (process- and drug-related)
- Inorganic impurities
- Residual solvents

Organic impurities can arise during the manufacturing process and/or storage of the new drug substance. They can be identified or unidentified, volatile or nonvolatile, and include:

- Starting materials
- By-products
- Intermediates
- Degradation products
- Reagents, ligands, and catalysts

Inorganic impurities can result from the manufacturing process. They are normally known and identified and include:

- Reagents, ligands and catalysts
- Heavy metals or other residual metals
- Inorganic salts
- Other materials (e.g., filter aids, charcoal)

Solvents are inorganic or organic liquids used as vehicles for the preparation of solutions or suspensions in the synthesis of a new drug substance. Since these are generally of known toxicity, the selection of appropriate controls is easily accomplished (see ICH Q3C on Residual Solvents).

Excluded from this document are: (1) extraneous contaminants that should not occur in new drug substances and are more appropriately addressed as good manufacturing practice (GMP) issues, (2) polymorphic forms, and (3) enantiomeric impurities.

III. RATIONALE FOR THE REPORTING AND CONTROL OF IMPURITIES (3)

A. Organic Impurities (3.1)

The applicant should summarize the actual and potential impurities most likely to arise during the synthesis, purification, and storage of a new drug substance. This summary should be based on sound scientific appraisal of the chemical reactions involved in the synthesis, impurities associated with raw materials that could contribute to the impurity profile of the new drug substance, and possible degradation products. This discussion can be limited to those impurities that might reasonably be expected based on knowledge of the chemical reactions and conditions involved.

In addition, the applicant should summarize the laboratory studies conducted to detect impurities in the new drug substance. This summary should include test results of batches manufactured during the development process and batches from the proposed commercial process, as well as the results of stress testing (see ICH Q1A(R) on stability) used to identify potential impurities arising during storage. The impurity profile of the drug substance batches intended for marketing should be compared with those used in development, and any differences discussed.

The studies conducted to characterize the structure of actual impurities present in a new drug substance at a level greater than (>) the identification threshold given in Attachment 1 (e.g., calculated using the response factor of the drug substance) should be described. Note that any impurity at a level greater than (>) the identification threshold in any batch manufactured by the proposed commercial process should be identified. In addition, any degradation product observed in stability studies at recommended storage conditions at a level greater than (>) the identification threshold should be identified. When identification of an impurity is not feasible, a summary of the laboratory studies demonstrating the unsuccessful effort should be included in the application. Where attempts have been made to identify impurities present at levels of not more than (≤) the identification thresholds, it is useful also to report the results of these studies.

Identification of impurities present at an apparent level of not more than (≤) the identification threshold is generally not considered necessary. However, analytical procedures should be developed for those potential impurities that are expected to be unusually potent, producing toxic or pharmacological effects at a level not more than (≤) the identification threshold**.** All impurities should be qualified as described later in this guidance.

B. Inorganic Impurities (3.2)

Inorganic impurities are normally detected and quantified using pharmacopoeial or other appropriate procedures. Carry-over of catalysts to a new drug substance should be evaluated during development. The need for inclusion or exclusion of inorganic impurities in a new drug substance specification should be discussed. Acceptance criteria should be based on pharmacopoeial standards or known safety data.

C. Solvents (3.3)

The control of residues of the solvents used in the manufacturing process for a new drug substance should be discussed and presented according to ICH *Q3C Impurities: Residual Solvents*.

IV. ANALYTICAL PROCEDURES (4)

A registration application should include documented evidence that the analytical procedures are validated and suitable for the detection and quantification of impurities (see ICH Q2A and Q2B on analytical validation). Technical factors (e.g., manufacturing capability and control methodology) can be considered as part of the justification for selection of alternative thresholds based on manufacturing experience with the proposed commercial process. The use of two decimal places for thresholds (see Attachment 1) does not necessarily reflect the precision of the analytical procedure used for routine quality control purposes. Thus, the use of lower precision techniques (e.g., thin-layer chromatography) can be appropriate where justified and appropriately validated. Differences in the analytical procedures used during development and those proposed for the commercial product should be discussed in the registration application. The quantitation limit for the analytical procedure should be not more than (≤) the reporting threshold.

Organic impurity levels can be measured by a variety of techniques, including those that compare an analytical response for an impurity to that of an appropriate reference standard or to the response of the new drug substance itself. Reference standards used in the analytical procedures for control of impurities should be evaluated and characterized according to their intended uses. The drug substance can be used as a standard to estimate the levels of impurities. In cases where the response factors of a drug substance and the relevant impurity are not close, this practice can still be appropriate, provided a correction factor is applied or the impurities are, in fact, being overestimated. Acceptance criteria and analytical procedures used to estimate identified or unidentified impurities can be based on analytical assumptions (e.g., equivalent detector response). These assumptions should be discussed in registration applications.

V. REPORTING IMPURITY CONTENT OF BATCHES (5)

Analytical results should be provided in an application for all batches of a new drug substance used for clinical, safety, and stability testing, as well as for batches representative of the proposed commercial process. Quantitative results should be presented numerically, and not in general terms such as “complies” or “meets limit.” Any impurity at a level greater than (>) the reporting threshold (see Attachment 1) and total impurities observed in these batches of the new drug substance should be reported with the analytical procedures indicated. Below 1.0 percent, the results should be reported to two decimal places (e.g., 0.06 percent, 0.13 percent); at and above 1.0 percent, the results should be reported to one decimal place (e.g., 1.3 percent). Results should be rounded using conventional rules (see Attachment 2). A tabulation (e.g., spreadsheet)

of the data is recommended. Impurities should be designated by code number or by an appropriate descriptor (e.g., retention time). If a higher reporting threshold is proposed, it should be fully justified. All impurities at a level greater than (>) the reporting threshold should be summed and reported as total impurities.

When analytical procedures change during development, reported results should be linked to the procedure used, with appropriate validation information provided. Representative chromatograms should be provided. Chromatograms of representative batches from analytical validation studies showing separation and detectability of impurities (e.g., on spiked samples), along with any other impurity tests routinely performed, can serve as the representative impurity profiles. The applicant should ensure that complete impurity profiles (e.g., chromatograms) of individual batches are available, if requested.

A tabulation should be provided that links the specific new drug substance batch to each safety study and each clinical study in which the new drug substance has been used.
For each batch of the new drug substance, the report should include:

- Batch identity and size
- Date of manufacture
- Site of manufacture
- Manufacturing process
- Impurity content, individual and total
- Use of batches
- Reference to analytical procedure used

VI. LISTING OF IMPURITIES IN SPECIFICATIONS (6)

The specification for a new drug substance should include a list of impurities. Stability studies, chemical development studies, and routine batch analyses can be used to predict those impurities likely to occur in the commercial product. The selection of impurities in a new drug substance specification should be based on the impurities found in batches manufactured by the proposed commercial process. Those individual impurities with specific acceptance criteria included in the specification for a new drug substance are referred to as *specified impurities* in this guidance. Specified impurities can be identified or unidentified.

A rationale for the inclusion or exclusion of impurities in a specification should be presented. The rationale should include a discussion of the impurity profiles observed in the safety and clinical development batches, together with a consideration of the impurity profile of batches manufactured by the proposed commercial process. Specified identified impurities should be included along with specified unidentified impurities estimated to be present at a level greater than (>) the identification threshold given in Attachment 1. For impurities known to be unusually potent or to produce toxic or unexpected pharmacological effects, the quantitation/detection limit of the analytical procedures should be commensurate with the level at which the impurities should be controlled. For unidentified impurities, the procedure used and assumptions made in establishing the level of the impurity should be clearly stated. Specified, unidentified impurities

should be referred to by an appropriate qualitative analytical descriptive label (e.g., "unidentified A," "unidentified with relative retention of 0.9"). A general acceptance criterion of not more than (≤) the identification threshold (see Attachment 1) for any unspecified impurity and an acceptance criterion for total impurities should be included.

Acceptance criteria should be set no higher than the level that can be justified by safety data and should be consistent with the level achievable by the manufacturing process and the analytical capability. Where there is no safety concern, impurity acceptance criteria should be based on data generated on batches of a new drug substance manufactured by the proposed commercial process, allowing sufficient latitude to deal with normal manufacturing and analytical variation and the stability characteristics of the new drug substance. Although normal manufacturing variations are expected, significant variation in batch-to-batch impurity levels can indicate that the manufacturing process of the new drug substance is not adequately controlled and validated (see ICH Q6A guidance on specifications, Decision Tree #1, for establishing an acceptance criterion for a specified impurity in a new drug substance). The use of two decimal places for thresholds (see Attachment 1) does not necessarily indicate the precision of the acceptance criteria for specified impurities and total impurities.

In summary, a new drug substance specification should include, where applicable, the following list of impurities:

Organic Impurities
- Each specified identified impurity
- Each specified unidentified impurity
- Any unspecified impurity with an acceptance criterion of not more than (≤) the identification threshold
- Total impurities

Residual Solvents
Inorganic Impurities

VII. QUALIFICATION OF IMPURITIES (7)

Qualification is the process of acquiring and evaluating data that establishes the biological safety of an individual impurity or a given impurity profile at the level(s) specified. The applicant should provide a rationale for establishing impurity acceptance criteria that includes safety considerations. The level of any impurity present in a new drug substance that has been adequately tested in safety and/or clinical studies would be considered qualified. Impurities that are also significant metabolites present in animal and/or human studies are generally considered qualified. A level of a qualified impurity higher than that present in a new drug substance can also be justified based on an analysis of the actual amount of impurity administered in previous relevant safety studies.

If data are unavailable to qualify the proposed acceptance criterion of an impurity, studies to obtain such data can be appropriate when the usual qualification thresholds given in Attachment 1 are exceeded.

Higher or lower thresholds for qualification of impurities can be appropriate for some individual drugs based on scientific rationale and level of concern, including drug class effects and clinical experience. For example, qualification can be especially important when there is evidence that such impurities in certain drugs or therapeutic classes have previously been associated with adverse reactions in patients. In these instances, a lower qualification threshold can be appropriate. Conversely, a higher qualification threshold can be appropriate for individual drugs when the level of concern for safety is less than usual based on similar considerations (e.g., patient population, drug class effects, clinical considerations). Proposals for alternative thresholds would be considered on a case-by-case basis.

The "Decision Tree for Identification and Qualification" (see Attachment 3) describes considerations for the qualification of impurities when thresholds are exceeded. In some cases, decreasing the level of impurity to not more than the threshold can be simpler than providing safety data. Alternatively, adequate data could be available in the scientific literature to qualify an impurity. If neither is the case, additional safety testing should be considered. The studies considered appropriate to qualify an impurity will depend on a number of factors, including the patient population, daily dose, and route and duration of drug administration. Such studies can be conducted on the new drug substance containing the impurities to be controlled, although studies using isolated impurities can sometimes be appropriate.

Although this guidance is not intended to apply during the clinical research stage of development, in the later stages of development, the thresholds in this guidance can be useful in evaluating new impurities observed in drug substance batches prepared by the proposed commercial process. Any new impurity observed in later stages of development should be identified if its level is greater than (>) the identification threshold given in Attachment 1 (see the “Decision Tree for Identification and Qualification” in Attachment 3). Similarly, the qualification of the impurity should be considered if its level is greater than (>) the qualification threshold given in Attachment 1. Safety assessment studies to qualify an impurity should compare the new drug substance containing a representative amount of the new impurity with previously qualified material. Safety assessment studies using a sample of the isolated impurity can also be considered.

GLOSSARY

Chemical Development Studies: Studies conducted to scale-up, optimize, and validate the manufacturing process for a new drug substance

Enantiomeric Impurity: A compound with the same molecular formula as the drug substance that differs in the spatial arrangement of atoms within the molecule and is a non-superimposable mirror image

Extraneous Contaminant: An impurity arising from any source extraneous to the manufacturing process

Herbal Products: Medicinal products containing, exclusively, plant material and/or vegetable drug preparations as active ingredients. In some traditions, materials of inorganic or animal origin can also be present.

Identified Impurity: An impurity for which a structural characterization has been achieved

Identification Threshold: A limit above (>) which an impurity should be identified

Impurity: Any component of the new drug substance that is not the chemical entity defined as the new drug substance

Impurity Profile: A description of the identified and unidentified impurities present in a new drug substance

Intermediate: A material produced during steps of the synthesis of a new drug substance that undergoes further chemical transformation before it becomes a new drug substance

Ligand: An agent with a strong affinity to a metal ion

New Drug Substance: The designated therapeutic moiety that has not been previously registered in a region or member state (also referred to as a new molecular entity or new chemical entity). It can be a complex, simple ester, or salt of a previously approved drug substance.

Polymorphic Forms: Different crystalline forms of the same drug substance. These can include solvation or hydration products (also known as pseudo-polymorphs) and amorphous forms.

Potential Impurity: An impurity that theoretically can arise during manufacture or storage. It may or may not actually appear in the new drug substance.

Qualification: The process of acquiring and evaluating data that establishes the biological safety of an individual impurity or a given impurity profile at the level(s) specified

Qualification Threshold: A limit above (>) which an impurity should be qualified

Reagent: A substance other than a starting material, intermediate, or solvent that is used in the manufacture of a new drug substance

Reporting Threshold: A limit above (>) which an impurity should be reported. Reporting threshold is the same as reporting level in Q2B.

Solvent: An inorganic or an organic liquid used as a vehicle for the preparation of solutions or suspensions in the synthesis of a new drug substance

Specified Impurity: An impurity that is individually listed and limited with a specific acceptance criterion in the new drug substance specification. A specified impurity can be either identified or unidentified.

Starting Material: A material used in the synthesis of a new drug substance that is incorporated as an element into the structure of an intermediate and/or of the new drug substance. Starting materials are normally commercially available and of defined chemical and physical properties and structure.

Unidentified Impurity: An impurity for which a structural characterization has not been achieved and that is defined solely by qualitative analytical properties (e.g., chromatographic retention time)

Unspecified Impurity: An impurity that is limited by a general acceptance criterion, but not individually listed with its own specific acceptance criterion, in the new drug substance specification

ATTACHMENT 1: THRESHOLDS

Maximum Daily Dose[1]	Reporting Threshold[2,3]	Identification Threshold[3]	Qualification Threshold[3]
≤ 2g/day	0.05%	0.10% or 1.0 mg per day intake (whichever is lower)	0.15% or 1.0 mg per day intake (whichever is lower)
> 2g/day	0.03%	0.05%	0.05%

[1] The amount of drug substance administered per day
[2] Higher reporting thresholds should be scientifically justified
[3] Lower thresholds can be appropriate if the impurity is unusually toxic

ATTACHMENT 2: ILLUSTRATION OF REPORTING IMPURITY RESULTS FOR IDENTIFICATION AND QUALIFICATION IN AN APPLICATION

The attachment is only illustrative and is not intended to serve as a template for how results on impurities should be presented in an application file. Normally, raw data are not presented.

Example 1: **0.5 g Maximum Daily Dose**
Reporting threshold = 0.05%
Identification threshold = 0.10%
Qualification threshold = 0.15%

"Raw" Result (%)	Reported Result (%) Reporting threshold =0.05%	Calculated Total Daily Intake (TDI) (mg) of the impurity (rounded result in mg)	Action	
			Identification (Threshold 0.10% exceeded?)	Qualification (Threshold 0.15% exceeded?)
0.044	Not reported	0.2	None	None
0.0963	0.10	0.5	None	None
0.12	0.12[1)]	0.6	Yes	None[1]
0.1649	0.16[1)]	0.8	Yes	Yes[1]

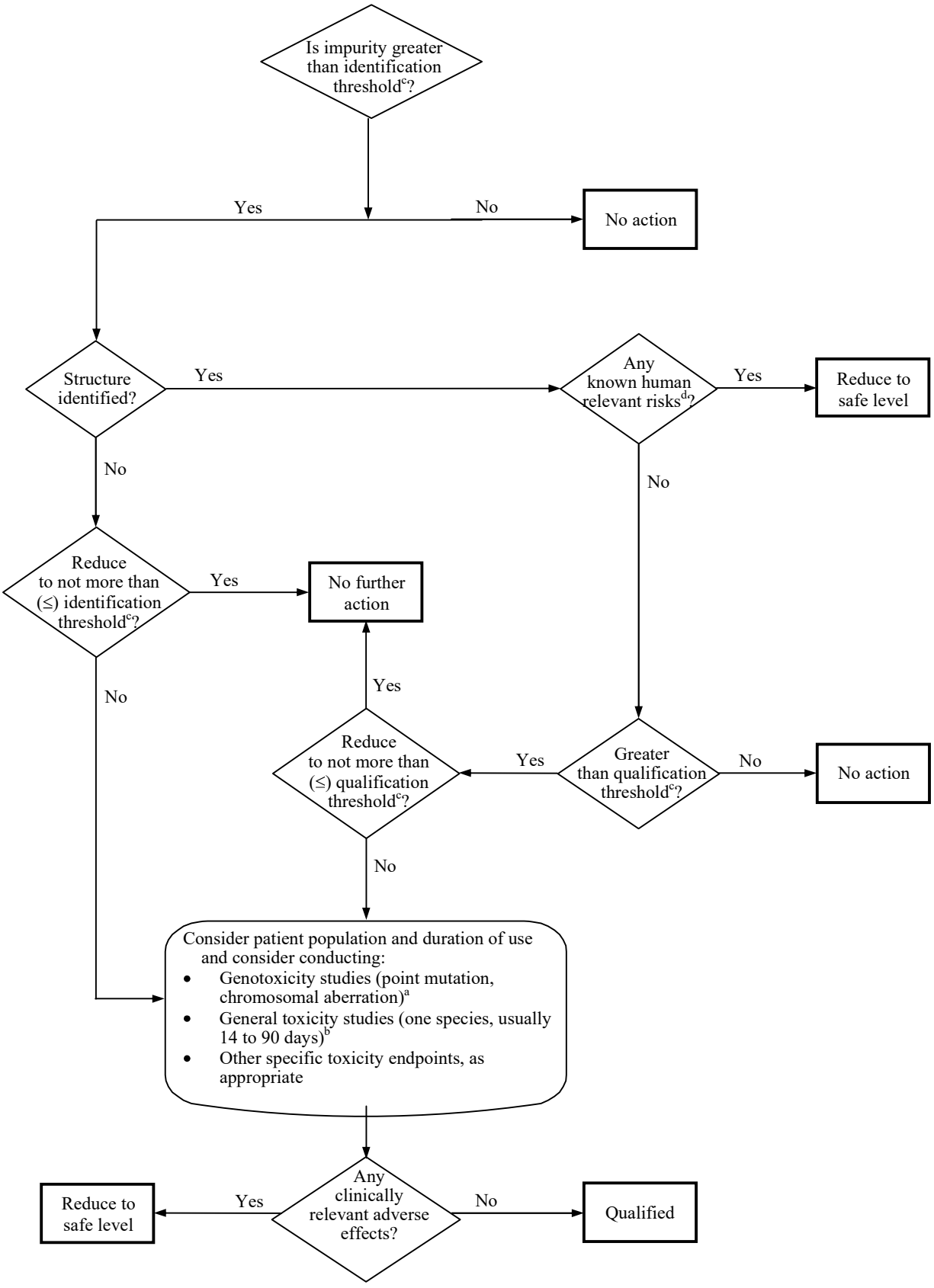
Example 2: **0.8 g Maximum Daily Dose**
Reporting threshold = 0.05%
Identification threshold = 0.10%
Qualification threshold = 1.0 mg TDI

"Raw" Result (%)	Reported Result (%) Reporting threshold =0.05%	Calculated Total Daily Intake (TDI) (mg) of the impurity (rounded result in mg)	Action	
			Identification (Threshold 0.10% exceeded?)	Qualification (Threshold 1.0 mg TDI exceeded?)
0.066	0.07	0.6	None	None
0.124	0.12	1.0	Yes	None[1, 2]
0.143	0.14	1.1	Yes	Yes[1]

[1] After identification, if the response factor is determined to differ significantly from the original assumptions, it may be appropriate to remeasure the actual amount of the impurity present and reevaluate against the qualification threshold (see Attachment 1).

[2] To verify if a threshold is exceeded, a reported result should be evaluated against the thresholds as follows: When the threshold is described in %, the reported result rounded to the same decimal place as the threshold should be compared directly to the threshold. When the threshold is described in TDI, the reported result should be converted to TDI, rounded to the same decimal place as the threshold, and compared to the threshold. For example, the amount of impurity at 0.12% level corresponds to a TDI of 0.96 mg (absolute amount), which is then rounded up to 1.0 mg; so the qualification threshold expressed in TDI (1.0 mg) is not exceeded.

ATTACHMENT 3: DECISION TREE FOR IDENTIFICATION AND QUALIFICATION



Notes on Attachment 3

a) If considered desirable, a minimum screen (e.g., genotoxic potential) should be conducted. A study to detect point mutations and one to detect chromosomal aberrations, both in vitro, are considered an appropriate minimum screen.

b) If general toxicity studies are desirable, one or more studies should be designed to allow comparison of unqualified to qualified material. The study duration should be based on available relevant information and performed in the species most likely to maximize the potential to detect the toxicity of an impurity. On a case-by-case basis, single-dose studies can be appropriate, especially for single-dose drugs. In general, a minimum duration of 14 days and a maximum duration of 90 days would be considered appropriate.

c) Lower thresholds can be appropriate if the impurity is unusually toxic.

d) For example, do known safety data for this impurity or its structural class preclude human exposure at the concentration present?

Exhibit 4

Guidance for Industry

ANDAs: Impurities in Drug Substances

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
November 1999
OGD #

Guidance for Industry

ANDAs: Impurities in Drug Substances

Additional copies are available from:

Office of Training and Communications
Division of Communications Management
Drug Information Branch, HFD-210
Center for Drug Evaluation and Research (CDER)
5600 Fishers Lane
Rockville, Maryland 20857
(Tel) 301-827-4573
(Internet) http://www.fda.gov/cder/guidance/index.htm

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
November 1999
OGD #

TABLE OF CONTENTS

GUIDANCE FOR INDUSTRY[1]

ANDAs: Impurities in Drug Substances

I. INTRODUCTION

This guidance provides recommendations for including information in abbreviated new drug applications (ANDAs) and supporting drug master files (DMFs) on the identification and qualification of impurities in drug substances produced by chemical syntheses for both monograph and nonmonograph drug substances.

Impurities in drug substances are addressed from two perspectives:

- Chemistry aspects, including classification and identification of impurities, generating reports, setting specifications, and a brief discussion of analytical procedures; and

- Safety aspects, including comparative studies and genotoxicity testing.

Specific guidance is provided for:

- Qualifying impurities found in a drug substance used in an ANDA by a comparison with impurities found in the related *U.S. Pharmacopeia* (USP) monograph, scientific literature, or innovator material;

- Qualifying impurities found at higher levels in a drug substance used in an ANDA than found in the related USP monograph, scientific literature, or innovator material;

- Qualifying impurities in a drug substance used in an ANDA that are **not** found in the related USP monograph, scientific literature, or innovator material; and

[1] This guidance has been prepared under the direction of the Chemistry, Manufacturing, and Controls Coordinating Committee (CMC CC) in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration. This guidance document represents the Agency's current thinking on the review of impurities in drug substances used in generic drug products. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes, regulations, or both.

- Threshold levels below which qualification is not needed.

This guidance is not applicable to biological/biotechnological, peptide, oligonucleotide, radiopharmaceutical, fermentation and semisynthetic products derived therefrom, herbal products, or crude products of animal or plant origin. The recommendations in this guidance are effective on publication and should be followed in preparing new applications and supplements for changes in drug substance synthesis or process. However, if the information in a drug substance DMF cited in such an ANDA or ANDA supplement has been reviewed prior to the publication of this final guidance, this guidance does not apply.

This guidance is intended to be a companion document to the International Conference on Harmonization (ICH) guidance *Q3A Impurities in New Drug Substances*.[2] The ICH Q3A guidance was published in the *Federal Register* on January 4, 1996 (61 FR 371), and issued as a Center for Drug Evaluation and Research (CDER) guidance. ICH Q3A provides recommendations for (1) inclusion of information regarding specified impurities in certain new drug applications (NDAs) (identified and unidentified impurities in new drug substance specifications) and (2) qualification of impurities (the process of acquiring and evaluating data that establishes the biological safety of individual impurities or a given impurity profile at the levels specified). Generic drugs are not covered by ICH Q3A; however, many of the recommendations in ICH Q3A are applicable to drug substances used in generic drug products. To provide, to the extent possible, comparable processes for new and generic drug review, this guidance was developed using the ICH Q3A framework.

At a meeting held June 22, 1993, an FDA Ad Hoc Advisory Committee recommended that there should be a 0.1 percent threshold above which isolation and characterization of individual impurities should apply to chemically synthesized drug substances including drug substances used in generic drug products. For compendial materials, the USP 23 in *General Notices and Requirements* (p. 7) states that it is manifestly impossible to include in each monograph a test for every impurity that may arise from a change in the source of material or a change in processing. Consequently, few USP monographs have acceptance criteria for individually identified impurities. However, USP has adopted a 0.1 percent threshold for impurity identification via the publication of *Other Impurities* in *General Notices and Requirements* (Sixth Supplement, p. 3636), which became official on November 15, 1996.

II. CLASSIFICATION OF IMPURITIES

Impurities can be classified into the following categories:

[2] *New drug substance* is defined in the Glossary.

- Organic Impurities (Process and Drug Related)
- Inorganic Impurities
- Residual Solvents

Organic impurities may arise during the manufacturing process and/or storage of the drug substance. They may be identified or unidentified, volatile or nonvolatile, and include:

- Starting materials
- By-products
- Intermediates
- Degradation products
- Reagents, ligands, and catalysts

Inorganic impurities may derive from the manufacturing process. They are normally known and identified and include:

- Reagents, ligands, and catalysts
- Heavy metals
- Inorganic salts
- Other materials (e.g., filter aids, charcoal)

Residual solvents are organic or inorganic liquids used during the manufacturing process. Because these are generally of known toxicity, the selection of appropriate controls is easily accomplished.

Excluded from this document are (1) extraneous contaminants, which should not occur in drug substances and are more appropriately addressed as good manufacturing practice issues; (2) polymorphic form, a solid state property of the drug substance; and (3) enantiomeric impurities.

III. RATIONALE FOR THE REPORTING AND CONTROL OF IMPURITIES

A. Organic Impurities

The DMF holder or the ANDA applicant should summarize those actual and potential impurities most likely to arise during the synthesis, purification, and storage of the drug substance. This summary should be based on sound scientific appraisal of the chemical reactions involved in the synthesis, impurities associated with raw materials that could contribute to the impurity profile of the drug substance, and possible degradation products. This discussion may include only those impurities that may reasonably be expected based on knowledge of the chemical reactions and conditions involved.

In addition, the DMF holder or the ANDA applicant should summarize the laboratory studies conducted to detect impurities in the drug substance. This summary should include test results of materials manufactured during the development process and batches from the proposed commercial process, as well as results of intentional degradation studies used to identify potential impurities that arise during storage. Assessment of the proposed commercial process may be deferred until the first batch is produced for marketing. The impurity profile of the drug substance lots intended for marketing should be compared with those used in development and any differences discussed.

The studies (e.g., NMR, IR, and MS) conducted to characterize the structure of actual impurities present in the drug substance at or above an apparent level of 0.1 percent (e.g., calculated using the response factor of the drug substance) should be described. All recurring impurities at or above an apparent level of 0.1 percent (see section IV) in batches manufactured by the proposed commercial process should be identified. Degradation products observed in stability studies at recommended storage conditions should be similarly identified. When identification of an impurity is infeasible, a summary of the laboratory studies demonstrating the unsuccessful effort should be included in the DMF or application. Where attempts have been made to identify impurities below the 0.1 percent level, it is useful also to report the results of these studies.

Identification of impurities below apparent levels of 0.1 percent is generally not considered necessary. However, identification should be attempted for those potential impurities that are expected to be unusually potent, producing toxic or pharmacologic effects at a level lower than 0.1 percent. In all cases, impurities should be qualified as described later in this guidance. Although it is common practice to round analytical results of between 0.05 and 0.09 percent to the nearest number (i.e., 0.1 percent), for the purpose of this guidance, such values should not be rounded to 0.1 percent in determining whether to identify the impurities.

B. Inorganic Impurities

Inorganic impurities are normally detected and quantitated using pharmacopeial or other appropriate procedures. Carryover of catalysts to the drug substance should be evaluated during development. The necessity for inclusion or exclusion of inorganic impurities in the drug substance specifications should be discussed. Acceptance criteria should be based on pharmacopeial standards or known safety data.

C. Residual Solvents

The control of residues of solvents used in the manufacturing process for the drug substance should be discussed. Any solvents that may appear in the drug substance should be quantified

using analytical procedures with an appropriate level of sensitivity. Pharmacopeial or other appropriate procedures should be used. Acceptance criteria should be based on pharmacopeial standards or known safety data, taking into consideration dose, duration of treatment, and route of administration. Particular attention should be given to quantitation of toxic solvents used in the manufacturing process as described in the ICH guidance *Q3C Impurities: Residual Solvents.*

IV. ANALYTICAL PROCEDURES

The DMF or abbreviated application should include documented evidence that the analytical procedures are validated and suitable for the detection and quantitation of impurities. Differences in the analytical procedures used during development and proposed for the commercial product should be discussed in the DMF or abbreviated application.

Organic impurity levels can be measured by a variety of techniques, including those that compare an analytical response for an impurity to that of an appropriate reference standard or to the response of the drug substance itself. Reference standards used in the analytical procedures for control of impurities should be evaluated and characterized according to their intended uses. It is considered acceptable to use the drug substance to estimate the levels of impurities when the response factors of the drug substance and impurities are close. In cases where the response factors are not close, this practice may still be acceptable, provided a correction factor is applied or the impurities are, in fact, being overestimated. Analytical procedures used to estimate identified or unidentified impurities are often based on analytical assumptions (e.g., equivalent detector response). These assumptions should be discussed in the DMF submission or abbreviated application.

V. REPORTING IMPURITY CONTENT OF BATCHES

Analytical results should be provided for all batches of the drug substance used for stability testing, as well as for batches representative of the proposed commercial process. The content of individual impurities, both identified and unidentified, and total impurities observed in these batches of the drug substance should be reported with the analytical procedures indicated. A tabulation (e.g., spreadsheet) of the data is recommended. Impurities should be designated by code number or by an appropriate descriptor, for example, name or retention time. Levels of impurities that are present but are below the validated limit of quantitation (LOQ) need not be reported.

If analytical procedures change during development, reported results should be linked with the procedure used, and appropriate validation information should be provided. Representative chromatograms should be provided. Chromatograms of such representative batches, from methods

validation studies showing separation and detectability of impurities (e.g., on spiked samples), along with any other impurity tests routinely performed, can serve as the representative impurity profiles. The ANDA applicant or DMF holder should ensure that complete impurity profiles (i.e., chromatograms) of stability batches are available if requested. A tabulation should be provided comparing impurity levels between stability and other batches.

For each batch of the drug substance, the report should include:

- Batch identity and size
- Date of manufacture
- Site of manufacture
- Manufacturing process
- Impurity content, individual and total
- Use of batches
- Reference to analytical procedures used

VI. ACCEPTANCE CRITERIA FOR IMPURITIES

The specification for a drug substance should include acceptance criteria for impurities. Stability studies, chemical development studies, and routine batch analyses can be used to predict those impurities likely to occur in the commercial product. The selection of impurities to include in the drug substance specification should be based on the impurities found in the batches manufactured by the proposed commercial process. Those impurities selected for inclusion in the specification for the drug substance are referred to as *specified impurities* in this guidance. Specified impurities may be identified or unidentified and should be individually listed in the drug substance specification (see below).

A rationale for the inclusion or exclusion of impurities in the specification should be presented. This rationale should include a discussion of the impurity profiles observed in batches under consideration, together with a consideration of the impurity profile of material manufactured by the proposed commercial process. Specific identified impurities should be included along with recurring unidentified impurities estimated to be at or above 0.1 percent. For impurities known to be unusually potent or to produce toxic or unexpected pharmacological effects, the quantitation and/or detection limit of the analytical methods should be commensurate with the level at which the impurities need to be controlled. For unidentified impurities, the procedure used and assumptions made in establishing the level of the impurity should be clearly stated. Unidentified impurities included in the specification should be referred to by some appropriate qualitative analytical descriptive label (e.g., "unidentified A," "unidentified with relative retention of 0.9"). Finally, a general acceptance criteria of not more than 0.1 percent for any unspecified impurity should be included.

Acceptance criteria should be set no higher than the level that can be justified (see the Impurities Decision Tree for generic drug substances, Attachment I) either by comparative studies or genotoxicity studies, and unless such data indicate otherwise, no lower than the level achievable by the manufacturing process and the analytical capability. In other words, where there is no safety concern, impurity acceptance criteria should be based on data generated on actual batches of the drug substance, allowing sufficient latitude to deal with normal manufacturing and analytical variation, and the stability characteristics of the drug substance. Although normal manufacturing variations are expected, significant variation in batch-to-batch impurity levels could indicate that the manufacturing process of the drug substance is not adequately controlled and validated.

In summary, the drug substance acceptance criteria should include, where applicable, acceptance criteria for:

- **Organic Impurities:**
  - Each specified identified impurity
  - Each specified unidentified impurity at or above 0.1 percent
  - Any unspecified impurity, with a limit of not more than 0.1 percent
  - Total impurities
- **Residual Solvents**
- **Inorganic Impurities**

A summation of assay value and impurity levels generally may be used to obtain mass balance for the test sample. The mass balance need not add to exactly 100 percent because of the analytical error associated with each analytical procedure. The summation of impurity levels plus the assay value may be misleading, for example, when the assay procedure is nonspecific (e.g., potentiometric titrimetry) and the impurity level is relatively high.

VII. QUALIFICATION OF IMPURITIES

Qualification is the process of acquiring and evaluating data that establishes the biological safety of an individual impurity or a given impurity profile at the levels specified. The DMF holder or the ANDA applicant should provide a rationale for selecting impurity acceptance criteria based on safety considerations. The level of any impurity present in a drug substance that is in compliance with a USP specification or has been adequately evaluated in comparative or in vitro genotoxicity studies or has been evaluated via an acceptable *Quantitative Structure Activity Relationships* (QSAR) database

program is considered qualified for ANDAs. Impurities that are also significant metabolites do not need further qualification.

If data are unavailable to qualify the proposed acceptance criteria of an impurity, studies to obtain such data may be needed when the usual qualification threshold levels given below are exceeded:

Maximum Daily Dose	**Qualification Threshold**
#2g/day	0.1 percent or 1 mg per day intake (whichever is lower)
>2g/day	0.05 percent

Higher or lower threshold levels for qualification of impurities may be appropriate for some individual drugs based on scientific rationale and level of concern, including drug class effects. For example, qualification may be especially important when there is evidence that such impurities in certain drugs or therapeutic classes have previously been associated with adverse reactions in patients. In these instances, a lower qualification threshold level may be appropriate. Technical factors (manufacturing capability and control methodology) may be considered as part of the justification for selection of alternative threshold levels. Proposals from applicants for alternative threshold levels will be considered by the FDA on a case-by-case basis.

The Impurities Decision Tree for generic drug substances (Attachment I) describes considerations for the qualification of impurities when thresholds are exceeded. In some cases, decreasing the level of impurity below the threshold, rather than providing additional data, may be the simplest course of action. Alternatively, adequate data may be available in the scientific literature to qualify an impurity. The studies that should be performed to qualify an impurity will depend on a number of factors, including the patient population, daily dose, and route and duration of drug administration. Such studies are normally conducted on the drug substance containing the impurities to be controlled, although studies using isolated impurities are acceptable.

Levels L1 through L4 are recommendations for the type of information that would be considered to provide assurance that the impurity in question is "innocuous by virtue of having no significant, undesirable biological activity in the amounts present" (see USP <1086> *Impurities in Official Articles*). Only in Level L5, where concern regarding possible toxicity is indicated, is additional testing recommended (e.g., by a battery of in vitro genotoxicity tests).

Level L6 would be for those rare instances where an impurity has not been qualified. In such cases, the ANDA would then fall outside the purview of section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act).

Additional clarification regarding the levels in the Impurities Decision Tree for generic drug substances is provided below:

- First level (L1): Is the impurity in question "above threshold"? See the threshold table in section VII. This level is identical to the corresponding level in the ICH Decision Tree for Safety Studies (Attachment II).

- Second Level (L2): Is the "structure elucidated"? This refers to structural identification or characterization exactly as in the ICH Decision Tree for Safety Studies. However, in those rare cases where it is not possible to identify the impurity by structure, the efforts made should be satisfactorily documented. Once the impurity has been structurally identified, one could go to level L3.

- Third Level (L3a): Compliance with a USP acceptance criterion for a known individual impurity (e.g., see impurity listed in the Clidinium Bromide USP monograph).

  Third Level (L3b): A comparison of the impurity profile of the generic drug substance with the process impurities profile on an average of three or more different lots of the innovator's drug product is recommended. This comparative study should be performed using appropriate discriminating analytical tests such as HPLC or Capillary Electrophoresis. The impurity is qualified if it is found at similar levels (no more than twofold higher, but not to exceed 1.0% for most drug substances). Twofold higher criteria are justified for several reasons. For example, the innovators' impurity acceptance criteria are set higher than levels observed in drug substances, and the safety studies that qualified the innovators' drug substances are carried out at significantly higher levels than the specifications agreed to under FDA's pharmacology and toxicology evaluations. In certain dosage forms where sensitivity or toxicity concerns arise, the impurity levels should be no higher than the innovator's level for toxic impurities. In generic drugs, an unidentified impurity may still be considered qualified in cases where the impurity is observed at similar levels in the innovator's product via a comparative study.

  Third Level (L3c): This level looks at an impurity at a "higher level, or a different new impurity." *New* means one that was not previously seen in the bulk drug substance. The level of the new impurity may be qualified from the scientific literature if it is substantiated that this impurity is an *ordinary impurity* (see USP <1086>) at the levels used. The scientific literature would include recognized scientific publications. Alternatively, the new impurity may be qualified by lowering

it to below the ICH threshold level, or by following the next level in the Impurities Decision Tree for generic drug substances.

! Fourth Level (L4): Is the impurity "related to others with known toxicity"? As one approach, the use of a *Quantitative Structure Activity Relationships* (QSAR) database program may be helpful in identifying whether an impurity is related to others of known toxicity. The use of such a program is acceptable to the Office of Generic Drugs (OGD). Modules currently recommended are: *Rodent Carcinogenicity, Developmental Toxicity Potential, Ames Mutagenicity* (five strains), and for topicals, *Skin Sensitization*.

If no potential for concern is indicated by QSAR evaluation, the impurity is considered qualified, but it should not exceed a level of 0.5 percent or 500 micrograms per day, whichever is less (equivalent to 0.5 percent of 100 mg of a drug substance), without other supporting data (such as genotoxicity test data). A determination to accept the QSAR data will be made on a case-by-case basis, taking into consideration the therapeutic use of the drug product, its intended duration of administration, and the results of the QSAR analysis.

However, if the QSAR evaluation does not provide sufficient information because the program cannot perform the evaluation due to the lack of relevant information in the database, the manufacturer should lower the impurity level to below the ICH threshold or qualify the new impurity at the L5 level.

! Fifth Level (L5): This level describes evaluation of the toxicity of an impurity via a battery of in vitro genotoxicity tests (see the ICH Decision Tree for Safety Studies regarding genotoxicity studies). If the result of genotoxicity testing raises a concern, the need for additional toxicity testing will be evaluated on a case-by-case basis. Factors to be considered include the therapeutic use of the drug product, its intended duration of use, and results of the QSAR analysis. However, even in those cases where no potential for concern is indicated by the genotoxicity testing, the necessity for further toxicity testing should be evaluated if the impurity level exceeds either 1 percent of the drug substance or 1 mg/day, whichever is lower, at the human therapeutic dose of the drug product.

If toxicity issues are confirmed by these in vitro tests, the DMF holder or ANDA applicant may either purify the drug substance to reduce the impurity to a level below the ICH threshold or go to the next level (L6) in the Impurities Decision Tree for generic drug substances.

! Sixth Level (L6): This level involves qualification of the impurity "by general toxicity testing" (see Attachment II, items 2 and 3). If this pathway is used, the ANDA would fall under section 505(b) of the Act. General toxicity testing involves animal testing, thus an application would not be deemed acceptable by OGD under section 505(j) of the Act. The drug substance

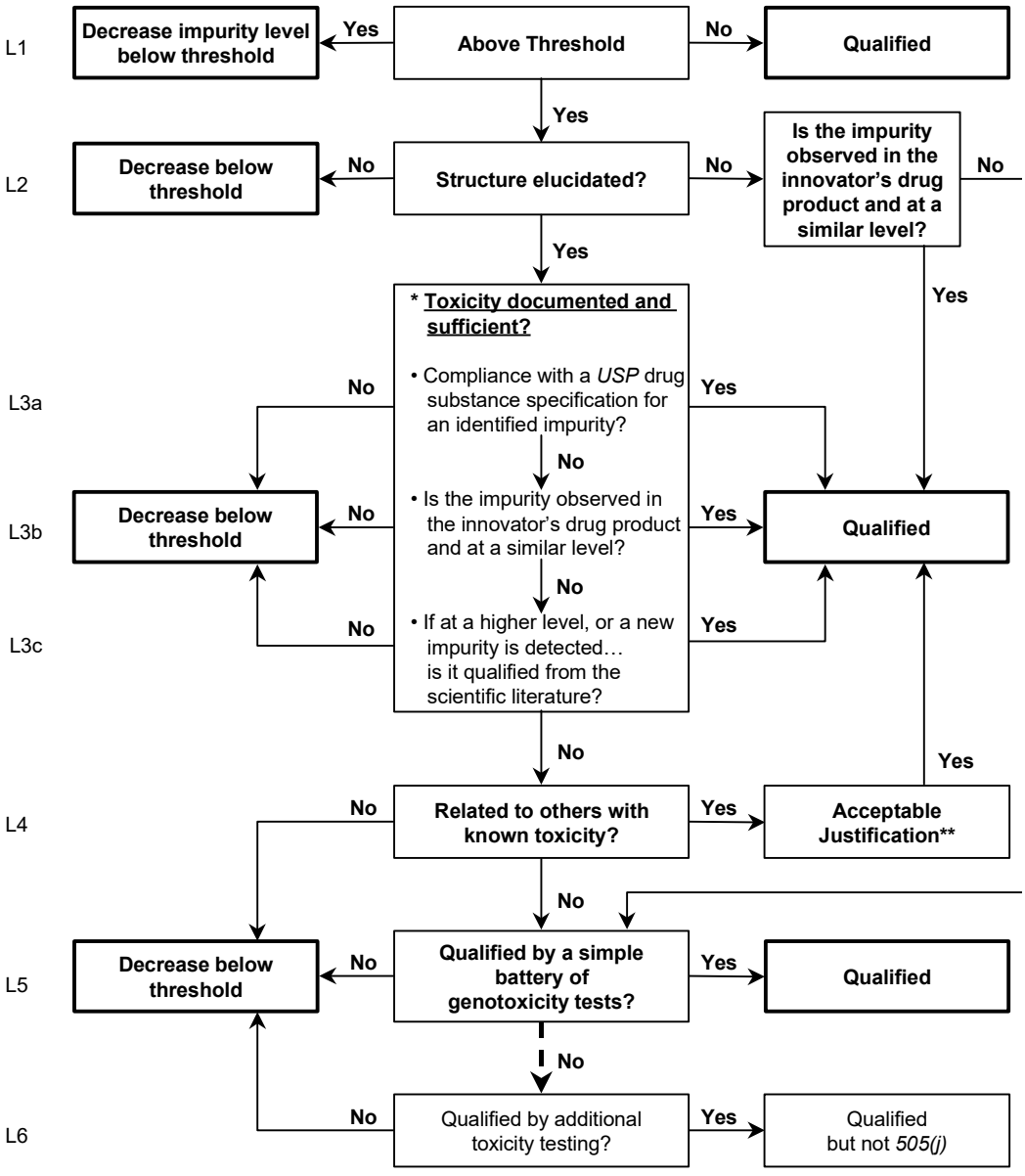
manufacturer as well as the ANDA applicant should be cognizant of this issue before the ANDA applicant commits to extensive studies with the bulk drug substance.

VIII. NEW IMPURITIES

During the course of a drug development program, the qualitative impurity profile of the drug substance may change or a new impurity may appear, for example, as a result of synthetic route changes, process optimization, or scale-up. New impurities may be identified or unidentified. Such changes call for consideration of the need for qualification of the level of the impurity unless it is below the threshold values as noted above. When a new impurity exceeds the threshold, the Impurities Decision Tree for generic drug substances (Attachment I) should be consulted. Studies should compare the drug substances containing a representative level of the new impurity with previously qualified material, although studies using the isolated impurity are also acceptable.

ATTACHMENT I

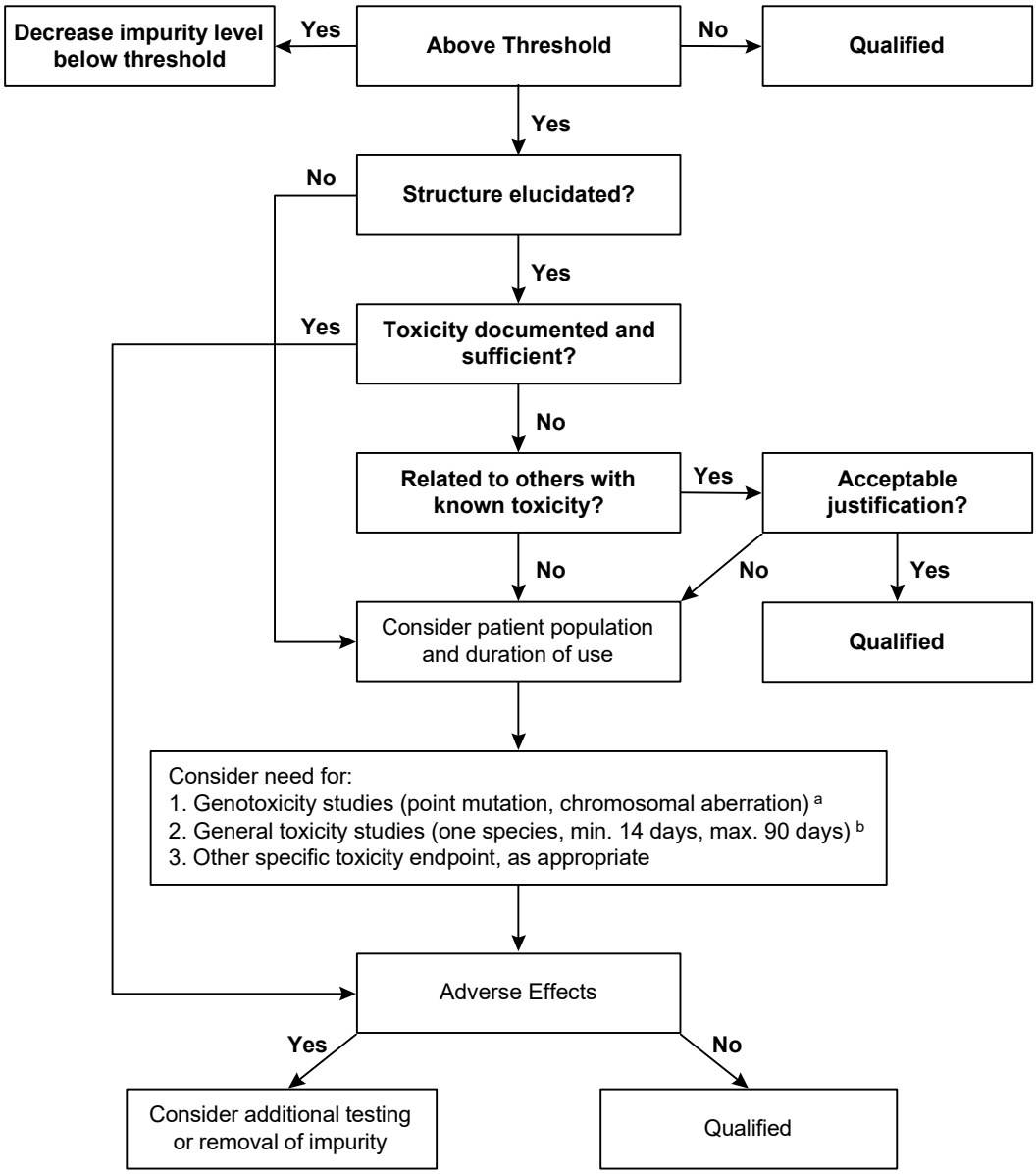
Impurities Decision Tree
(Generic Drug Substance)



* Generic Drug Pathway
** e.g., qualified by QSAR

Attachment II

ICH Decision Tree for Safety Studies



[a] If considered desirable, a minimum screen for genotoxic potential should be conducted. A study to detect point mutations and one to detect chromosomal aberrations, both in vitro, are seen as an acceptable minimum screen.

[b] For NDAs, if general toxicity studies are desirable, study(ies) should be designed to allow comparison of unqualified to qualified material. The study duration should be based on available relevant information and performed in the species most likely to maximize the potential to detect the toxicity of an impurity. In general, a minimum duration of 14 days and a maximum duration of 90 days will be acceptable.

ATTACHMENT III

Glossary

Acceptance Criteria: Numerical limits, ranges, or other suitable measures for acceptance of the results of analytical procedures

Chemical Development Studies: Studies conducted to scale-up, optimize, and validate the manufacturing process for a drug substance

Drug Substance: The designated therapeutic moiety. See also the definition in 21 CFR 314.3.

Enantiomers: Compounds with the same molecular formula as the drug substance, which differ in the spatial arrangement of atoms within the molecule and are nonsuperimposable mirror images

Extraneous Substance: An impurity arising from any source extraneous to the manufacturing process

Genotoxicity Tests: Genotoxicity tests can be defined as in vitro tests designed to detect compounds that induce genetic damage directly or indirectly by various mechanisms. Compounds that are positive in tests that detect such kinds of genetic damage have potential to be human carcinogens and/or mutagens (i.e., may induce cancer and/or heritable damage).

Herbal Products: Medicinal products containing, exclusively, plant material and/or vegetable drug preparations as active ingredients. In some traditions, materials of inorganic or animal origin may also be present.

Identified Impurity: An impurity for which a structural characterization has been achieved

Impurity: Any component of the drug substance that is not the chemical entity defined as the drug substance

Impurity Profile: A description of the identified and unidentified impurities present in a drug substance

Intermediate: A material produced during steps of the synthesis of a drug substance that must undergo further molecular change before it becomes the drug substance

Ligand: An agent with a strong affinity to a metal ion

Mass Balance: The process of adding together the assay value and levels of degradation products to see how closely these add up to 100 percent of the initial value, with due consideration of the margin of analytical precision

New Drug Substance: The designated therapeutic moiety that has not been previously registered in a region or member state (also referred to as a new molecular entity or new chemical entity). It can be a complex, simple ester, or salt of a previously approved drug substance.

Polymorphism: The occurrence of different crystalline forms of the same drug substance

Potential Impurity: An impurity that, from theoretical considerations, may arise from or during manufacture. It may or may not actually appear in the drug substance.

Qualification: The process of acquiring and evaluating data that establishes the biological safety of an individual impurity or a given impurity profile at the levels specified

Quantitative Structure Activity Relationship (QSAR): Used for rationalization and prediction of in vivo mammalian toxicity of chemicals on the basis of their overall and/or local properties, as defined by their chemical structure and evaluated by using an appropriate database and modules

Reagent: A substance, other than a starting material or solvent, used in the manufacture of a drug substance

Safety Information: The body of information that establishes the biological safety of an individual impurity or a given impurity profile at the levels specified

Solvent: An inorganic or an organic liquid used as a vehicle for the preparation of solutions or suspensions in the synthesis of a drug substance

Specification: A list of tests, references to analytical procedures, and appropriate acceptance criteria that are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which a drug substance or drug product should conform to be considered acceptable for its intended use. *Conformance to specifications* means that the drug substance and/or drug product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria. Specifications are binding quality standards that are agreed to between the appropriate governmental regulatory agency and the applicant.

Specified Impurity: An identified or unidentified impurity that is selected for inclusion in the drug substance specifications and is individually listed and limited to ensure the safety and quality of the drug substance

Starting Material: A material used in the synthesis of a drug substance that is incorporated as an element into the structure of an intermediate and/or of the drug substance. Starting materials normally are commercially available and of defined chemical and physical properties and structure.

Toxic Impurity: Impurities having significant undesirable biological activity

Unidentified Impurity: An impurity that is defined solely by qualitative analytical properties (e.g., chromatographic retention time)

Validated Limit of Quantitation: For impurities at a level of 0.1 percent, the validated limit of quantitation should be less than or equal to 0.05 percent. Impurities limited at higher levels may have higher limits of quantitation.

Exhibit 5

Prescription Drug Advertising | Questions and Answers

These are some frequently asked questions about direct-to-consumer (DTC) advertising. FDA requirements, as well as activities of the Office of Prescription Drug Promotion (OPDP), are shown in this section. Contact us (/about-fda/about-center-drug-evaluation-and-research/contact-opdp) if you have any additional questions.

- Does the FDA control advertisements for all drugs?
- Does the FDA review and approve all advertisements for drugs before their release?
- Does Federal law ban ads for drugs that have serious risks?
- Does the FDA require drug companies to use hard-to-understand medical language in ads directed to consumers?
- Can the FDA limit the amount of money spent on prescription drug ads?
- Does the FDA work with drug companies to create prescription drug ads?
- Does the FDA approve ads for prescription drugs before they are seen by the public?
- What must product claim ads tell you?
- What are ads not required to tell you?
- How do the "brief summary," "prescribing information," "major statement," and "adequate provision" differ?
- Does the law say anything about the design of ads for prescription drugs?
- Has FDA done research on DTC advertising?
- How can an ad violate the law?
- Who should I tell if I think that a prescription drug ad violates the law?
- What does FDA do if it determines that an ad violates the law?
- How can I learn more about a medical condition or a drug?

Does the FDA control advertisements for all drugs?

- No. The FDA *does not* oversee the advertising of over-the-counter (OTC) drugs. The Federal Trade Commission (FTC) is responsible for regulating OTC drug ads. The FDA regulates advertising only for prescription drugs. We also oversee the advertising for certain kinds of medical devices, such as hearing aids, the lasers used in LASIK procedures, and contact lenses.

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Does the FDA review and approve all advertisements for drugs before their release?

- No. In most cases, federal law does not allow the FDA to require that drug companies submit ads for approval before the ads are used. We see many ads at about the same time the public sees them. Many drug companies voluntarily seek advice from us before they release TV ads. However, if we believe that an ad violates the law, we send a letter to the drug company asking that the ads be stopped right away.

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Does Federal law ban ads for drugs that have serious risks?

- No. Federal law does not bar drug companies from advertising any kind of prescription drugs, even ones that can cause severe injury, addiction, or withdrawal effects. However, companies cannot use reminder ads (/drugs/prescription-drug-advertising/reminder-ad-correct) for drugs with certain serious risks (drugs with "boxed warnings" (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#boxed_warning)).

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Does the FDA require drug companies to use hard-to-understand

medical language in ads directed to consumers?

- No. We encourage drug companies to use language that is clear and understandable to the general public. The law requires that all risks be communicated. However, it is sometimes difficult to express scientific and medical language in simpler terms without changing the meaning.

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Can the FDA limit the amount of money spent on prescription drug ads?

- No. We do not have any authority to affect the amount of money drug companies spend on ads.

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Does the FDA work with drug companies to create prescription drug ads?

- We do not help create any prescription drug ads. Drug companies create these ads themselves, often with help from advertising agencies.

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Does the FDA approve ads for prescription drugs before they are seen by the public?

- No, generally we do not. Except in unusual instances, we cannot require drug companies to submit ads for approval before they are used. Drug companies must only submit their ads to us when they first appear in public. This rule is the same whether the ads are aimed toward healthcare providers or consumers. This means that the public may see ads that violate the law before we can stop the ad from appearing or seek

corrections to the ad. Consumers should know that they may not necessarily be able to tell whether any specific DTC ad includes false or misleading information.

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What must product claim ads tell you?

- At least one approved use for the drug
- The generic (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#generic_name) name of the drug
- All the risks of using the drug
    - Under certain circumstances, ads can give only the most important risks
    - For more detail, see brief summary (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#brief_summary) and adequate provision (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#adequate_provision)

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What are ads not required to tell you?

- Cost
- If there is a generic (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#generic_name) version of the drug (a drug with the same active ingredient that might be cheaper)
- If there is a similar drug with fewer or different risks that can treat the condition
- If changes in your behavior could help your condition (such as diet and exercise)
    - Sometimes this information is required. It depends on the prescribing information for the particular drug
- How many people have the condition the drug treats
- How the drug works (its "mechanism of action")

- How quickly the drug works
    - However, if the ad claims that the drug works quickly, the ad must explain what "quickly" means
- How many people who take the drug will be helped by it

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How do the "brief summary," "prescribing information," "major statement," and "adequate provision" differ?

- These terms refer to different rules for how risk information must be included with materials that advertise prescription drugs. We require different types of benefit and risk disclosures for different types of promotions.
- "Prescribing information" (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#prescribing_information) (also called product information, product labeling, package insert, and the PI) includes the most complete information about a prescription drug. It includes technical information about the chemistry of the drug, its proper use overall and in specific types of patients, and details about possible side effects. It is written for healthcare providers. When we approve a drug for marketing, we also approve the prescribing information.
- The "brief summary" (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#brief_summary) includes all the risk information about a prescription drug and is generally based on the prescribing information. The brief summary may leave out non-risk information, such as the chemical description of the drug, how it works in the body, and directions for using it. For DTC ads, we recommend that brief summaries be written in language that consumers can understand.
- A "major statement" (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#M) is required only for broadcast (TV, radio and telephone) ads. It consists of the drug's most important risks. The major statement must be presented in a clear, conspicuous, and neutral manner. The risks are generally similar to the risks required for "fair balance" (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#fair_balance) in print ads.
- "Adequate provision" (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#adequate_provision) applies only to broadcast ads. Broadcast ads must include either the "brief summary" or make "adequate provision" for the audience to

find the drug's prescribing information. This requirement can be met by offering a variety of sources, including a healthcare provider, a toll-free telephone number, the current issue of a magazine containing a print ad for the drug, and a Web site address.

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Does the law say anything about the design of ads for prescription drugs?

- Yes. The layout of an ad — the way information is presented — can affect whether an ad meets the fair balance (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#fair_balance) requirement. For example, ads must present side effect information in a manner similar to that used for the benefit (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#benefit) information. Various ways of presenting information that can affect fair balance include type size, bulleting, amount of white space, and headlines.

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Has FDA done research on DTC advertising?

- Yes. The Office of Prescription Drug Promotion (OPDP) of the FDA's Center for Drug Evaluation and Research (CDER) conducts research on direct-to-consumer (DTC) advertising. This includes telephone surveys of DTC-related patient and physician attitudes and behaviors. This research helps OPDP make decisions about DTC advertisements. For more about the research conducted by OPDP, go to OPDP Research (/about-fda/about-center-drug-evaluation-and-research/office-prescription-drug-promotion-opdp-research).

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How can an ad violate the law?

- These are a number of ways in which an ad may violate the law. For example, the ad could:
    - State or imply that the drug can treat a condition when the FDA has not approved the drug for such use
    - Make claims that are not supported by adequate evidence
    - Misrepresent data from studies
    - Overstate the drug's benefits
    - Suggest that the drug can be used in patients with specific characteristics when the drug hasn't been shown to work or to be safe in such patients
    - Leave out or downplay risk information
        - Fail to present a "fair balance" (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#fair_balance) of information relating to the drug's risks and benefits (required for "product claim ads" (/drugs/prescription-drug-advertising/product-claim-ad-correct) and "promotional labeling" (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#promotional_labeling))
        - Leave out a "brief summary" (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#brief_summary) (required for "product claim ads" (/drugs/prescription-drug-advertising/product-claim-ad-correct))
        - Fail to attach the drug's prescribing information (required for "promotional labeling" (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#promotional_labeling))
        - Fail to include sources to help the audience find the "prescribing information" (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#prescribing_information) for the drug (for product claim ads on TV, radio, or by telephone)
        - Fail to include the required information about where negative side effects can be reported
    - Appear to be a "reminder ad" (/drugs/prescription-drug-advertising/reminder-ad-correct) but make a claim about the drug
    - Appear to be a "reminder ad" (/drugs/prescription-drug-advertising/reminder-ad-correct) but is about a drug that has certain very serious risks (one with a boxed warning (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#boxed_warning)) — reminder ads are not allowed for such drugs
    - Appear to be a "help-seeking" (/drugs/prescription-drug-advertising/correct-

help-seeking-ad) or disease awareness ad but recommend or suggest a particular prescription drug

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Who should I tell if I think that a prescription drug ad violates the law?

- Contact FDA's Office of Prescription Drug Promotion (OPDP) about prescription drug ads you believe violate the law by being false, misleading, or lacking in "fair balance" (/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#fair_balance). Consumers can call OPDP at 301-796-1200. Or, consumers may submit their complaint in written form to OPDP at:

    - Food and Drug Administration
      Center for Drug Evaluation and Research
      Office of Prescription Drug Promotion
      5901-B Ammendale Road
      Beltsville, MD 20705-1266

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What does FDA do if it determines that an ad violates the law?

- We have different ways to enforce the laws that apply to advertisements for prescription drugs. The simplest and most common way is to send a letter to the drug company. The letter explains how the ad has violated the law. It generally asks the drug company to remove the ad and stop the unlawful behavior.
- In some cases, we will ask the drug company to fix the misimpression made by the violative ad. The fix could include publishing a corrective ad. We are most likely to take this action when the misimpression poses a serious threat to public health.
- We post the enforcement letters issued by OPDP on the Warning Letters (/warning-letters-and-notice-violation-letters-pharmaceutical-companies) web page.
- Sometimes we take additional enforcement action. This may include taking drug

companies to court and even taking ("seizing") supplies of the drug. Court actions can include asking for an injunction (court-enforced ban of specific activities) and bringing criminal charges against the drug company.

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How can I learn more about a medical condition or a drug?

- Browse Information for Consumers (Drugs) (/information-consumers-drugs) for links to information on medical conditions. Or, use Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/) to search for specific brand and generic drugs.
- To find out if a medical condition is something you should be concerned about or if a particular drug is right for you, talk with your doctor or other healthcare provider.

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Note: This website does not purport to set forth all the ways in which an ad may violate the law, but rather to explain to the public some of the basic concepts related to drug advertising.

This site was developed as a collaborative effort between FDA (http://www.fda.gov/) and EthicAd to educate consumers about DTC prescription drug advertisements.

Exhibit 6

Laboratory Tests | Ranitidine

Laboratory analysis of ranitidine and nizatidine products

FDA continues to investigate the presence of the N-Nitrosodimethylamine (NDMA) impurity in ranitidine and is now aware of NDMA in nizatidine, which is chemically similar to ranitidine. Both medicines are H2 blockers which decrease the amount of acid in the stomach. FDA has identified NDMA in ranitidine and nizatidine active pharmaceutical ingredient (API) and finished drugs.

FDA is posting its laboratory results in the table below showing NDMA levels in all ranitidine and nizatidine samples it tested, including API and finished drug which included tablets and syrup. NDMA was present in all samples tested. Testing of ranitidine for injection is still ongoing.

For reference, consuming up to 0.096 micrograms or 0.32 parts per million (ppm) of NDMA per day is considered reasonably safe for human ingestion based on lifetime exposure. FDA has set the acceptable daily intake limit for NDMA at 0.096 micrograms or 0.32 ppm for ranitidine. Although many manufacturers have already recalled ranitidine voluntarily, FDA will recommend recalls to manufacturers with NDMA levels above the acceptable daily intake limit.

The methods FDA used in the laboratory testing are available here (/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine).

FDA also developed a simulated gastric fluid (SGF) model to be used with the LC-MS testing method (/media/131868/download) to estimate the biological significance of in vitro findings. The SGF and simulated intestinal fluid (SIF) models are intended to detect the formation of NDMA in systems that approximate the stomach and intestinal fluids, respectively. The results of these tests showed no additional NDMA generated in the stomach.

NDMA ESTIMATED RISK:

FDA has determined that the levels of NDMA in ranitidine and nizatidine are similar to the levels you would expect to be exposed to if you ate common foods like grilled or smoked meats.

Company	Product	Lots Tested	NDMA level ppm	NDMA level (micrograms-mcg/tablet or oral dose)
Sanofi Pharmaceutical	OTC Ranitidine 150mg	19E413M, 19D554, 19A432U, 19C540, 19D431I, 19D442N, 19D423M, 19D464M,	0.07-2.38	0.01-0.36
Sanofi Pharmaceutical	OTC Ranitidine 75mg	18L012U, 9A003U, 19B006M, 18M025M, 18N023U, 19B005N, 19A002U, 18N026U	0.10-0.55	0.01-0.04
Cardinal Health	OTC Ranitidine 150mg	9FE2953	1.02	0.15
Watson	Rx Nizatidine 150mg	1350798M	0.05	0.01
Watson	Rx Nizatidine 300mg	1333973A	0.04	0.01
Strides Shasun Ltd	Rx Nizatidine 150mg	7704758A	0.11	0.02
Strides Shasun Ltd	Rx Nizatidine 300mg	7704022A	0.09	0.03
Novitium	Rx Ranitidine 300mg	S18038B	2.85	0.86
Dr Reddy's	Rx Ranitidine 300mg	C805265	0.68	0.20
Strides Shasun Ltd	Rx Ranitidine 300mg	7702255A	0.11	0.03
Sandoz	Rx Ranitidine 300mg	HU2207	0.82	0.25
Strides Shasun Ltd	Rx Ranitidine 300mg	7704537A	0.02	0.00
Aurobindo	Rx Ranitidine 300mg	RA3019001-A	1.86	0.56
Ajanta Pharma USA Inc	Rx Ranitidine 300mg	PA1229B	0.23	0.07
Silarx Pharma	Ranitidine 150mg Syrup	3652081-02661	1.37	0.20

Company	Product	Lots Tested	NDMA level ppm	NDMA level (micrograms-mcg/tablet or oral dose)
Pharma Associates	Ranitidine 150mg Syrup	BE00, BF75, BF77, BF78, BDFF, COAC	0.03-0.07	0.004-0.012
Amneal Pharmaceuticals	Ranitidine 300mg	AR181795A, AR190878A, AR190876A, AR191177A, HB05819, HB06119, HL08718	0.52-2.17	0.16-0.65
Sanofi Pharmaceutical	Ranitidine 150mg	19D570, 19D428U, 19E408M	0.08-2.17	0.01-0.33

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Exhibit 7

COMPANY ANNOUNCEMENT

Sanofi Provides Update on Precautionary Voluntary Recall of Zantac OTC in U.S.

Summary

Company Announcement Date:

October 22, 2019

FDA Publish Date:

October 23, 2019

Product Type:

Drugs

Reason for Announcement:

May Contain N-Nitrosodimethylamine (NDMA)

Company Name:

Sanofi

Brand Name:

Sanofi

Product Description:

Zantac 150, Zantac 150 Cool Mint, Zantac 75 (OTC Products)

Company Announcement

As a precautionary measure, Sanofi on Friday, October 18, intiated a voluntary recall of all Zantac OTC (over-the-counter) in the United States. This includes Zantac 150®, Zantac 150® Cool Mint, and Zantac 75®. Zantac tablets are an oral, over-the-counter product to prevent and relieve heartburn associated with acid ingestion and sour stomach.

On September 13, 2019, the U.S Food and Drug Administration issued a public statement

alerting that some ranitidine medicines, including Zantac OTC, could contain NDMA at low levels and asked manufacturers to conduct testing.

Evaluations are ongoing on both drug substance (active ingredient) and finished drug product. Due to inconsistencies in preliminary test results of the active ingredient used in the U.S. products, Sanofi has made the decision to conduct the voluntary recall as the investigation continues.

Active ingredients used in Sanofi's ranitidine products outside of the U.S. and Canada are sourced from different suppliers. Sanofi has also issued a voluntary recall in Canada. The company is committed to transparency and will continue to communicate results with health authorities from the ongoing testing, and work with them to make informed decisions based on available data and evidence.

Risk Statement: NDMA is classified as a probable human carcinogen (a substance that could cause cancer) based on results from laboratory tests. NDMA is a known environmental contaminant and found in water and foods, including meats, dairy products, and vegetables.

Sanofi will be notifying its distributors and customers via email and via the Sanofi web site, and will arrange for return of all recalled products. Wholesalers (direct customers) will be asked to immediately stop distribution and return any stock to Sanofi, and contact the retail outlets in their group to do the same. Retailers will be asked to immediately stop dispensing Zantac tablets and return remaining stock to Sanofi by contacting INMAR at 877-275-0993 (option 1) or via fax at 336-499-8145 or email at zantacrecall@inmar.com (mailto:zantacrecall@inmar.com). Consumers are asked to speak to their physician or pharmacist about alternate heartburn relief options.

Adverse reactions or quality problems experienced with the use of this product may be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax.

- Complete and submit the report Online (/node/360543)
- Regular Mail or Fax: Download form (/node/360547) or call 1- 800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

This recall is being conducted with the knowledge of the U.S. Food and Drug Administration

Company Contact Information

Consumers:

INMAR

877-275-0993 (option 1)

zantacrecall@inmar.com (mailto:zantacrecall@inmar.com)

Media:

Ashleigh Koss

908-981-8745

Ashleigh.Koss@sanofi.com (mailto:Ashleigh.Koss@sanofi.com)

More Recalls, Market Withdrawals, & Safety Alerts (/safety/recalls-market-withdrawals-safety-alerts)

Exhibit 37

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CENTER FOR ENVIRONMENTAL HEALTH

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

Case No. RG 20-054985

ASSIGNED FOR ALL PURPOSES TO:
Hon. Winifred Smith, Department 21

PLAINTIFF'S REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF OMNIBUS OPPOSITION TO DEFENDANTS' DEMURRERS

Date: April 21, 2021
Time: 10:00 a.m.

Reservation Numbers: R-2240281, R-2240282, R-2240283, R-2240276, R-2242157

SAC Filed: January 4, 2021
Trial Date: None Set

[Filed concurrently with Plaintiff's Omnibus Opposition to Defendants' Demurrers; Declaration of Mark N. Todzo]

TO THE COURT, DEFENDANTS, AND THEIR ATTORNEYS OF RECORD:

Please take notice that, pursuant to California Evidence Code §452, Plaintiff Center for Environmental Health ("CEH") hereby requests that this Court take judicial notice of the following documents in support of CEH's Omnibus Opposition to Defendants' Demurrers, true and correct copies of which are attached to the concurrently filed Declaration of Mark N. Todzo:

EXHIBIT NO.	**DESCRIPTION OF DOCUMENT**
1.	Proposition 65 Ballot Pamphlet. A true and correct copy of this document is attached to the Todzo Declaration as **Exhibit 1**.
2.	The U.S. Food and Drug Administration's ("FDA") publicly available webpage on "Questions and Answers: NDMA impurities in ranitidine (commonly known as Zantac)." A true and correct copy of this document is attached to the Todzo Declaration as **Exhibit 2**.
3.	The FDA's "Guidance for Industry – Q3A Impurities in New Drug Substances" (June 2008). A true and correct copy of this document is attached to the Todzo Declaration as **Exhibit 3**.
4.	The FDA's "Guidance for Industry – ANDAs: Impurities in Drug Substances" (Nov. 1999). A true and correct copy of this document is attached to the Todzo Declaration as **Exhibit 4**.
5.	The FDA's publicly available webpage on "Prescription Drug Advertising – Questions and Answers." A true and correct copy of this document is attached to the Todzo Declaration as **Exhibit 5**.
6.	The FDA's publicly available webpage on "Laboratory Tests – Ranitidine." A true and correct copy of this document is attached to the Todzo Declaration as **Exhibit 6**.
7.	Defendant Sanofi-Aventis U.S. LLC's "Company Announcement – Sanofi Provides Update on Precautionary Voluntary Recall of Zantac OTC in U.S.," as posted to FDA's publicly available website. A true and correct copy of this document is attached to the Todzo Declaration as **Exhibit 7**.

MEMORANDUM OF POINTS AND AUTHORITIES

CEH requests that the Court take judicial notice of the Proposition 65 ballot materials identified above as Exhibit 1 pursuant to Evidence Code §452(c) as these materials reflect an official act of the legislative departments of the State of California. *See Moore v. Sup. Ct.* (2004) 117 Cal.App.4th 401, 406 n.5 (taking judicial notice of a "ballot pamphlet, which may properly be considered to show the intent of the voters in passing an initiative measure").

In addition, CEH requests that the Court take judicial notice of the FDA documents identified above as Exhibits 2 through 6 pursuant to Evidence Code §452(c) as each is an official record and each reflects an official act of the executive departments of the United States. *See Brescia v. Angelin* (2009) 172 Cal.App.4th 133, 142 (taking judicial notice of official records of the U.S. Patent and Trademark Office); *Tamas v. Safeway, Inc.* (2015) 235 Cal.App.4th 294, 297-98 (taking judicial notice of "question and answer" statements from FDA's website); *cf. Rodas v. Spiegel*, 87 Cal.App.4th 513, 518 (2001) (taking judicial notice of "records, reports and orders" of the California Contractors' State License Board). CEH further notes that Defendants have all asked the Court to take judicial notice of essentially analogous FDA documents in their own moving papers. *See, e.g.*, Brand Name Manufacturers Request for Judicial Notice ("RJN"), Exh. A-I, M; Generic Manufacturers RJN, Exh. A-D; Apotex RJN, Exh. 1-4, 7-9; Private Label Retailers RJN, Exh. A. Thus, the FDA documents are all "not reasonably subject to dispute" and "capable of immediate and accurate determination by resort to courses of reasonable accuracy" under Evidence Code §452(h).

Finally, CEH requests that the Court take judicial notice of Defendant Sanofi-Aventis U.S. LLC's press release as formally posted on FDA's website, identified above as Exhibit 7, pursuant to Evidence Code §452(c) as it is an official record and reflects an official act of the executive departments of the United States. *See* 21 C.F.R. §§7.49, 7.50 (imposing notification duties on both the recalling entity and FDA); *see also, e.g.*, Apotex RJN, Exh. 4 (conceding that its own press release, submitted to FDA for the same regulatory reason, is judicially noticeable under Evidence Code § 452(c) as a "record" of FDA). Furthermore, the Sanofi press release is listed on FDA's website as a "company announcement" that has been submitted by Sanofi and posted by

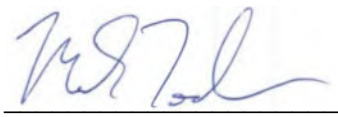
FDA "as a public service." Since this is the company's own document, it is "not reasonably subject to dispute" and "capable of immediate and accurate determination by resort to courses of reasonable accuracy" under Evidence Code §452(h).

For the foregoing reasons, Plaintiff respectfully requests that Exhibits 1 through 7 of the concurrently filed Declaration of Mark N. Todzo be judicially noticed.

DATED: March 29, 2021

Respectfully submitted,

LEXINGTON LAW GROUP



Mark N. Todzo
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CENTER FOR ENVIRONMENTAL HEALTH

Exhibit 38

FILED BY FAX
ALAMEDA COUNTY
April 08, 2021
CLERK OF
THE SUPERIOR COURT
By Xian-xii Bowie, Deputy
CASE NUMBER:
RG20054985

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation, Plaintiff, v. PERRIGO COMPANY, *et al.*, Defendants.	Case No. RG 20-054985 ASSIGNED FOR ALL PURPOSES TO: Hon. Winifred Smith, Department 21 **PROOF OF SERVICE**

PROOF OF SERVICE

I, Owen Sutter, declare:

I am a citizen of the United States and employed in the County of San Francisco, State of California. I am over the age of eighteen (18) years and not a party to this action. My business address is 503 Divisadero Street, San Francisco, CA 94117 and my email address is osutter@lexlawgroup.com.

On March 29, 2021 I served the following document(s) on all interested parties in this action by placing a true copy thereof in the manner and at the addresses indicated below:

PLAINTIFF'S OMNIBUS OPPOSITION TO DEFENDANTS' DEMURRERS

PLAINTIFF'S REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF OMNIBUS OPPOSITION TO DEFENDANTS' DEMURRERS

DECLARATION OF MARK N. TODZO IN SUPPORT OF PLAINTIFF'S OMNIBUS OPPOSITION TO DEFENDANTS' DEMURRERS

☐ **BY MAIL**: I am readily familiar with the firm's practice for collecting and processing mail with the United States Postal Service ("USPS"). Under that practice, mail would be deposited with USPS that same day with postage thereon fully prepaid at San Francisco, California in the ordinary course of business. On this date, I placed sealed envelopes containing the above mentioned documents for collection and mailing following my firm's ordinary business practices.

☐ **BY FACSIMILE**: I caused all pages of the document(s) listed above to be transmitted via facsimile to the fax number(s) as indicated and said transmission was reported as complete and without error.

☒ **BY ELECTRONIC MAIL**: I transmitted a PDF version of the document(s) listed above via email to the email address(es) indicated on the attached service list [or noted above] before 5 p.m. on the date executed.

Please see attached service list

☐ **BY PERSONAL DELIVERY**: I placed all pages of the document(s) listed above in a sealed envelope addressed to the party(ies) listed above, and caused such envelope to be delivered by hand to the addressee(s) as indicated.

☐ **BY OVERNIGHT DELIVERY**: I deposited such document(s) in a box or other facility regularly maintained by FedEx, or delivered such document(s) to a courier or driver authorized by FedEx, with delivery fees paid or provided for, and addressed to the person(s) being served below.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed on March 29, 2021 at San Francisco, California.

Owen Sutter

SERVICE LIST
CEH v. Perrigo Company, et al.
RG 20-054985

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Exhibit 39

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et. al.*,

Defendants.

Case No. RG-20-054985

[*Assigned to Honorable Winifred Y. Smith, Dept. 21*]

DEFENDANT APOTEX CORP.'S REPLY IN SUPPORT OF DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT AND JOINDER TO REPLY OF DEFENDANT PERRIGO COMPANY

Date: April 30, 2021
Time: 10:00 a.m.
Dept: 21

Complaint Filed: February 19, 2020
SAC Filed: January 4, 2021
Trial Date: None Set

Hearing Reservation ID # R2240282

BY FAX

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REPLY MEMORANDUM OF POINTS AND AUTHORITIES

In support of its demurrer ("Demurrer") to the second amended complaint ("SAC") filed by plaintiff Center for Environmental Health ("CEH"), defendant Apotex Corp. ("Apotex") represents as follows in the instant reply, and joins in the joint reply brief of defendants Perrigo Company, Granules USA, Inc., Dr. Reddy's Laboratories Louisiana, LLC, and Dr. Reddy's Laboratories, Inc.:

I. INTRODUCTION

In an attempt to sidestep the glaring deficiencies of its pleading, CEH downplays the proactive, wide-ranging remedial efforts Apotex took by withdrawing its medication ranitidine from the national market, over six months prior to the issuance of CEH's Notice of Violation under Proposition 65.[1] This is not surprising given that CEH is now seeking a windfall, but does so via the façade of attributing the positive implications of Apotex's voluntary recall to the Notice it issued half a year later. The fact remains that CEH 's action did nothing and will provide no public benefit, thereby defeating the purpose of private party lawsuits under Proposition 65.

Thus, CEH's opposition ("Opposition") confirms that its cause of action for violation of Proposition 65 fails. CEH's "Enforcement Action" remains moot, as it was brought long after Apotex's nationwide recall of the Products. The fundamentally equitable nature of Proposition 65 confirms that CEH's action is rendered ineffective following Apotex's voluntary recall six months prior. CEH's claims for injunctive relief and attorneys' fees are equally mooted as there is no conduct to enjoin and because CEH does not meet the definition of a "successful party" for purposes of Proposition 65. Similarly, Civil penalties are not warranted here, where there is no conduct to deter. Finally, CEH's cause of action fails because FDA's comprehensive investigation, oversight, and management of the narrow field of potential NDMA content in ranitidine products confirms that field preemption applies.

Accordingly, Apotex's Demurrer should be sustained, without leave to amend.

[1] Unless otherwise noted, all defined terms herein have the same meaning as those in Apotex's Demurrer.

II. ARGUMENT

A. CEH's "Enforcement Action" is Moot

1. The Equitable Nature of Proposition 65 Confirms That CEH's "Enforcement" Action Remains Moot Following Apotex's Voluntary Recall

CEH declines to address Apotex's argument that Proposition 65 is "fundamentally equitable," and that the "statutory remedies afforded by the Act, including civil penalties, are not damages at law, but instead constitute equitable relief appropriate as incidental to enforcement of the Act." Demurrer, at p. 3-4 (citing *DiPirro v. Bondo Corp.*, 153 Cal.App.4th 150, 150, 183-84 (2007). CEH therefore concedes this argument in favor of Apotex. *See Nelson v. Pearson Ford Co.*, 186 Cal.App.4th 983, 1021 (2010) (issues not addressed in opposition briefs are conceded to the moving party); *see also Wurzl v. Holloway,* 46 Cal.App.4th 1740, 1755 (1996) (a point not presented in a party's opening brief is deemed to have been abandoned or waived).

CEH instead contends that Apotex's Demurrer is "procedurally defective" because CEH's allegations as to injunctive relief, civil penalties, and attorneys' fees "only arise" in the context of the Prayer for Relief of the SAC. Opp., 40:9-13. Not so. The overarching theme of CEH's SAC is that CEH is entitled to such relief pursuant to its enforcement actions. Indeed, the SAC itself is styled as the "Second Amended Complaint for Injunctive Relief and Civil Penalties." *See* SAC. In any event, CEH misconstrues Apotex's contention. Apotex is not challenging only parts of CEH's prayer for relief. Apotex is challenging CEH's ability to bring its cause of action at all where there is no relief to be had. Stated differently, a claim for violation of Proposition 65 is a "remedial law, designed to protect the public," and there is nothing for Apotex to remediate following Apotex's voluntary recall of its ranitidine Products on September 25, 2019, six months prior to CEH's Notice of Violation. RJN ¶ 4, Ex. 4.

Moreover, the cases relied upon by CEH are inapposite as they do not involve situations where the demurrer asserted that the cause of action was rendered moot based on the language of the statute and the conduct of the defendant. *See* Opp., 40:14-27; *see also Venice Town Council, Inc. v.*

City of Los Angeles, 47 Cal. App. 4th 1547, 1561 (1996), as modified on denial of reh'g (Aug. 22, 1996) (noting that while certain aspects of the prayer of the complaint conflicted with the statute in question, the demurrer tests the sufficiency of the factual allegations of the complaint); *Grieves v. Superior Ct.*, 157 Cal. App. 3d 159, 167 (1984) (reiterating the view that the adequacy of punitive damage allegations may not properly be tested by demurrer, but acknowledging that cases examining the sufficiency of punitive damage allegations raised by demurrer).

Accordingly, Apotex's Demurrer is proper.

2. CEH's Claims for Injunctive Relief and Attorneys' Fees Are Moot Due to the Nationwide Recall of the Products Prior to CEH's Enforcement Efforts

CEH's Opposition does not and cannot dispute that the Apotex-manufactured Products were recalled six months prior to the Notice, and over a year before Apotex was named as a defendant in this case. An injunction is appropriate only where it appears "with reasonable certainty that the wrongful acts will be continued or repeated." *Gold v. Los Angeles Democratic League*, 49 Cal. App. 3d 365, 372 (1975) (declined to follow on other grounds by *Youst v. Longo*, 43 Cal. 3d 64, 72 (1987)). An injunction should "neither serve as punishment for past acts, nor be exercised in the absence of any evidence establishing the reasonable probability the acts will be repeated." *Scripps Health v. Marin*, 72 Cal. App. 4th 324, 333 (1999). Where there is a change in circumstances, "rendering injunctive relief moot or unnecessary," or where the "defendant has voluntarily discontinued the wrongful conduct," there is no equitable reason for a court to issue an injunction. *Id.* In California, good faith assertions regarding the intent to discontinue offending conduct are sufficient to merit denial of an injunction. *Lee v. Gates*, 141 Cal. App. 3d 989, 993-94 (1983).

CEH claims that Apotex's voluntary recall does not moot its request for injunctive relief or attorneys' fees and cost, relying on *Marin Cty. Bd. of Realtors, Inc. v. Palsson*, 16 Cal. 3d 920, 931, (1976) (*Palsson*) and *California Common Cause v. Duffy*, 200 Cal. App. 3d 730, 742 (1987) (*Duffy*). Opp., 42:23-43:3. CEH further claims that these so-called "rules" "make sense because the alleged violator may restart the illegal conduct at any time." Opp., 43:3-4. As is further discussed below,

Apotex has demonstrated no intention to reintroduce its Products. Even if it had, it could not do so unilaterally due to the comprehensive guidelines and oversight promulgated by FDA.

In *Palsson*, an antitrust case, the court considered whether a board of realtor's assertion that a certain challenged bylaw requiring that members be primarily engaged in the real estate business was deleted, thereby rendering the pending appeal moot. *Id.* at 928. Noting that there was no indication that the board had changed other rules at issue in the litigation (pertaining to access to the multiple listing service), the court concluded that appellate review remained appropriate. *Id.* at 928-29. As to the deleted bylaw, in declining the mootness argument, the court emphasized that there "is no assurance that the board will not reenact it in the future." *Id.* at 929.

In *Duffy*, a taxpayers' suit for declaratory and injunctive relief against a sheriff, which sought to establish the illegality of the sheriff's use of departmental funds to distribute postcards opposing the Chief Justice of the state Supreme Court, both parties appealed an award of attorneys' fees to the taxpayers. *Id.* at 738-41. The sheriff contended the taxpayers were not the prevailing party for purposes of the attorney fee award because they failed to cause any action to be enjoined since, by the time of the judgment, the sheriff had voluntarily ceased the practice of distributing the postcards in question. *Id.* at741-42. The court disagreed, explaining that for purposes of determining prevailing party status in connection with a fee award, an award should not be denied because resolution was reached through the defendant's voluntary cessation of the unlawful practice, among other things. *Id.*

The instant case is markedly different from *Palsson* and *Duffy* for two reasons. First, Apotex voluntarily recalled the Products over a year before CEH brought suit against it. *See* RJN ¶ 4, Ex. 4. Unlike the board of realtors in *Palsson*, Apotex's voluntary recall did not occur pending appeal, and unlike the sheriff in *Duffy*, the recall was not prompted by CEH's initiation of litigation. Perhaps most importantly, there is no risk here that Apotex will voluntarily reintroduce the Products to the nationwide market. Apotex discussed this fact in detail in its Demurrer. *See* Demurrer, 6:23-8:2. Significantly, *Apotex cannot unilaterally return its ranitidine Products to the market in California—*

or anywhere else—without prior FDA approval. RJN ¶ 9, Ex. 9. Moreover, FDA's Information Request to Apotex states:

> The Agency will not approve any pending supplement until FDA finds appropriate controls have been implemented and stability data submitted demonstrating adequate control of drug quality, specifically NDMA. To reintroduce your product to the market, submit a supplemental application with the results of your analysis of the cause(s) and extent of NMDA formation, proposed changes to manufacturing process or other controls, and at least 12 months stability data; 3 months of accelerated stability data; and months 1, 2, and 3 and the 12 month (or midpoint) in-use stability data per the table above.

Id.

Thus, judicially noticeable documents confirm that Apotex cannot reenter the ranitidine product market without meeting FDA's high reentry threshold. It cannot simply "change its mind" and reenter the market, as CEH suggests. Opp., 44:7-10. And, while CEH asserts that injunctive relief remains appropriate because there could be ongoing exposures to NDMA for any purchasers who are not aware of the recall or the NDMA contamination issues (Opp. 43:13-16), an injunction that seeks to enjoin conduct not occurring, could in no way protect these individuals any more than Apotex's nationwide recall already has. *See* Cal. Code Civ. Proc., § 525 ("injunction is a writ or order requiring a person to refrain from a particular act"); *Madrid v. Perot Sys. Corp.*, 130 Cal. App. 4th 440, 463 (2005) ("Injunctive relief is appropriate only when there is a threat of continuing misconduct."). CEH appears to be grasping at straws to concoct relief that the Court could simply not award or enforce; Apotex cannot control and an injunction would not reach the actions of individuals who obtained the product prior to the recall and who declined to dispose of any residual ranitidine Products in their possession, regardless of the reason.

In its Opposition, CEH makes a further brief argument regarding the availability of attorneys' fees, based primarily on numerous overbroad, and unsupported assertions. Among these assertions is the sweeping generalization that, if CEH can prove that its pre-suit Notice was the catalyst for "any change" in Apotex's conduct, it *may* be entitled to attorneys' fees. Opp., 44:12-15.

Despite CEH's overarching claims, it cannot duck the California Attorney General's Proposition 65 settlement guidelines, which confirm that, in order to be a "successful party for

purposes of obtaining an award of attorneys' fees, the action must have "resulted in the enforcement of an important right affecting the public interest if: (a) a significant benefit . . . has been conferred on the general public or a large class of persons, (b) the necessity and financial burden of private enforcement . . . are such as to make the award appropriate, and (c) such fees should not in the interest of justice be paid out of the recovery, if any." Cal. Code Regs. tit. 11, § 3201; Cal. Civ. Proc. Code § 1021.5. That is, CEH cannot demonstrate or allege the necessity of its private enforcement action *after* the recall of the ranitidine Products by Apotex, or that it has conferred or will confer any benefit on the general public when the conduct it seeks to prevent has long ceased.

CEH's inability to plead entitlement to injunctive relief or attorneys' fees remains fatal to the SAC.

3. Civil Penalties Are Not Warranted Because There is No Basis for the Required Equitable or Injunctive Relief

CEH further claims that the determination of penalties under Proposition 65 is "intensely fact-based," suggesting that it is inappropriate for a demurrer. Opp., 40:22-41:1; 42:19-20. However, given Proposition 65's inherently equitable nature, civil penalties are not warranted where the purportedly improper conduct ceased well before initiation of litigation and is not at risk of occurring in the future. As outlined above, Proposition 65 is inherently equitable in nature. *DiPirro*, 153 Cal. App. 4th, at 183-84. Civil penalties available pursuant to Proposition 65 are merely incidental to its equitable nature. *Id.* Thus, without a basis for equitable or injunctive relief, civil penalties are not warranted in this case, and CEH does not allege otherwise.

Apotex does not dispute that in assessing the amount of a civil penalty for violations of Proposition 65, courts may consider a variety of factors. Cal. Health & Safety Code § 25249.7(b)(2). However, the existence of these factors does not mean that civil penalties are automatically warranted in a case such as this, where Apotex's voluntary recall occurred six months prior to CEH's Notice. *See* Cal. Code Regs. tit. 11, § 3203(a). Not only did it issue a recall, but Apotex did so early, and independently. RJN ¶ 4, Ex. 4. Apotex also directed those with existing inventory of Apotex Products to quarantine the recalled lots, and advised as to the return of Products

as to either their place of purchase or a specified point of contact with Apotex. *Id.* Even if the factors were considered, they confirm that civil penalties should not be assessed here. Due to Apotex's proactive measures, the nature extent, number of, and severity of any violation was drastically curbed half a year prior to CEH's issuance of the Notice, and over a year prior to CEH joining Apotex to this litigation. *See* Cal. Health & Safety Code § 25249.7(b)(2)(A)-(B). Further, the economic effect of the penalty likely pales in comparison to the costs associated with a voluntary nationwide recall. *See* Cal. Health & Safety Code § 25249.7(b)(2)(C). Apotex clearly took good faith measures when it undertook its own voluntary compliance measures even prior to any action by FDA, and did so willingly. *See* Cal. Health & Safety Code § 25249.7(b)(2)(D)-(E).

As to the final factor, the "deterrent effect that the imposition of the penalty would have on both the violator and the regulated community as a whole," CEH claims the "necessity of deterrence appears to be particularly strong here." Opp., 41:18. CEH speculates that Apotex could have remedied any NDMA contamination sooner by "cleaning its production facilities, properly storing the Products, or simply testing its Products." Opp., 41:18-20. CEH cites no authority in support of this illogical assertion which, in any event, is not what Proposition 65 requires. Contrary to CEH's claims, Apotex acted swiftly, and in conjunction with FDA, when it issued its nationwide voluntary recall on a precautionary basis due to the potential for detection of NDMA on September 25, 2019, and the FDA published its announcement the same day. RJN ¶ 4, Ex. 4. Apotex did not, for example, hold off on the recall until after it received CEH's 60-day Notice in March 2020. Furthermore, the Opposition fails to comprehend the lack of a deterrent effect here, where FDA has indefinitely requested removal of the Products on a nationwide basis while it implements and oversees its own strict control and approval process.

Thus, in addition to CEH's claim being moot, there is no basis for injunctive relief, attorneys' fees, or the imposition of a civil penalty and the Demurrer should be sustained without leave to amend.

B. CEH's Claims Remain Federally Preempted Under the Theory of Field Preemption Due to FDA's Comprehensive Investigation, Oversight, and Management of Potential NDMA Content in Ranitidine Products

CEH attempts to discredit Apotex's field preemption argument on the grounds that none of the other Defendants have raised it and that it is "absurd." Opp., 38:17-19. However, CEH does little to substantively address Apotex's position, which is that CEH's claim is preempted under the theory of field preemption in this unique situation in which FDA has taken affirmative and drastic steps to regulate the sale, marketing, manufacture, stability, and testing of the NDMA content in ranitidine drugs. While CEH asserts that the federal statute that provides the authority for any preemption of the field "expressly preserves state authority in a number of circumstances" (*see* Opp., at pp. 38:17-39:2), Apotex acknowledges in its Demurrer that general federal regulation alone is not sufficient to preempt state law claims on a field preemption basis. *See* Dem. at 20, citing *Dowhal v. SmithKline Beecham Consumer Healthcare*, 32 Cal. 4th 910, 924 (2004).

Apotex's argument is more nuanced and involves the specific oversight of FDA as to NDMA content in ranitidine medication. CEH attempts to distinguish *R.F. v. Abbott Labs.*, 162 N.J. 596, 604, 745 A.2d 1174 (2000) (*Abbott*) on the grounds that it involved "specific, affirmative statements by the FDA that state regulation would necessarily conflict with the agency's own findings." Opp., 39:15-18 (citing *Abbott*, at 745 A.2d at 1177-84.). Not so. In fact, none of the eight pages of the *Abbott* decision that CEH cites discuss the direct issue of specific state regulations. Rather, CEH cites to the factual portion of the *Abbott* opinion, which outlines, in significant detail, FDA's exercise of control and initiative over the HIV test's development, packaging, and field performance monitoring. *Id.* at 601-14, 620.

The facts of *Abbott* are on par with the facts here. Just as with the manufacturer at issue in *Abbott*, so too here is *Apotex* prohibited from unilaterally altering the label on its ranitidine medication. *Id.* at 621. So too here has FDA exercised control via aggressive, severe, and comprehensive action to address the issue of NDMA in ranitidine medications. *Id.* at 620; RJN ¶¶ 8,

9, Exs. 8-9. So too here is FDA undertaking a "whole host" of monitoring efforts as to the NDMA content in ranitidine medications. *Id.* at 611; RJN ¶ 8, Ex. 8.

Apotex is not asserting that the Court should conclude that field preemption applies here "just because" FDA required a recall of all ranitidine products from the market. Opp., 39:20-40:2. FDA did not simply require a recall. Rather, FDA is conducting a thorough investigation of NDMA content in ranitidine medications, it will be responsible for "find[ing] adequate a supplemental application that demonstrates adequate control over NDMA in ranitidine medications," and is reviewing manufacturers' "proposed changes to manufacturing process and other controls" before allowing reintroduction of the Products to the market, among other controls. RJN ¶ 9, Ex. 9.

FDA's "extensive control and continuous scrutiny" over the issue of NDMA in ranitidine medications confirms that it "left no room for the state[s] to supplement it." *Abbott*, 162 N.J. at 925. Accordingly, the Opposition confirms that this Court should dismiss the SAC without leave to amend, as CEH remains unable to plead around the fact of FDA's complete occupation of the field of ranitidine medications – the very field which CEH's state law claim seeks to concurrently occupy.

III. CONCLUSION

Based on the foregoing, the Court should sustain Apotex's Demurrer to CEH's SAC in its entirety, without leave to amend.

DATED: April 12, 2021

BLANK ROME LLP

By: */s/ Cheryl S. Chang*
Cheryl S. Chang
Jessica A. McElroy
Attorneys for Defendant,
APOTEX CORP.

PROOF OF SERVICE

STATE OF CALIFORNIA, COUNTY OF LOS ANGELES

I am employed in the county of Los Angeles, State of California. I am over the age of 18 and not a party to the within action; my business address is **BLANK ROME LLP**, 2029 Century Park East, 6th Floor, Los Angeles, California 90067.

On April 12, 2021, I served the foregoing document(s): **DEFENDANT APOTEX CORP.'S REPLY IN SUPPORT OF DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT AND JOINDER TO REPLY OF DEFENDANT PERRIGO COMPANY** on the interested parties in this action addressed and sent as follows:

SEE ATTACHED SERVICE LIST

☒ **BY ENVELOPE:** by placing ☐ the original ☒ a true copy thereof enclosed in sealed envelope(s) addressed as indicated and delivering such envelope(s):

☒ **BY MAIL:** I caused such envelope(s) to be deposited in the mail at Los Angeles, California with postage thereon fully prepaid to the office or home of the addressee(s) as indicated. I am "readily familiar" with this firm's practice of collection and processing documents for mailing. It is deposited with the U.S. Postal Service on that same day, with postage fully prepaid, in the ordinary course of business. I am aware that on motion of party served, service is presumed invalid if postal cancellation date or postage meter date is more than one day after the date of deposit for mailing in affidavit.

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☒ **BY ELECTRONIC SERVICE (EMAIL):** Pursuant to Temporary Emergency Rule #12 related to electronic service of documents via email enacted by the California Judicial Counsel due to the National Emergency and public health orders in California related to the coronavirus and COVID-19 pandemic, I caused the document(s) listed above to be transmitted to the person(s) at the e-mail address(es) as indicated. I did not receive, within a reasonable time after the transmission, any electronic message or other indication that the transmission was incomplete or unsuccessful.

☒ **STATE:** I declare under penalty of perjury under the laws of the State of California that the above is true and correct.

Executed on **April 12, 2021**, at Los Angeles, California.

/s/ Hannah No
Hannah No

SERVICE LIST

Center for Environmental Health v. Perrigo Company, et al.
Alameda Case No. RG 20-054985

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By SUE PESKO
Deputy

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

CASE NO. RG20054985

ASSIGNED FOR ALL PURPOSES TO:
HON. WINIFRED Y. SMITH
DEPT. 21

DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S REPLY IN SUPPORT OF DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT

Date: April 30, 2021
Time: 10:00 a.m.
Dept.: 21
Judge: Hon. Winifred Y. Smith

Reservation No.: R-2240283

Reservation No.: R-2242157

SAC Filed: January 4, 2021

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MEMORANDUM OF POINTS AND AUTHORITIES

I. INTRODUCTION

In the Demurrer of Defendants Chattem, Inc. and Sanofi-Aventis U.S. LLC (together, "Brand Defendants"), Brand Defendants demonstrated why the Proposition 65 warnings sought by Plaintiff Center for Environmental Health are preempted by federal regulations governing over-the-counter ("OTC") drugs. Nothing in Plaintiff's Omnibus Opposition to Defendants' Demurrers compels a different result.

First, a Proposition 65 warning conflicts with the Food and Drug Administration's content and format requirements for OTC drugs established by 21 C.F.R. § 201.66. Plaintiff does not refute the mandatory nature of 21 C.F.R. § 201.66 (Opp. at 29-30) and concedes that noncompliance with the labeling requirements for OTC drugs under 21 C.F.R. § 201.66 would subject the Brand Defendants to adverse regulatory action. *See* Opp. at 30, n.19. It is self-evident that manufacturers cannot violate federal law to appease contrary requirements under California law.

Second, as argued in Brand Defendants' Demurrer (Br. at 20-22), a Proposition 65 warning is not a "warning" that could be added to OTC labeling through the Changes Being Effected ("CBE") process. 21 C.F.R. § 314.70. Plaintiff argues in response only that the FDA has determined that the products should not be sold (Opp. at 32-33), a false characterization of the FDA's actions regarding Zantac, and which does not address the express limitations on the CBE process that would prohibit a manufacturer from unilaterally changing an FDA-approved label to add a Proposition 65 warning.[1]

Third, Plaintiff fails to plausibly plead that the Brand Defendants could deliver the hypothesized alternatives to Proposition 65 warnings on the Zantac label—such as providing a warning on retail store shelf labels, internet notices, or other public advertising (see Opp. at 29-32)—where the Brand Defendants do not control retail store shelf signage, do not sell Zantac to consumers through the internet, and cannot plausibly provide warnings to consumers through advertising unconnected to the point of sale or affixed to the product itself. Moreover, because FDA-regulated "labeling" includes written materials that accompany an OTC drug, a store-shelf label may not

[1] To the extent Plaintiff relies on documents subject to judicial notice, this Court need not accept the contents of these documents as true. *See, e.g., Fremont Indem. Co. v. Fremont Gen. Corp.*, 148 Cal. App. 4th 97, 113 (2007).

include information that conflicts with federal OTC labeling requirements. 21 U.S.C. § 321(m); *see Am. Meat Inst. v. Leeman*, 180 Cal. App. 4th 728, 752-53 (2009) (describing caselaw demonstrating that "labeling" includes store-shelf warnings and other items "given away with the sale of products") (citing *Kordel v. United States*, 335 U.S. 345 (1948)).

Finally, Plaintiff's argument that Brand Defendants could have somehow reduced or eliminated NDMA from Zantac is not relevant to a Proposition 65 claim. Plaintiff concedes that its Proposition 65 claim does not depend on whether defendants could have reduced NDMA; rather the essential elements of the claim are that there was an exposure to a toxicant and that no warning was provided. *Physicians Comm. for Responsible Med. v. KFC Corp.*, 224 Cal. App. 4th 166, 181 (2014) (noting it is an "essential element of a Proposition 65 claim that the [defendants] failed to give 'clear and reasonable warning' that its customers were being exposed to a carcinogenic chemical").

The Second Amended Complaint should be dismissed with prejudice because the Brand Defendants could not comply with both Proposition 65 and federal law.

II. FEDERAL OTC DRUG REGULATIONS PREEMPT A REQUIREMENT TO PROVIDE A PROPOSITION 65 WARNING

A. Federal Regulations Govern OTC Drug Labeling and a Proposition 65 Warning Cannot Be Added to the Label Under 21 C.F.R. 201.66

The Brand Defendants have demonstrated that 21 C.F.R. § 201.66 does not permit a Proposition 65 warning on the label of an OTC drug, and Plaintiffs do not argue otherwise. That is because a Proposition 65 warning, unlike the warnings permitted on OTC labels, does not communicate clinical or therapeutic information that advises the consumer whether they should or should not use the product. *See* Br. at 18-19. Moreover, as argued in the Brand Defendants' Demurrer, federal regulations dictate every aspect of an OTC product label down to the format and the font and § 201.66 limits warnings to specific categories, such as warnings for allergic reaction, liver or stomach issues, flammability, sexually transmitted diseases, serious contraindications ("Do not use"), preexisting conditions ("Ask a doctor before use if you have"), serious side effects ("Stop use and ask a doctor if"), and pregnancy-related information. *See* 21 C.F.R. §201.66(c)(5). A Proposition 65 warning is not within the scope of any warning contemplated by § 201.66. Accordingly, under § 201.66, Proposition 65 warnings are barred from OTC labeling.

Moreover, the inclusion of additional warnings outside those in the format specified by FDA would frustrate FDA's objective of providing clear, readable, and simple product labels for OTC drugs. In 1999, the FDA enacted § 201.66 to simplify the OTC label after conducting "extensive research on how consumers use OTC drug product labels," and finding that a "standardized format" was required to "help people compare and select OTC medicines."[2] The inclusion of a Proposition 65 warning would frustrate FDA's objective of standardized and clear labeling for OTC drug products. *See Dowhal v. SmithKline Beecham Consumer Healthcare*, 32 Cal. 4th 910, 929 (2004) (finding federal law preempted Proposition 65 warning because it would "stand as an obstacle" to FDA's policy of encouraging pregnant women to use smoking cessation product).[3]

Plaintiff has no response other than citation to the exclusion of Proposition 65 claims from federal law's *express* preemption of state-law regulation of OTC products, 21 U.S.C. § 379r(d)(2), which says nothing about whether *implied conflict* preemption nonetheless applies. *See Dowhal*, 32 Cal. 4th at 926 (noting U.S. Supreme Court "has never interpreted a savings clause so broadly as to permit a state enactment to conflict with a federal regulation scheme"); *see also Sprietsma v. Mercury Marine*, 537 U.S. 51, 65 (2002) (noting "Congress' inclusion of an express pre-emption clause 'does *not* bar the ordinary working of conflict pre-emption principles'" (quoting *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 869 (2000)).

B. <u>Plaintiff Fails To Allege That A Proposition 65 Warning Is Made Possible By The CBE Regulation's Narrow Exception For Warnings For Clinically Significant Hazards</u>

Plaintiff fails to plead facts to show Brand Defendants were permitted to unilaterally add a Proposition 65 warning through the CBE process. In the context of preemption, to state a failure-to-warn claim that survives FDCA preemption, "a plaintiff must plead a labeling deficiency that [Defendants] could have corrected using the [CBE process]." *See Gibbons v. Bristol-Myers Squibb*

[2] FDA, "OTC Drug Facts Label," *available at* https://www.fda.gov/drugs/information-consumers-and-patients-drugs/otc-drug-facts-label (last visited April 11, 2021).

[3] Plaintiff is incorrect that *Dowhal* is an "outlier" because it included "direct agency statements confirming the unavoidable conflict between state and federal law." Opp. at 23. To the contrary, the U.S. Supreme Court has not required express agency statements to find implied conflict preemption. *See, e.g., Geier*, 529 U.S. at 883 (finding obstacle preemption and placing only "some weight" on the Department of Transportation's interpretation of Congress' objectives and rejecting the requirement for "a specific expression of agency intent to pre-empt").

Co., 919 F.3d 699, 708 (2nd Cir. 2019). The CBE process permits Brand Defendants to add a warning to the label for Zantac only in specific, narrow circumstances that do not include a Proposition 65 warning. Br. at 20-22. As argued (*see* Br. at 12-13, 20-22), a Proposition 65 warning noting possible exposure to a listed chemical does not constitute a "contraindication, warning, precaution, or adverse reaction," nor does it pertain to a "clinically significant hazard" for which "reasonable evidence of a causal association" with the drug exists. *See* 21 C.F.R. § 314.70(c)(6)(iii); § 201.57(c)[4]; *see also Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1679 (2019) ("[M]anufacturers cannot propose a change that is not based on reasonable evidence.").

Plaintiff nevertheless insists that a Proposition 65 warning could be added to Zantac through the CBE process by relying on the bare assertion that "NDMA is a potential carcinogen." *See* Opp. at 32-33. But the SAC alleges neither the existence of a clinically significant cancer risk associated with Zantac, nor any explanation of how the message allegedly required by Proposition 65 would communicate clinically significant information about such a hazard, all of which must be pleaded to invoke the CBE process and defeat preemption. *See* Br. at 20-21; *Cryolife, Inc. v. Superior Court*, 110 Cal. App. 4th 1145, 1152 (2003); *see also* SAC ¶¶ 22-23 (pleading the presence of NDMA at unspecified levels without pleading a reasonable causal association between Zantac and cancer).

The CBE process and its requirements are "intended to ensure that scientifically valid and appropriately worded warnings will be provided in the approved labeling for medical products, and to prevent overwarning, which may deter appropriate use of medical products, or overshadow more important warnings." 73 Fed. Reg. at 49,605-06; *see also Albrecht*, 139 S. Ct. at 1673 (observing that overwarning "could discourage appropriate use of a beneficial drug").

Finally, neither the pleadings nor judicially noticeable record suggests that FDA exercised its recall authority or otherwise came to any conclusions about the safety of Zantac or any causal association with cancer. Plaintiff misconstrues the FDA's response to the discovery of the potential

[4] S*ee* 21 C.F.R. § 314.70(c)(6)(iii)(A) ("To add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter[.]").

presence of NDMA in ranitidine to argue, falsely, that the FDA determined Zantac presents a risk of cancer. The FDA did not "ban" Zantac, nor did it issue a recall pursuant to 21 C.F.R. § 7.45. *See* Opp. at 33 (citing SAC ¶36; Apotex RJN, Exh. 8). Rather, as the record makes clear, the FDA issued a request for voluntary market withdrawal. Apotex RJN, Exh. 8.

III. PLAINTIFF'S ALTERNATIVE WARNINGS METHODS ARE NOT AVAILABLE TO BRAND DEFENDANTS, NOR WOULD THEY COMPLY WITH FEDERAL LAW

Plaintiff's insistence that Brand Defendants—which are manufacturers but not retailers of Zantac—could have supplied consumers with a Proposition 65 warning by displaying signs or shelf tags in physical retail locations, posting internet warnings, or engaging in public advertising is both factually implausible and unavailing as a matter of law. *See* Opp. at 30-32. "Promotional materials" not regulated by the FDA cannot reasonably be said to include a Proposition 65 warning about carcinogens, the purpose and effect of which is to discourage use. Regardless, such warnings cannot deviate from the language approved in the NDA for Zantac, without compliance with both federal labeling requirements and the CBE process.

First, Brand Defendants are not retailers, and the SAC does not allege otherwise. Contrary to the Opposition (Opp. at 31-32), but consistent with the SAC, Brand Defendants neither maintain retail locations, online stores, nor otherwise engage in direct to consumer sales of Zantac. As such, Brand Defendants have no ability to post physical warning signs or shelf tags. Plaintiff fails to explain, because it cannot, how such warnings could ever be employed by Brand Defendants. Opp. at 31-32. Likewise, Brand Defendants cannot provide internet warnings to consumers (*contra* Opp. at 29), when they do not sell Zantac directly to consumers through online channels—nor does the SAC allege otherwise. *See* SAC ¶¶ 11, 12 (asserting only generally that Brand Defendants "manufacture[], distribute[], and/or sell[] the Products"). The Opposition's argument to the contrary is irreconcilable with how Brand Defendants operate, and Plaintiff's own pleadings.

Second, beyond the hurdle of posting warnings on physical shelf space to which manufacturers lack access, such warnings would still require the approval of the FDA, whose regulations regulating and defining labeling encompass and control Plaintiff's proposed alternative mediums. *See* Br. at 10-12. Under the FDCA, "labeling" embraces "all labels and *other written,*

printed, or graphic matter (1) upon any article or any article or any of its containers or wrappers, or (2*) accompanying such article*." 21 U.S.C. § 321(m) (emphasis added). This definition includes materials that supplement or explain the product, and therefore "accompany" it, such as warnings. *Strayhorn v. Wyeth Pharmaceuticals, Inc.*, 737 F.3d 378, 394 (6th Cir. 2013) (quoting *Kordel v. United States*, 335 U.S. 345, 349-50 (1948)) (noting an article or thing "is accompanied by another when it supplements or explains it … No physical attachment one to the other is necessary").[5]

The case cited by Plaintiff, *American Meat Institute v. Leeman*, is in accord. 180 Cal. App. 4th 728 (2010). There, the Court of Appeal held that point of sale warnings, like those suggested by Plaintiff here, constituted "labeling" within the meaning of the Federal Meat Inspection Act, which the Court found mirrored the definition of "labeling" in the FDCA. *Id*. at 757.[6] In *American Meat Institute*, the Court of Appeal considered and distinguished the reasoning of *Chem. Specialties Mfrs. Ass'n, Inc. v. Allenby*, 958 F.2d 941 (9th Cir. 1992), which limited the definition of labeling under the Federal Insecticide, Fungicide, and Rodenticide Act to materials accompanying the product during the period of use. *Am. Meat Inst.*, 180 Cal. App. 4th at 758-59. Plaintiff's point-of-sale warning is regulated as "labeling" under the FDCA, and cannot be added to the Zantac label under 21 C.F.R. § 201.66 or through the CBE process, as demonstrated above. In fact, the sole case Plaintiff cites to support for his non-labeling warning proposal, *Dowhal*, held that federal law preempted point-of-sale and other public advertising warnings for the same reason as label-based warnings. *See Dowhal*, 32 Cal. 4th at 929 ("[W]arnings through point-of-sale posters or public advertising" were preempted by the FDCA where they "could have the same effect of frustrating the purpose of the federal policy").

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[5] The FDA's Guidance to Industry on Labeling OTC Human Drug Products advises that the Food, Drug and Cosmetic Act "defines labeling in *broad* terms," that includes for example, not only the "outer carton" or "package insert," but also "a brochure about the drug product." *Available at* https://www.fda.gov/media/76481/download.

[6] The other cases cited by Plaintiff fail to definitively interpret "labeling" under the FDCA. In *Allenby*, the court limited "labeling" under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) to be restricted to material that will "accompany the product during the period of use," but the court did not consider whether materials supplementing or explaining the product can be said to "accompany" the product. *Chem. Specialties Mfrs. Ass'n, Inc. v. Allenby*, 958 F.2d 941, 946 (9th Cir. 1992). The definition of labeling at issue in *Cotter*, under the Federal Hazardous Substances Act (FHSA), included accompanying literature only where it contained "directions for use." *People ex rel. Lungren v. Cotter & Co.*, 53 Cal. App. 4th 1373, 1396 (1997). Those cases are therefore distinguishable on their facts and involve different regulatory schemes that offer different definitions of labeling.

Plaintiff attempts to circumvent this result by arguing that the FDCA does not regulate the *advertising* of OTC drugs, citing only to a "Questions and Answers" webpage on the FDA's website for support, which states that the "Federal Trade Commission (FTC) is responsible for regulating OTC drug ads." Opp. at 30.[7] Plaintiff fails to explain how a point-of-sale warning of a carcinogen could somehow qualify as promotional advertisement for an OTC drug, rather than supplemental and explanatory material accompanying the product.

Finally, California law compels the same result. Proposition 65 expressly exempts from its warning requirements any exposures "for which federal law governs warning in a manner that preempts state authority." Cal. Health & Safety Code § 25249.10(a). Yet, Plaintiff offers no support for the proposition that the legislature intended to apply a different meaning to the plain language of the statute. Where federal law governs a product's warnings and precludes a Proposition 65 warning, as it does here, Proposition 65 does not apply.

IV. THE ALLEGED POSSIBILITY OF DIFFERENT MANUFACTURING PROCESSES OR FORMULATIONS CANNOT DEFEAT PREEMPTION OR AVOID DISMISSAL

Perhaps recognizing that any Proposition 65 warning is foreclosed by federal law, Plaintiff instead focuses its Opposition on claims that the Branded Defendants could have avoided liability by making changes to manufacturing, storage, or transportation methods, implementation of additional testing that would reduce or eliminate the risk of NDMA formation, or by ceasing to sell ranitidine altogether. Opp. at 23-26. Plaintiff cannot avoid federal preemption by recharacterizing a Proposition 65 claim to regulate the composition, manufacturing, or storage of products, rather than as a warning claim.

Nothing in Proposition 65 or its regulations requires a defendant to reformulate an FDA-approved product or modify its manufacturing, storage, and testing processes to reduce or eliminate a purported toxicant. Rather, under the statute that authorizes Plaintiff's actions, Cal. Health & Safety Code § 25249.6, exposures to listed carcinogens, by themselves, are not actionable; the law

[7] Plaintiff appears to base this argument on a 1971 Memorandum of Understanding between the FDA and FTC, which delegates the enforcement of the truth or falsity of statements in OTC drug advertising, but not labeling, to the FTC. *See* https://www.fda.gov/about-fda/domestic-mous/mou-225-71-8003.

only prohibits exposures to listed chemicals *without a clear and reasonable warning*. To adjudicate liability here, the court need not determine whether defendants could have reduced NDMA; only that there was an exposure and that no warning was provided. *Physicians Comm. for Responsible Med. v. KFC Corp.*, 224 Cal. App. 4th 166, 181 (2014) (noting it is an "essential element of a Proposition 65 claim that the [defendants] failed to give 'clear and reasonable warning' that its customers were being exposed to a carcinogenic chemical").

Although Plaintiff argues that Brand Defendants could have complied with Proposition 65 by reducing or eliminating NDMA (Opp. at 23-27), Plaintiff's allegations in the Complaint confirm that its Proposition 65 claim are predicated on a failure to warn, rather than about reducing the risk of NDMA formation. Plaintiff accordingly framed its claim as a failure to warn, and Plaintiff alleged that Defendants failed to provide "clear and reasonable warnings" about NDMA to consumers. SAC ¶2; *see, e.g.*, SAC ¶1 ("continuing failure to warn"), ¶3 ("Defendants' conduct thus violates the warning provision of Proposition 65"), ¶26 ("No clear and reasonable warning is provided"), ¶27 ("failure to provide warnings"). The face of Plaintiff's Complaint confirms that this court need not determine whether defendants could have reduced NDMA in considering Plaintiff's Proposition 65 claim.

To determine whether a preemption defense applies, courts must determine "whether a private party can act sufficiently independently under federal law to do what state law requires." *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 623 (2011). Plaintiff alleges both elements of a Proposition 65 cause of action, exposure and failure to warn, but where federal law prohibits Brand Defendants from providing the warning, state law is preempted. *See id.* Plaintiff cites no authority to the contrary[8] and ignores the vast body of case law rejecting its position.

Finally, as pleaded, Plaintiff's hypothetical possibilities that Brand Defendants could have

[8] The district court's decision in the Zantac MDL is in accord. *In re Zantac (Ranitidine) Prods. Liab. Litig.* (S.D. Fla. Jan. 8, 2021) 2021 U.S. Dist. LEXIS 4006, 2020 WL 7864213 ("The Court similarly is not aware of any authority providing that generic drug manufacturers or repackagers can change storage and transportation information on labeling without FDA pre-approval while remaining in compliance with federal law."). Indeed, so are the MDL plaintiffs. *Id*. ("Plaintiffs acknowledged during the Hearing that "changing the storage and transport conditions to the extent that it could impact the identity, quality, and purity profile of the drug and pose risk to the ultimate consumer would constitute a major change.").

used "cleaner ingredients and manufacturing processes and more careful storage techniques," SAC ¶24, do not necessarily defeat preemption here. *Mensing*, 564 U.S. at 623 (rejecting various hypothetical possibilities for compliance with state and federal law).[9]

Accordingly, Plaintiff's arguments that Brand Defendants should have reduced or eliminated NDMA exposures in Zantac to comply with both federal law and Proposition 65 fail.

V. CONCLUSION

Brand Defendants cannot fulfill, and could not have fulfilled, the requirements of Proposition 65 as sought in Plaintiff's SAC without violating federal law. Such requirements under state law are preempted and unenforceable under the Supremacy Clause. For these reasons, and the reasons stated in Brand Defendants' Demurrer, the SAC must be dismissed with prejudice.

Dated: April 12, 2021

DLA PIPER LLP (US)

By: _____

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[9] Plaintiffs acknowledge that Branded Defendants need not have stop selling Zantac to avoid Proposition 65 liability. Opp. at 26, n.14; *see also Mutual Pharmaceutical Co. v. Bartlett*, 570 U.S. 472, 489 (2013) (holding that plaintiffs' "stop selling rationale" is squarely rejected by the U.S. Supreme Court in *Bartlett* "as incompatible with [the Court's] preemption jurisprudence.").

PROOF OF SERVICE

I, Selena Paradee, declare:

I am a citizen of the United States and employed in Sacramento, California. I am over the age of eighteen years and not a party to the within-entitled action. My business address is DLA Piper LLP (US), 400 Capitol Mall Ste 2400, Sacramento, CA 95814. On April 12, 2021, I served a copy of the within document(s):

DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S REPLY IN SUPPORT OF DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT

☐ by transmitting via facsimile the document(s) listed above to the fax number(s) set forth below on this date before 5:00 p.m.

☐ by placing the document(s) listed above in a sealed envelope with postage thereon fully prepaid, the United States mail at Sacramento, California addressed as set forth below.

☐ by personally delivering the document(s) listed above to the person(s) at the address(es) set forth below.

☒ by transmitting via e-mail or electronic transmission the document(s) listed above to the person(s) at the e-mail address(es) set forth below.

SEE ATTACHED SERVICE LIST

I declare under penalty of perjury under the laws of the State of California that the above is true and correct.

Executed on April 12, 2021, at Sacramento, California.

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY; TARGET CORPORATION; APOTEX CORP.; GRANULES PHARMACEUTICALS, INC.; GRANULES USA, INC.; 7-ELEVEN, INC.; SANOFI-AVENTIS U.S. LLC; CHATTEM INC.; DR. REDDY'S LABORATORIES LOUISIANA, LLC; DR. REDDY'S LABORATORIES, INC. and DOES 1 to 20, inclusive.

Defendants.

Case No. RG20054985

Assigned for All Purposes to
Hon. Winifred Y. Smith - Dept 21

REPLY IN SUPPORT OF GENERIC MANUFACTURER DEFENDANTS' AND RETAILER DEFENDANTS' DEMURRERS TO PLAINTIFF'S SECOND AMENDED COMPLAINT

RESERVATION NOS: R-2242700; R-2240283; R-2242157; R-2240276;

Hearing Date	**April 30, 2021**
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Trial Date:	None Set

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Perrigo Company, Granules Pharmaceuticals, Inc., Granules USA, Inc., Dr. Reddy's Laboratories Louisiana, LLC, and Dr. Reddy's Laboratories, Inc. ("Generic Manufacturer Defendants") and Target Corporation and 7-Eleven, Inc. ("Retailer Defendants") file this Reply in support of their respective demurrers, and further state as follows:

I. INTRODUCTION

Under well-settled controlling authority, reinforced by a vast body of persuasive authorities, any claim brought against a generic-drug manufacturer or seller premised on issuing a new or different warning to consumers is preempted as matter of federal impossibility-preemption law. The Supreme Court's *Mensing* and *Bartlett* opinions,[1] and dozens of decisions applying them,[2] hold that such warnings claims are preempted because they conflict with the duty of "sameness" imposed by the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 301 *et seq.* and its implementing regulations to use only the warnings on the equivalent brand-name drug's label. Contrary to Plaintiff's arguments, this substantial body of preemption law applies here and mandates the dismissal of Plaintiff's one-count Proposition 65 claim.

Plaintiff tries to save its preempted claim by mischaracterizing it as something more than a warnings claim. Plaintiff presents the Proposition 65 provision underlying its claim—Cal. Health & Safety Code Section 25249.6 ("Section 6")—as a statute that can be satisfied by either (1) issuing a warning or (2) reducing or "eliminating the exposure." Pl.'s Opp. at 11, 24. But this argument is completely irrelevant because it ignores Cal. Health & Safety Code Section 25249.10(a) ("Section 10(a)"), which unambiguously states that when there is "exposure for which federal law governs warning in a manner that preempts state authority" Proposition 65's requirements "shall not apply." Section 10(a)'s plain language and *Mensing's* holding that Generic Manufacturer and Retailer Defendants ("Generic Defendants") are preempted from issuing novel *warnings* to consumers are sufficient, alone, to mandate dismissal of Plaintiff's claim.

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[1] *PLIVA, Inc. v. Mensing* (2011) 564 U.S. 604; *Mut. Pharm. Co. v Bartlett* (2013) 570 U.S. 472.

[2] This includes numerous authorities cited in Retailer Defendants' demurrer holding that state-law claims brought against retailers and other companies that do not hold ANDAs for the generic drugs they sell must be dismissed as preempted. Plaintiff failed to respond to any of these authorities.

Plaintiff's brief also mischaracterizes Section 6 as more than a warnings provision. It is not. Even the operative complaint recognizes Section 6 as "the warning provision of Proposition 65." *See* Second Am. Compl. ¶ 3. Indeed, a company manufacturing a product for sale in California can comply with Proposition 65 *even if* the product will expose consumers to cancer-causing chemicals above regulatory safe harbor levels, so long as it is accompanied by an appropriate warning. Thus, applying the principles of *Mensing* to Section 6 produces the same result: preemption and dismissal of Plaintiff's claim.

Plaintiff's remaining arguments are no better. Plaintiff repeats the already-rejected view that it can elude impossibility preemption by simply framing its alternative warnings as something other than "labeling," such as "advertising." But dozens of courts, including every federal Circuit Court to consider the issue, have held that such "failure to communicate" claims are also preempted under *Mensing* because warnings publicized to consumers by means other than the actual label fixed to the product are still "labeling" under the FDCA. The Court cannot simply ignore these rulings. As the *Zantac* MDL court recently held, a trial court is not free to issue a preemption ruling that would "render the vast body of pre-emption caselaw in the drug context, including binding Supreme Court decisions, meaningless."[3] Plaintiff also misrepresents the *Zantac* MDL court's recent decision to defer judgment on preemption of some *unpleaded* theories of liability as a decisive final judgment in its favor. It invents an OTC drugs loophole, suggesting that all claims related to non-prescription drugs are not preempted under *Mensing*—a proposition rejected by numerous courts applying implied preemption to OTC generic drug products.

Last, Plaintiff speculates that various adjustments to ranitidine's design or manufacture *might* reduce or remove the NDMA risk, allegations that are entirely irrelevant to Section 6's warning requirement or to the preemption of Plaintiff's claim. The Demurrer should be sustained with prejudice.

[3] *In re Zantac (Ranitidine) Prods. Liab. Litig.* (S.D. Fla. 2020) No. 2924 20-MD-2924, 2020 WL 7864213 at *13.

II. ARGUMENT

A. *Mensing* preemption disposes of Plaintiff's Proposition 65 claim.

1. Applying *Mensing* and Section 10(a), Plaintiff's Proposition 65 claim is preempted and must be dismissed.

Generic Defendants' threshold argument (*see* Generic Manufacturer Defendants' Mem. at 4-6) is that Section 10(a) means exactly what it says: Proposition 65's requirements "shall not apply to . . . [a]n exposure for which federal law governs warning in a manner that preempts state authority." Cal. Health & Safety Code 25249.10(a). Applying the clear and unambiguous wording of Section 10(a) along with the controlling holding of *Mensing* (*i.e.*, that federal law preempts generic-drug manufacturers or sellers from issuing a novel warning because it is impossible for them to do so without violating the federal duty of "sameness"), requires the dismissal of Plaintiff's one-count complaint.

Contrary to Plaintiff's straw-man argument, Generic Defendants are not attempting to construe Section 10(a) as "operat[ing] more broadly than the Federal Constitution." *See* Pl.'s Opp. at 11, 36-38. In fact, Generic Defendants' position is simply that Section 10(a) requires deference to the controlling authority of *Mensing*, *i.e.*, "federal law [that] governs warning in a manner that preempts state authority." Thus, Generic Defendants are not asking the Court to exceed *Mensing's* already broad preemptive scope but rather to apply *Mensing* as it is. The significance of Section 10 (a) is that it explicitly clarifies that the existence of federal law preempting **warnings** suffices to exempt a company from liability under Proposition 65 Section 6. Thus, Plaintiff's discussion of potential changes to manufacturing or storage practices is irrelevant to the preemption analysis here.

In response, Plaintiff insists that Section 10 (a) "simply recognizes where the state's authority under Proposition 65 is *preempted as to a particular exposure*, Proposition 65 does not apply to that exposure." Pl.'s Opp. at 37 (emphasis added). Thus, while the actual text of Section 10(a) *provides* that "[Section 6] shall not apply to . . . an exposure for which federal law **governs warning in a manner that** preempts state authority," *see* Cal. Health & Safety Code Section 25249.10 (emphasis added), Plaintiff effectively proposes that Section 10(a) should be

interpreted to mean that "[Section 6] shall not apply to . . . an exposure for which federal law . . . preempts state authority."

The flaw in this proposal is immediately obvious—it would require the Court to ignore language at the heart of Section 10(a). But the Court cannot simply ignore the words of Section 10(a), as doing so would offend the bedrock principle that when "faced with a question of statutory interpretation," courts "look first to the language of the statute" and "strive to give effect and significance to every word and phrase." *See Copley Press, Inc. v. Superior Court* (2006) 39 Cal. 4th 1272, 1284. "In interpreting a voter initiative," like Proposition 65, courts "apply the same principles that govern statutory construction." *See Styrene Info. & Research Ctr. v. Office of Envtl. Health Hazard Assessment* (2012) 210 Cal. App. 4th 1082, 1096. As the *Styrene Info.* court held in the context of interpreting Proposition 65, when the statutory language is clear, courts "need go no further." *Id.* Here, Section 10(a) provides that when federal law governs warnings in a preemptive manner (which *Mensing* held is true for generic drugs) then no Proposition 65 claim may lie. Thus, the Court should grant Generic Defendants' demurrers based on *Mensing* and the plain and unambiguous terms of Section 10(a)

There is no reason for the Court to strain to avoid Section 10(a)'s plain language by, as Plaintiff suggests, ignoring key statutory text entirely in favor of Proposition 65 ballot materials or other policy considerations. *See* Pl.'s Opp. at 36-38. But even if such extrinsic materials are considered, it would not sway the result. Plaintiff's primary argument is that construing Section 10(a) "to mean that any time a federal warning requirement precludes a warning relating to a given exposure, Proposition 65 is wholly preempted" would produce "surprising" or "absurd" results in that it would exempt companies from the requirements of Section 6 even though, according to Plaintiff, Section 6's requirements can also be met through taking actions "other than a warning (such as reformulation)." *Id.* Of course, there is no discrepancy between the two sections if the Court concludes (as it should) that when read in concert they show Proposition 65 is a right-to-know warnings statute that requires only giving a warning to consumers about the presence of a carcinogenic or toxic chemical. That is the position taken by Plaintiff in its own complaint and echoed in the cases Plaintiff relies on. *See infra*, Part A.2. Moreover, even if the

Court were willing to overlook the flaws in Plaintiff's argument that there are multiple pathways to satisfy Proposition 65—*i.e.*, that it lacks legal support and contradicts CEH's own pleaded allegations—the argument still would not justify interpreting Section 10(a) contrary to its plain language. Even if there are multiple pathways to satisfy Section 6, it would hardly be "absurd" to interpret Section 10(a) as exempting a company from liability when the more straightforward of those pathways (adding a warning) is foreclosed by the preemptive force of federal law.

2. Applying *Mensing* to Section 6 also requires the preemption and dismissal of Plaintiff's Proposition 65 claim.

This is a failure-to-warn case under Proposition 65, which seeks to compel an NDMA cancer warning as its remedy. The opening paragraph of Plaintiff's Second Amended Complaint leaves no doubt that it "seeks to remedy Defendants' continuing *failure to warn* individuals in California that they are being exposed to n-nitrosodimethylamine ("NDMA"), a chemical known to the State of California to cause cancer." Second Am. Compl. ¶ 1 (emphasis added). The next paragraph alleges that Defendants violated Proposition 65 by not "providing clear and reasonable warnings" about NDMA to ranitidine consumers. *Id.* ¶ 2. The third paragraph reiterates that Defendants' conduct "violates the warning provision of Proposition 65, Health & Safety Code § 25249.6." *Id.* ¶ 3.

Plaintiff's factual allegations likewise reinforce that its Proposition 65 claim is one for failure to warn. Plaintiff alleges that NDMA forms "when nitrates and amino acids combine" (*id.* ¶ 23), that "individuals are exposed to NDMA through the average use of the Products" (*id.* ¶ 25), and the "primary route of exposure is through ingestion when individuals use the Product." *Id.* Plaintiff complains that "[n]o clear and reasonable warning is provided" regarding NDMA and criticizes the "failure to provide warnings regarding the carcinogenicity of NDMA in Products . . . in light of evidence that ingestion of NDMA causes cancer." *Id.* ¶¶ 26, 27.

Likewise, the operative complaint's single cause of action alleges that "Defendants have failed, and continue to fail, to provide clear and reasonable warnings regarding the carcinogenicity of NDMA to users" and "violated Proposition 65 by . . .exposing individuals to NDMA without first giving clear and reasonable warnings . . . regarding the carcinogenicity of

NDMA." *Id.* ¶¶ 44-45. The prayer for relief calls for civil fines and injunctive relief preventing "Defendants from offering Products for sale in California without providing prior clear and reasonable warnings." *See id.*

In light of these allegations throughout the operative complaint, there is no basis for Plaintiff's belated and unconvincing attempt to reframe its Proposition 65 Section 6 claim as some claim other than a failure to issue warnings. The statute's plain and unambiguous text shows that an enforcement action under Section 6 is based on a failure to warn: the section unambiguously prohibits businesses from "knowingly and intentionally" exposing individuals to listed chemicals "without first giving clear and reasonable warning to such individuals."[4] And Plaintiff's own cited cases reinforce that Section 6 only "requires that businesses provide warnings before consumers are exposed to [any listed] chemicals." *See Am. Meat Inst. v. Leeman* (2009) 180 Cal. App. 4th 728, 735-36; *see also People ex rel. Lungren v. Cotter & Co.* (1997) 53 Cal. App. 4th 1373, 1376 (holding that "[Section 6] requires warnings for products causing cancer or reproductive toxicity."); *Comm. of Dental Amalgam Mfrs. & Distribs. v. Stratton* (9th Cir. 1996) 92 F.3d 807, 809-10 (Section 6 required "consumer warnings for dental amalgam" after the State of California listed mercury, a chemical present in dental amalgam, as a chemical known to cause reproductive harm).

Plaintiff itself drives home that Section 6 is a warning provision, and that the preemption analysis is therefore concerned **only** with whether federal law conflicts with the issuance of a consumer warning. It quotes *Stratton* as standing for the proposition that "[t]o find that Proposition 65 is preempted [by a federal law], we must determine that ***all*** possible consumer product warnings that would satisfy Proposition 65 conflict with provisions of [that law]." Pl.'s

[4] Plaintiff attempts to sew confusion about the plain language of Section 6 by referring the Court to a materially different provision of Proposition 65, Health & Safety Code Section 25249.5 ("Section 5"). As Plaintiff acknowledges, Section 5 is limited to "drinking water" exposures and has no warning requirement, meaning that it contemplates a remediation of drinking water and not a warning. It is undisputed that Section 5 does not apply to the alleged exposure to NDMA in Generic Defendants' OTC ranitidine product. And Section 6, which *does* apply to the exposure at issue here, is the opposite in expressly requiring clear and reasonable warnings for other exposures to listed substances. Thus, Section 5 is entirely irrelevant to this case and does not lend any support to Plaintiff's proposed construction of Section 6.

Opp. at 22 (quoting *Stratton*, 92 F.3d at 810). Thus, *Stratton* shows that Plaintiff's Section 6 claim is only a warnings claim.

Therefore, based on the allegations in the operative complaint, the plain language of the statute, and the cases on which Plaintiff relies, Plaintiff's Proposition 65 claim is a failure-to-warn claim that is preempted under *Mensing*.

B. Alternative warnings to consumers are still generic-drug "labeling," and the *Mensing* decision preempts all generic-drug labeling claims.

Plaintiff suggests that the U.S. Supreme Court's *Mensing* decision—and the vast body of preemption law applying it—can be negated by simply calling publicized cancer warnings "advertising" instead of FDCA "labeling." Plaintiff has it wrong. A massive body of case law already holds that using alternatives to standard labeling to publicize additional warnings to generic-drug consumers still amounts to a preempted *labeling* change—regardless of whether the product is available by prescription or over the counter. *See, e.g., Greager v. McNeil-PPC, Inc.* (N.D. Ill. 2019) 414 F. Supp. 3d 1137, 1141-42. Product warnings issued by online announcements, letters to doctors or consumers, shelf signs, and any other means are all "labeling" that a generic-drug manufacturer cannot unilaterally alter.

If presenting additional product warnings through public notices or shelf tags were all that was required to defeat federal preemption, failure-to-warn claims against generic-drug manufacturers or retailers would *never* be preempted. As Plaintiff emphasizes, every case that applied impossibility preemption did so because it was *impossible* for the defendant to simultaneously follow both federal and state law. *See* Pl.'s Opp. at 11. If thwarting impossibility preemption in failure-to-warn claims against generic-drug manufacturers or retailers were so simple, every plaintiff would do so. But it is not. The claim here against Generic Defendants is preempted.

1. Warnings to generic-drug consumers are preempted labeling.

Every federal circuit court to consider the "failure to communicate" theory has held that state-law claims that would require generic-drug manufacturers to communicate warning information to physicians or consumers in some fashion different from the FDA-approved

prescribing information or patient labeling are impliedly preempted because, to do so, the generic manufacturer would violate the federal "duty of sameness" in labeling. *Strayhorn v. Wyeth Pharm., Inc.* (6th Cir. 2013) 737 F.3d 378, 394; *Morris v. PLIVA, Inc.* (5th Cir. 2013) 713 F.3d 774, 777; *Lashley v. Pfizer, Inc.* (5th Cir. 2014) 750 F.3d 470, 474; *Johnson v. Teva Pharm. USA, Inc.* (5th Cir. 2014) 758 F.3d 605, 611; *In re Darvocet, Darvon, & Propoxyphene Prods. Liab. Litig.* (6th Cir. 2014) 756 F.3d 917, 932-33; *McDaniel v. Upsher-Smith Labs., Inc.* (6th Cir. 2018) 893 F.3d 941, 945-47; *Brinkley v. Pfizer, Inc.* (8th Cir. 2014) 772 F.3d 1133, 1139; *Schrock v. Wyeth, Inc.* (10th Cir. 2013) 727 F.3d 1273, 1286.

Trial courts that have considered the issue, including the *Zantac* MDL court, have held likewise:

- The *Zantac* MDL court held that "claims against generic drug manufacturers for failure to communicate information to consumers or medical providers, where the manufacturers of the listed brand-name drugs have not done so, are pre-empted." *In re Zantac (Ranitidine) Prods. Liab. Litig.* (S.D. Fla. Dec. 31, 2020) No. 2924 20-MD-2924, 2020 WL 7864585 ("*Zantac II*"), at *15.
- The *Fosamax* MDL court joined "the majority of other courts to consider this issue in holding that any claims stemming from the generic manufacturer defendants' alleged failure to communicate additional warnings through **some method other than** their [standard labeling] are preempted." *In re Fosamax Prods. Liab. Litig.* (S.D.N.Y. 2013) 965 F. Supp. 2d 413, 419 (emphasis added);
- The Southern District of New York also held that when a plaintiff "allege[d] inadequate warnings not only in [the generic contraceptive's] packaging but also in Defendants' communications with healthcare providers and **advertisements to the public** . . . [t]he preemption of failure-to-warn claims extends to these latter types of communications as well." *Montero v. Teva Pharm. USA Inc.* (S.D.N.Y. 2020) 2020 WL 1862693, at *3 (emphasis added); *see also Gardley-Starks v. Pfizer, Inc.* (N.D. Miss. 2013) 917 F. Supp. 2d 597, 609 (holding similarly); *Moretti v. Mut. Pharm. Co.* (D. Minn. 2012) 852 F. Supp. 2d 1114, 1118 (holding similarly);

- The federal Middle District of Florida held that a claim against a manufacturer of generic metoclopramide was preempted to the extent that the plaintiff argued that the manufacturer should have provided different or additional information to consumers beyond the existing warnings on the equivalent brand-name label. *Metz v. Wyeth* (M.D. Fla. 2012) 872 F. Supp. 2d 1335, 1340; and
- The federal District of Nevada rejected the argument that a manufacturer of generic metoclopramide can be held liable for "failure to communicate" warnings by "tools" *other than* standard labeling—exactly the theory that Plaintiff here contends would defeat implied federal preemption. *Moretti v. PLIVA, Inc.* (D. Nev. 2012) No. 2:08-CV-00396-JCM (CWH), 2012 WL 628502.

This large and steadily growing body of law repeatedly rejects Plaintiff's brisk assurance that this Court can sidestep *Mensing* by viewing Proposition 65 NDMA warnings as information communicated to ranitidine consumers that somehow does not supplement the product labeling or conflict with generic manufacturers' duty of sameness. Plaintiff invites legal error.

2. Proposition 65 point-of-sale shelf signs are preempted labeling.

Controlling California case law aligns with the federal cases discussed above, and supports a holding here that posting Proposition 65 NDMA warning signs on store shelves next to ranitidine would likewise impose a "labeling" requirement under the FDCA and, thus, be preempted as a matter of law under *Mensing*. The *only* on-point California state appellate authority—*American Meat Institute. v. Leeman* (2009) 180 Cal. App. 4th 728, which is binding authority on this Court—holds that point-of-sale warnings signs **are** "labeling" under the FDCA. In arguing to the contrary, Plaintiff grossly mischaracterizes the facts and holding of *American Meat*, as well as the significance of other California state and federal cases discussing point-of-sale labeling.

Presenting three opinions as the purported authoritative body of law addressing "the precise question of whether Proposition 65 point of sale warnings are precluded by federal statutes with the same broad definition of labeling as the FDCA," Plaintiff incorrectly argues that the "weight of authority" holds that such warnings are not "labeling." *See* Pl.'s Opp. at 31-32

(citing *Chem. Specialties Mfrs. Ass'n v. Allenby* (9th Cir. 1992) 958 F.2d 941, *People ex rel. Lungren v. Cotter & Co.* (1997) 53 Cal. App. 4th 1373, and *American Meat Institute. v. Leeman* (2009) 180 Cal. App. 4th 728). Of the three opinions, only two (*American Meat* and *Cotter*) are precedential California state court opinions. And only one controlling precedent (*American Meat*) construes the FDCA's definition of labeling.

Although Plaintiff tries to dismiss it as a "dissenting" case, the *American Meat* opinion is the *only* controlling authority addressing "the precise question of whether Proposition 65 point of sale warnings are precluded by federal statutes with the same broad definition of labeling as the FDCA." *See* Pl.'s Opp. at 32. The *American Meat* plaintiff, like Plaintiff here, had argued that Proposition 65 "point of sale warnings do not constitute 'labeling,' and thus, Proposition 65" shelf warnings would not change any "labeling" under the definition used by the FDCA. 180 Cal. App. 4th at 749. Although the case applied the express-preemption provision of the Federal Meat Inspection Act ("FMIA") (which is not at issue here), the court recognized that the FMIA had adopted the FDCA's definition of "labeling." *Id.* at 749, 752, 757. The court, thus, applied the U.S. Supreme Court's 1948 *Kordel* opinion on what constitutes FDCA labeling and rejected the plaintiff's argument. *Id.* at 752-61 (applying *Kordel v. United States* (1948) 335 U.S. 345). The Court of Appeal held that Proposition 65 "point of sale warnings are 'labeling' within the meaning of the FMIA," a federal statute that uses the FDCA's definition of "labeling." 180 Cal. App. 4th at 761.

In doing so, it not only thoroughly analyzed *Kordel* and decisions applying it, but also distinguished the Ninth Circuit's *Allenby* decision. *Id.* at 752-61. In *Allenby*, the Ninth Circuit had construed the meaning of "labeling" under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"), and restricted FIFRA's definition of "labeling" to material that will "accompany the product during the period of use." 180 Cal. App. 4th at 752-61. (quoting *Allenby*, 958 F.2d at 946). Rejecting *Allenby's* restriction of FIFRA "labeling" to material that is visible "during the period of use," as inapplicable to the FDCA, *American Meat* leaves no room for any California state trial court to apply *Allenby's* definition of labeling for FDA-regulated generic drugs. This Court is just as bound by the *American Meat* decision as by *Mensing*.

The only other published California appellate opinion that Plaintiff cites for this Court, *People ex rel. Lungren v. Cotter & Co.* (1997) 53 Cal. App. 4th 1373, does not help Plaintiff either. *Cotter* applies a much narrower statutory definition of "labeling" under a fundamentally different statute, the Federal Hazardous Substances Act (FHSA). *See* 53 Cal. App. 4th at 1389. As the *Cotter* court explained, Congress "limited a label under the FHSA to mean accompanying literature providing 'directions for use.'" *Id.*; *see also Allenby*, 958 F.2d at 949 (recognizing that FHSA labeling is limited to directions for use). No one has argued—or could seriously argue—that *Mensing* and the FDCA limit the definition of generic-drug "labeling" to only the directions for use.

3. FTC regulation of the truth or falsity of statements in OTC advertising does not strip FDA of its central role in regulating all drug labeling and warnings.

Without citing a single case recognizing an impossibility-preemption loophole for all OTC drugs, Plaintiff nonetheless asks this Court to create just such a loophole. *See* Pl.'s Opp. at 30-31. But the request contradicts existing case law, which upholds impossibility preemption for generic drugs without regard for whether they are prescription or OTC. *See, e.g., Gaeta v. Perrigo Pharms. Co.* (N.D. Cal. 2008) 562 F. Supp. 2d 1091, 1098, *aff'd by* (9th Cir. 2012) 469 F. App'x 556; *Greager v. McNeil-PPC, Inc.* (N.D. Ill. 2019) 414 F. Supp. 3d 1137.

In *Gaeta*, the federal trial court (in a decision initially reversed by the Ninth Circuit but ultimately vindicated by the U.S. Supreme Court's *Mensing* decision) held "that Plaintiffs' causes of action are preempted to the extent that they allow for liability based on a lack of adequate warning on the company's **OTC generic** drug labeling for its 200mg ibuprofen product." *Gaeta* 562 F. Supp. 2d at 1098 (emphasis added); *see PLIVA, Inc. v. Mensing* (2011) 564 U.S. 604, 614-15 (rejecting reasoning of Ninth Circuit's initial *Gaeta* decision).

More recently, the *Greager* court expressly rejected the plaintiff's argument that "the 'duty of sameness' does not apply to over-the-counter drugs." 414 F. Supp. 3d at 1141. In language equally applicable here, the *Greager* court explained that the "key distinction in the relevant regulatory structure and case law is *not between prescription and non-prescription drugs* but between NDA holders and ANDA holders." *Id.* at 1142 (emphasis added). And

because the impossibility-preemption analysis for generic prescription and generic OTC drugs is the same, the *Greager* court held that failure to warn claims against a generic-drug manufacturer and retailer of an OTC generic drug were preempted and must be dismissed. *See id.*

Finally, the *Zantac II* court found that all failure-to-warn claims brought against generic-drug manufacturers and retailers of ranitidine—including those claims related to OTC generic ranitidine—were preempted as a matter of law. 2020 WL 7864213 at *9, *14; 2020 WL 7864585 at *13, *16-*17. Those holdings would not make any sense if, as Plaintiff here suggests, FDCA labeling and impossibility preemption somehow did not apply to OTC products.

Plaintiff's purported contrary authority is no authority at all. Rather, it is a "Questions and Answers" page on the FDA website, which states that the Federal Trade Commission (FTC) oversees OTC drug advertising. *See* Pl.'s Opp. at 30. That website statement, in turn, is based on a 1971 Memorandum of Understanding between the FDA and FTC, which delegates to the FTC the enforcement of the *truth or falsity* of statements in OTC drug advertising, while leaving the FDA responsible for enforcing requirements for OTC drug "labeling." *See* https://www.fda.gov/about-fda/domestic-mous/mou-225-71-8003. Plaintiff's Proposition 65 claim does not implicate the "truth or falsity" of ranitidine "advertising." Rather, it seeks to compel communication of a **warning** about NDMA to consumers. Under the FDCA and controlling case law, such a warning is "labeling" even if communicated via television or the internet. *See* 21 U.S.C. 321(n); *Kordel*, 335 U.S. at 348-50; *Strayhorn*, 737 F.3d at 394

Neither the FDCA nor its federal regulations support Plaintiff's argument that the FDCA does not apply to warning labeling for OTC drugs. To the contrary 21 U.S.C. § 355(j) lists generic ANDA requirements, including labeling requirements, without distinguishing OTC and prescription drugs. *Id.* § 355(j)(2)(A)(v). 21 U.S.C. § 352, relied on by Plaintiff, *see* Pl.'s Opp. 29-30, not only contains certain advertising-specific requirements for prescription drugs, *see* 21 U.S.C. § 352(n) but **also** contains requirements for drug labeling for all forms of human drugs, OTC and prescription. *See* 21 § U.S.C. § 352(a)(1). Likewise, 21 U.S.C. § 321(m) defines FDCA "labeling" without distinguishing between OTC and prescription drugs. Finally, under relevant federal regulations, the FDA expressly regulates the "content and format requirements for the

labeling of all OTC drug products." *See* 21 C.F.R. § 201.66; *see also* §§ 201.60-201.72. Plaintiff's purported loophole for OTC drug preemption simply does not exist, and Plaintiff's claim is preempted.

C. Plaintiff wholly mischaracterizes the *Zantac II* opinion.

Plaintiff's gross mischaracterizations of the *Zantac* MDL court's rulings epitomize its flawed preemption arguments. Dismissing three master complaints, the MDL court held that a wide swath of claims—those alleging a failure to warn of NDMA and that the ranitidine molecule is defective—were federally preempted as a matter of law and dismissed with prejudice. *See In re Zantac (Ranitidine) Prods. Liab. Litig.*, No. 2924 20-MD-2924 ("*Zantac II*") 2020 WL 7864213 (S.D. Fla. Dec. 31, 2020). Among the claims that the MDL court has already found preempted as a matter of law are claims based on generic manufacturers' "product labeling [and] other communications" that must match those of brand manufacturers and "claims based on failure to warn consumers that the products contained NDMA":

> . . . Plaintiffs' claims based on alleged defects in ranitidine products, product labeling, or other communications that Generic Manufacturer Defendants could not independently change while remaining in compliance with federal law are **pre-empted. This includes**, but is not limited to, claims based on allegations that ranitidine products were defectively designed because they break down into NDMA and **claims based on failure to warn consumers** that the products contained NDMA or could break down into NDMA when ingested.

Zantac II, 2020 WL 7864213 at *14 (emphasis added). The MDL court also issued a similar ruling dismissing as preempted all claims against the MDL Retailer Defendants, including dismissal with prejudice of warnings claims. 2020 WL 7864585 at *14, *16. The crux of Plaintiff's claim here remains Generic Defendants' purported failure to warn consumers that ranitidine allegedly contained NDMA. Second Am. Compl. ¶¶ 1-3. That remains preempted as a matter of law.

Although it dismissed all claims, the *Zantac II* court reserved judgment on whether preemption also applied to vaguely pleaded liability theories related to ranitidine's testing, storage, transportation, and expiration dates because the then-operative master complaints failed to adequately plead these theories. Plaintiff misrepresents the *Zantac II* court's decision to defer judgment as a decisive final judgment in its favor. Indeed, the *Zantac II* opinion repeatedly

refrained from deciding whether federal preemption doctrine bars claims over testing, storage and transportation, expiration dates, and manufacturing defects because they were not properly pleaded.[5] The MDL court required re-pleading and supplemental briefing before it would substantively address whether such claims are preempted.

Yet, Plaintiff misconstrues the unremarkable fact that the MDL plaintiffs were given leave to amend their master complaints as creating an ironclad class of "***not*** federally preempted" claims in ranitidine litigation. *See id.* at 24. The *Zantac II* opinion, which dismissed all claims against the generic manufacturers, did not do this. The plain text of the *Zantac II* opinion, which Plaintiff conspicuously avoids quoting, disproves Plaintiff's erroneous summary of the opinion.

D. Plaintiff cannot thwart federal preemption of its Proposition 65 warning claim by raising irrelevant design-defect, manufacturing-defect and expiration date allegations.

As discussed above, Section 6 of Proposition 65 (the sole basis for Plaintiff's one-count claim) is a warnings statute and does not compel manufacturers to re-design products or change their manufacturing practices. Nor has Plaintiff alleged any design- or manufacturing-defect claims. Likewise, Plaintiff has not pleaded any claim for liability based on over-long expiration dates—indeed, the term "expiration date" appears nowhere in the operative complaint. Yet, Plaintiff hopes to muddy the preemption inquiry with vague allegations of *possible* changes that Defendants purportedly could make to their storage or manufacturing processes, or to expiration dates, that *might* eliminate *some* NDMA. None of these allegations matter in a case with no design-defect, manufacturing-defect, or expiration date claims.

[5] *Zantac II*, 2020 WL 7864213 at *16-*17 (holding that the MDL plaintiffs had failed to "state claims based on expiration dates . . . upon which relief can be granted," including failing to identify the basis in state law for a duty to shorten expiration dates and reliance on "allegations that expiration dates for ranitidine products should have been shortened because the products became dangerous over time [that] are inconsistent with their allegations that the products were dangerous upon being manufactured."); *id.* at *19 ("[T]o the extent that it is Plaintiffs' intent to hold Defendants liable for storing ranitidine products under the wrong conditions, such a theory is not pled."); *id.* at *21 ("Plaintiffs have not pled a plausible manufacturing-defect claim. . . . in this posture of the pleadings, the Court is unable to evaluate Defendants' contention that the manufacturing-defect claims are pre-empted.").

"The question for 'impossibility' [preemption] is whether the private party could independently do under federal law what state law **requires** of it." *Mensing*, 564 U.S. at 618, 620 (emphasis added). Here, Proposition 65 does not compel adjustments to expiration dates, manufacturing practices, or storage conditions. Rather, the statute requires just one thing: communicating a Proposition 65-compliant warning to consumers. Because Generic Defendants could not independently do so without violating federal law, the Proposition 65 claim is preempted irrespective of Plaintiff's vague manufacturing, design, and expiration date allegations.

III. CONCLUSION

For these reasons, and those stated in the opening brief, the Court should sustain the Generic Defendants' respective demurrers to Plaintiff's Second Amended Complaint, in their entirety, without leave to amend.

DATED: April 12, 2021

STEPTOE & JOHNSON LLP

By: _____
Dennis Raglin
Attorneys for Defendant
PERRIGO COMPANY

DATED: April 12, 2021

LEWIS BRISBOIS BISGAARD & SMITH LLP

By: _____
Paul Desrochers
Attorneys for Defendant
GRANULES USA, INC.

DATED: April 12, 2021

GORDON REESE SCULLY MANSUKHANI LLP

By: *"signed on behalf of with permission"*
Brian Ledger
Attorneys for Defendants
DR. REDDY'S LABORATORIES, INC.
DR. REDDY'S LABORATORIES LOUISIANA, LLP

DATED: April 12, 2021

NORTON ROSE FULBRIGHT US LLP

"SIGNED ON BEHALF OF WITH PERSMISSION"
BY:
JEFFERY MARGULIES
LAUREN A. SHOOR
ATTORNEYS FOR DEFENDANT TARGET CORPORATION

DATED: April 12, 2021

GREENBERG TRAURIG, LLP

"SIGNED ON BEHALF OF WITH PERSMISSION"
BY:
WILL WAGNER
ATTORNEYS FOR DEFENDANT 7-ELEVEN, INC.

PROOF OF SERVICE

F.R.C.P. 5 / C.C.P. 1013a(3)/ Rules of Court, Rule 2060

I am a resident of, or employed in the County of Los Angeles, State of California. I am over the age of 18 and not a party to this action. My business address is: Gordon Rees Scully Mansukhani 101 W. Broadway, Suite 2000, San Diego, California 92101.

On **April 12, 2021** , I served the following listed document(s), by method indicated below, on the parties in this action: **GENERIC DEFENDANTS' JOINT MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT**

SERVICE LIST ATTACHED

☐ **BY U.S. MAIL**
By placing ☐ the original / ☐ a true copy thereof enclosed in a sealed envelope(s), with postage fully prepaid, addressed as per the attached service list, for collection and mailing at Steptoe & Johnson, LLP 633 West Fifth Street, Suite 1900 in Los Angeles, California 90071, following ordinary business practices. I am readily familiar with the firm's practice for collection and processing of document for mailing. Under that practice, the document is deposited with the United States Postal Service on the same day in the ordinary course of business. Under that practice, the document is deposited with the United States Postal Service on the same day as it is collected and processed for mailing in the ordinary course of business.

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By delivering the document(s) listed above in a sealed envelope(s) or package(s) designated by the express service carrier, with delivery fees paid or provided for, addressed as per the attached service list, to a facility regularly maintained by the express service carrier or to an authorized courier or driver authorized by the express service carrier or to an authorized courier or deliver authorized by the express service carrier to receive documents. **Note:** Federal Court requirement: service by overnight delivery was made ☐ pursuant to agreement of the parties, confirmed in writing, or ☐ as an additional method of service as a courtesy to the parties or ☐ pursuant to Court Order.

☐ **BY PERSONAL SERVICE**
☐ By personally delivering the document(s) listed above to the offices at the addressee(s) as shown on the attached service list.
☐ By placing the document(s) listed above in a sealed envelope(s) and instructing a registered process server to personally delivery the envelope(s) to the offices at the address(es) set forth on the attached service list. The signed proof of service by the registered process server is attached.

☐ **BY ELECTRONIC SERVICE**
(via electronic filing service provider)
By electronically transmitting the document(s) listed above to File & ServeXpress, an electronic filing service provider, at www.fileandservexpress.com . To my knowledge, the transmission was reported as complete and without error. *See* Cal. R. Ct. R. 2.253, 2.255, 2.260.

☒ **BY EMAIL**
(to individual persons)
By electronically transmitting the document(s) listed above to the email address(es) of the person(s) set forth on the attached service list. To my knowledge, the transmission was reported as complete and without error. Service my email was made ☐ pursuant to agreement of the parties, confirmed in writing, or ☐ as an additional method of service as a courtesy to the parties or ☐ pursuant to Court Order. *See* Cal. Rules of Court, rule 2.260.

☐ **BY FACSIMILE**
By transmitting the document(s) listed above from Steptoe & Johnson in Los Angeles, California to the facsimile machine telephone number(s) set forth on the attached service list. Service by facsimile transmission was made ☐ pursuant to agreement of the parties, confirmed in writing, or ☐ as an additional method of service as a courtesy to the parties or ☐ pursuant to Court Order.

I declare under penalty of perjury under the laws of the *State of California* and the *United States of America* that the above is true and correct. Executed on this 12th day of April, 2021, at San Diego, California.

Maria Gonzalez

SERVICE LIST

Center for Environmental Health v. Perrigo Corp., et al.
Case No.: RG20054985

Matter No.: 26550-0005

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4845-9550-3332, v. 2

Exhibit 42

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

Case No. RG 20-054985

ASSIGNED FOR ALL PURPOSES TO:
Hon. Winifred Y. Smith, Department 21

PLAINTIFF'S OMNIBUS SURREPLY TO DEFENDANTS' REPLIES TO PLAINTIFF'S OPPOSITION TO DEMURRERS

Date: April 30, 2021
Time: 10:00 a.m.

Reservation Nos.: R-2240281, R-2240282, R-2240283, R-2240276, R-2242157

SAC Filed: January 4, 2021
Trial Date: None Set

As authorized by the Stipulated Order entered by the Court on February 24, 2021, Plaintiff Center for Environmental Health ("CEH") respectfully submits this surreply brief in response to the three reply briefs filed by (1) Defendants Sanofi-Aventis U.S. LLC and Chattem, Inc. (hereinafter, the "Brand Name Manufacturers"); (2) Defendants Perrigo Company, Granules USA, Inc., Dr. Reddy's Laboratories, Inc., Dr. Reddy's Laboratories Louisiana, LLC, Target Corporation, and 7-Eleven, Inc. (hereinafter, the "Generic Manufacturers/Retailers"); and (3) Defendant Apotex Corp. (hereinafter, "Apotex"), another generic manufacturer of over-the-counter ("OTC") antacid products made with ranitidine as the active ingredient (the "Products").[1]

I. INTRODUCTION

Defendants' reply briefs confirm two fundamental premises of CEH's opposition, each of which undermine Defendants' contention that CEH's claim is preempted by the impossibility doctrine: (1) Defendants can use non-label warning methods such as public advertising to provide Proposition 65 warnings for NDMA exposures; and (2) there are many options to reduce exposures to NDMA – which is an undisclosed contaminant found in the Products – such that no Proposition 65 warning would be required. CEH's opposition details how each of these two methods of compliance with Proposition 65 is not prohibited by any federal statute or U.S. Food and Drug Administration ("FDA") regulation. Defendants' replies fail to provide any meaningful response.

Instead, Defendants submit new authorities for the incorrect assertions that advertising is labeling (it is not) and that the FDA regulates OTC drug advertising (it does not), as well as an entirely new argument: that providing a Proposition 65 warning via public advertising is barred under the "frustration of purpose" doctrine of federal preemption (also known as "obstacle" preemption). Defendants also offer an expansion of their earlier argument that where federal law preempts ***some*** state authority, ***all*** state authority under Proposition 65 is precluded by Health and Safety Code §25249.10(a) ("Section 10(a)"). In their opening briefs, Defendants argued that because federal law preempts all types of Proposition 65 warnings, they did not need to address

[1] The term "Defendants" applies collectively to all Defendants in the case.

CEH's contention that Defendants can comply with Proposition 65 by reducing or eliminating the NDMA exposures. Recognizing the flaws in their argument that all forms of public communication regarding NDMA in Products are regulated by federal law, Defendants now contend that where federal law preempts ***any form*** of Proposition 65 warning (such as a label warning), Section 10(a) operates to preempt a Proposition 65 claim in its entirety (*i.e.*, even where non-label warnings ***or*** alternate, non-warning methods of compliance are readily permitted). CEH submits this surreply to respond to these new authorities and arguments.

II. OTC DRUG ADVERTISING IS NOT REGULATED BY THE FDA

As set forth in CEH's opposition – and not disputed in Defendants' replies – Proposition 65 warnings may be provided by public advertising. Opp. at 17, 30 & n.20. Furthermore, as CEH noted earlier, OTC drug advertising is not subject to FDA regulation. *Id.* at 30-31; *see also Mylan Pharms., Inc. v. Procter & Gamble Co.* (S.D.N.Y. 2006) 443 F.Supp.2d 453, 460 (citing *Sandoz Pharm. Corp. v. Richardson-Vicks, Inc.* (3rd Cir. 1990) 902 F.2d 222, 227, and *Bristol-Myers Co. v. Federal Trade Comm'n* (2nd Cir. 1984) 738 F.2d 554, 559-60); *Terry v. McNeil-PPC, Inc.* (E.D. Pa. Nov. 13, 2015) 2015 U.S. Dist. LEXIS 153970, at *8. Accordingly, providing Proposition 65 warnings using some form of public advertising is not prohibited by FDA regulations. This alone defeats Defendants' impossibility preemption argument.

Defendants raise two new arguments on reply in an attempt to blunt the fatal impact of these legal premises: (1) that the FDA ***does*** regulate OTC drug advertising (Brand Name Manufacturers Reply at 11; Generic Manufacturers/Retailers Reply at 11-13); and (2) that OTC drug advertising is "labeling" under the Food, Drug, and Cosmetic Act ("FDCA") and therefore subject to FDA regulation (Brand Name Manufacturers Reply at 11; Generic Manufacturers/Retailers Reply at 7-9). Neither proposition is well taken.

In support of their contention that the FDA's regulation of OTC drugs broadly preempts all "failure to communicate" claims, even where such claims are premised on advertisements, Defendants cite to a host of new cases. *See, e.g.*, Generic Manufacturers/Retailers Reply at 8-9.[2]

[2] Defendants did not cite to the *In re Fosamax*, *Montero*, *Gardley-Starks*, *Moretti*, or *Metz* decisions in their opening briefs.

The problem for Defendants is that of the 15 cases they cite for this proposition, 14 of them involve prescription rather than OTC drugs. These cases are irrelevant, as there is no dispute among the parties that the FDA regulates prescription drug advertising under the FDCA. *See* 21 U.S.C. §352(n). What is conspicuously missing from Defendants' briefs is a citation to ***any*** provision in the FDCA or the FDA's regulations thereunder granting the agency authority over OTC drug advertising. *See also* Opp. at 30-31 & n.21 (noting this absence). The one case cited by Defendants that involves OTC drugs – the Florida MDL's decision in the *In re Zantac* case – does not address advertising at all. Generic Manufacturers/Retailers Reply at 8 (citing *In re Zantac (Ranitidine) Prods. Liab. Litig.* (S.D. Fla. Dec. 31, 2020) 2020 U.S. Dist. LEXIS 245302 ("*Zantac II*")). Accordingly, Defendants have no support for their argument that the FDA regulates OTC drug advertising.

Defendants' argument that any type of public advertising that includes a warning constitutes "labeling" under the FDCA (and thus falls within the FDA's regulatory purview) also lacks support. As an initial matter, Defendants ignore that the same statutory provision authorizing the FDA to regulate prescription drug advertising (1) expressly distinguishes "advertisements" from "labeling," and (2) nowhere states that any and all warning statements are "labeling." 21 U.S.C. §352(n); *see also* 21 U.S.C. §321(m) & (n) (defining "labeling" but also referring to "labeling or advertising" as separate concepts). Indeed, the law regarding prescription drug advertisements affirmatively provides for certain types of warnings to be included in advertisements (relating to "side effects" and "contraindications") without such advertisement becoming "labeling." 21 U.S.C. §352(n) ("This paragraph (n) shall not be applicable to any printed matter which the Secretary determines to be labeling as defined in [21 U.S.C. §321(m)]."). Moreover, there is no requirement that OTC drug advertising be limited to language that is approved in an NDA or ANDA. *See Terry*, 2015 U.S. Dist. LEXIS 153970, at *8 ("Advertisers of OTC drugs are not limited to using FDA-approved labeling language when advertising an OTC drug for an FDA-approved purpose.").[3] Consequently, Proposition 65 warnings for the Products

[3] Brand Name Manufacturers' unsupported statement that "such warnings cannot deviate from the language approved in the NDA for Zantac" thus is wrong. Brand Name Manufacturers Reply at 9.

may be provided using public advertising.

Defendants' only authority for this proposition relating to OTC drugs – *Gaeta v. Perrigo Pharms. Co.* (N.D. Cal. 2008) 562 F.Supp.2d 1091 – does not provide that all warnings or advertisements are labeling. Rather, the only mention of advertising by the *Gaeta* court is that advertising "that goes with the package in which the articles are transported" is labeling. *Id*. at 1096. Including a Proposition 65 warning on a radio or television advertisement for the Products clearly does not "go with the package" and clearly is not labeling.

To the extent that there is any lingering doubt as to whether Defendants may independently communicate with the public regarding the hazards of NDMA in the Products without FDA approval, Defendants themselves have already provided conclusive evidence in the affirmative. All of the manufacturer Defendants – the Brand Name Manufacturers and Generic Manufacturers alike – widely disseminated recall notices over the internet in which they communicated hazards associated with NDMA in the Products to the public. *See*, *e.g.*, Opp. at 31 (describing the notices issued by Brand Name Manufacturers and Apotex). Notably, when Defendants chose to communicate with the public about such hazards, they were able to do so without prior FDA approval and without subsequent FDA admonishment. In a significant concession, none of the reply briefs address CEH's argument that Defendants' recall notices undermine their contention that they are unable to communicate with the public using language that was not approved during the NDA or ANDA process.[4] Nor do the Generic Manufacturers address the point that the differences between their recall notices and the Brand Name Manufacturer's recall notice undermine their contention that the so-called "duty of sameness" precludes their ability to communicate with the public.[5] Opp. at 35-36.

[4] Apotex again boasts about its "independent" action to widely and publicly disseminate its recall notice (Apotex Reply at 6), but again overlooks that this shows the FDA does not regulate OTC drug advertising.

[5] It is also telling that neither the Generic Manufacturers nor Apotex address CEH's argument that the "duty of sameness" is undermined by the significant variance in the NDMA content of different manufacturers' Products. Opp. at 34-35. This lack of sameness regarding the NDMA levels in the Products supports CEH's view that the FDA does not exclusively regulate undisclosed contaminants such as the NDMA in the Products. Indeed, Defendants fail to cite a single case or regulation in any of their extensive briefing that explicitly addresses FDA regulation of undisclosed contaminants. *Id.* at 34 (noting this absence).

Given the lack of any legal authority supporting Defendants' contention that they are barred from communicating hazards associated with the Products to the public through means of public advertising – as well as the conclusive empirical proof that they may, in fact, do so – Defendants' impossibility argument fails.

III. USE OF PUBLIC ADVERTISING TO PROVIDE A PROPOSITION 65 WARNING FOR THE PRODUCTS DOES NOT TRIGGER OBSTACLE PREEMPTION

In their reply, Brand Name Manufacturers advance an argument that no Defendant made in any opening brief, and that no other Defendants join on reply: that "the inclusion of additional warnings outside [of] those in the format specified by FDA [in 21 C.F.R. §201.66] would frustrate FDA's objective of providing clear, readable, and simple product labels for OTC drugs." Brand Name Manufacturers Reply at 7 (citing *Dowhal v. SmithKline Beecham Consumer Healthcare* (2004) 32 Cal.4th 910, 929 on "obstacle" preemption). This is a drastic pivot from the unavailing "impossibility" rationale on which these entities relied in their opening brief. In any event, this new "obstacle" preemption argument fails for reasons similar to those that defeat the spurious "field" preemption argument made by fellow Defendant Apotex. *See* Opp. at 38-40.

Obstacle preemption "permits courts to strike state law that stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Quesada v. Herb Thyme Farms, Inc.* (2015) 62 Cal.4th 298, 312. "It requires proof Congress had particular purposes and objectives in mind, a demonstration that leaving state law in place would compromise those objectives, and reason to discount the possibility the Congress that enacted the legislation was aware of the background tapestry of state law and content to let that law remain as it was." *Id.* As with other forms of implied preemption, "a high threshold must be surmounted before obstacle preemption will be found." *Solus Indus. Innovs., LLC v. Sup. Ct.* (2018) 4 Cal.5th 316, 345 (citation omitted). This is especially true where Congress is legislating in health and safety fields traditionally occupied by the states or where Congress has expressly carved out areas in which state law may still operate. *See Bronco Wine Co. v. Jolly* (2004) 33 Cal.4th 943, 957, 988, 993. Furthermore, the presumption against preemption is even greater where the alleged obstacle preemption is founded on a federal regulation rather than a federal statute. *See id.* at 992

("[B]ecause agencies normally deal with problems in far more detail than does Congress … we can expect that [agencies] will make their intentions clear if they intend for their regulations to be exclusive.").

All of these factors cut against a finding of obstacle preemption here. As noted in CEH's opposition brief, the purpose of Congress in enacting the FDCA was to protect consumers from harmful products – an objective that is wholly consonant with Proposition 65. Opp. at 18; *see also id.* at 20 (Proposition 65 is an exercise of traditional state police powers). Congress was not only ***aware*** of Proposition 65, but expressly ***exempted*** it from the FDCA's national uniformity provisions as to OTC drugs. *See id.* at 21 (citing legislative history of 21 U.S.C. §379r demonstrating that Congress deemed federal and California law on OTC drugs to be complementary, not conflicting). Congress has now had over twenty years since the 1997 passage of 21 U.S.C. §379r(d)(2) to change its mind on this point, but it has not. The FDA's intent as to OTC drug warnings is not at variance with that of Congress, and the sole regulation on which Brand Name Manufacturers rely – 21 C.F.R. §201.66 – does not indicate otherwise. This provision merely sets forth certain restrictions on "[t]he outside container or wrapper of the retail package, or the immediate container label if there is no outside container or wrapper" – it says nothing about the content of off-label warnings, and gives no "clear" indication that the operation of any state laws are foreclosed. *See* Opp. at 29-30 & n.19. Yet, Brand Name Manufacturers construe the FDA's ***silence*** in this regard to mean not only that off-label warnings ***are*** regulated, but that any and all state laws requiring such off-label warnings are implicitly ***precluded***. Suffice it to say, this is at least a bridge too far. Also, this situation is nothing at all like *Dowhal* – the only case at any level finding Proposition 65 to be impliedly preempted by federal law – in which the FDA was addressing a rare "lesser of two evils" situation and where the agency had made express statements that a conflict between federal and state law was inevitable.[6] *See id.* at 22-23.

[6] Brand Name Manufacturers contend that "the U.S. Supreme Court has not required express agency statements to find implied conflict preemption." Brand Name Manufacturers Reply at 7 n.3 (citing *Geier v. Am. Honda Motor Co.* (2000) 529 U.S. 861, 869). Actually, the *Geier* case only held that such preemptive statements need not be formally made "after notice-and-comment rulemaking," not that no such agency statements need be made at all. *Id.* at 884. Indeed, the U.S. Supreme Court in *Geier* ***did*** rely on affirmative agency statements, made in the context of an amicus brief, that the suit at issue would "stand as an obstacle to the accomplishment and

Consequently, Brand Name Manufacturers' belated (and undeveloped) obstacle preemption argument is without merit.

IV. SECTION 10(a) DOES NOT ACT TO EXPAND PREEMPTION FROM A SINGLE TYPE OF WARNING TO THE ENTIRE CAUSE OF ACTION

Section 10(a) provides that Health & Safety Code §25249.6 shall not apply to "an exposure for which federal law governs warning in a manner that preempts state authority." Without citing any authority (other than one trial court case that was overturned on this point), Defendants argued in their opening briefs that if the FDCA precludes all warnings under Proposition 65, Defendants need not address whether alternative compliance with Proposition 65 by reducing or eliminating the NDMA contamination in the Products is possible. *See* Opp. at 38 & n.29. CEH's opposition pointed out that, in essence, Defendants are arguing that where federal law governs warning in a manner that preempts ***some*** state authority, ***all*** state authority is preempted. *Id.* at 36. On reply, Defendants confirm that CEH's construction of their argument is correct, as they now advance an even broader principle of law: that preemption of even a single method of Proposition 65 warning results in preemption of CEH's Proposition 65 claim in its entirety. *See* Brand Name Manufacturers Reply at 11 ("Where federal law governs a product's warnings and precludes a Proposition 65 warning, as it does here, Proposition 65 does not apply."); Generic Manufacturers/Retailers Reply at 4 ("Section 10(a) provides that when federal law governs warnings in a preemptive manner (which *Mensing* held is true for generic drugs) then no Proposition 65 claim may lie.").

As discussed in CEH's opposition, Defendants' initial interpretation runs contrary to the express language of Section 10(a), to the ballot materials that serve as the legislative history for Proposition 65, and to prior case law demonstrating that courts analyzing Section 10(a) do not hold this provision to have raised the bar for conflict preemption above the constitutional standard. Opp. at 36-38. Defendants' attempt on reply to expand Section 10(a) runs even further afoul of

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execution" of federal objectives. *Id.* at 883. Likewise, in *Dowhal*, the FDA submitted an amicus brief stating its position that any Proposition 65 warning would frustrate federal policies. *See Dowhal*, 32 Cal.4th at 927. Here, the FDA has made no such statements regarding warnings as to NDMA in ranitidine specifically, or as to the operation of Proposition 65 generally.

governing case law, which consistently holds that Proposition 65 warnings are only preempted where all possible warning methods are preempted. *See, e.g.*, *Committee of Dental Amalgam Mfrs. & Distribs. v. Stratton* (9th Cir. 1996) 92 F.3d 807, 810 ("[T]o find that Proposition 65 is preempted by [a federal law], we must determine that ***all*** possible consumer product warnings that would satisfy Proposition 65 conflict with provisions of [that law].") (emphasis in original) (citation omitted); *People ex rel. Lungren v. Cotter & Co.* (1997) 53 Cal.App.4th 1373, 1379 (same). Thus, Defendants' new argument, like its initial one, is wrong.

DATED: April 19, 2021

LEXINGTON LAW GROUP

Mark N. Todzo
Joseph Mann
Attorneys for Plaintiff
Center for Environmental Health

PROOF OF SERVICE

I, Owen Sutter, declare:

I am a citizen of the United States and employed in the County of San Francisco, State of California. I am over the age of eighteen (18) years and not a party to this action. My business address is 503 Divisadero Street, San Francisco, CA 94117 and my email address is osutter@lexlawgroup.com.

On April 19, 2021, I served the following document(s) on all interested parties in this action by placing a true copy thereof in the manner and at the addresses indicated below:

PLAINTIFF'S OMNIBUS SURREPLY TO DEFENDANTS' REPLIES TO PLAINTIFF'S OPPOSITION TO DEMURRERS

☐ **BY MAIL**: I am readily familiar with the firm's practice for collecting and processing mail with the United States Postal Service ("USPS"). Under that practice, mail would be deposited with USPS that same day with postage thereon fully prepaid at San Francisco, California in the ordinary course of business. On this date, I placed sealed envelopes containing the above mentioned documents for collection and mailing following my firm's ordinary business practices.

☐ **BY FACSIMILE**: I caused all pages of the document(s) listed above to be transmitted via facsimile to the fax number(s) as indicated and said transmission was reported as complete and without error.

☒ **BY ELECTRONIC MAIL**: I transmitted a PDF version of the document(s) listed above via email to the email address(es) indicated on the attached service list [or noted above] before 5 p.m. on the date executed.

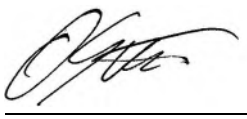
Please see attached service list

☐ **BY PERSONAL DELIVERY**: I placed all pages of the document(s) listed above in a sealed envelope addressed to the party(ies) listed above, and caused such envelope to be delivered by hand to the addressee(s) as indicated.

☐ **BY OVERNIGHT DELIVERY**: I deposited such document(s) in a box or other facility regularly maintained by FedEx, or delivered such document(s) to a courier or driver authorized by FedEx, with delivery fees paid or provided for, and addressed to the person(s) being served below.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed on April 19, 2021 at San Francisco, California.



Owen Sutter

SERVICE LIST
CEH v. Perrigo Company, et al.
RG 20-054985

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Exhibit 43

SUPERIOR COURT OF THE STATE OF CALIFORNIA

IN AND FOR THE COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, et al, Plaintiffs/Petitioners, v. PERRIGO COMPANY, et al, Defendants/Respondents.	No. RG20-054985 [TENTATIVE] ORDER SUSTAINING DEMURRER WITH LEAVE TO AMEND. Date: 5/5/21 Time: 10:00 a.m. Dept.: 21

Several demurrers came on for hearing on 5/5/21, in Department 21 of this Court, the Honorable Winifred Y. Smith presiding. Counsel appeared on behalf of Plaintiff and on behalf of Defendant. After consideration of the points and authorities and the evidence, as well as the oral argument of counsel, IT IS ORDERED:

The demurrer of Chattem and Sanofi-Aventis (Brand Name Defendant (R#2240283) is SUSTAINED WITH LEAVE TO AMEND.

The demurrer of Apotex (Generic Manufacturer Defendant) (R#2240282), the demurrer of Perrigo (Generic Manufacturer Defendant) (R#2242700), the demurrer of Granules USA, Inc. (Generic Manufacturer Defendant) (R#2242703), and the demurrer of Dr. Reddy's Laboratories,

Inc. (Generic Manufacturer Defendant) (R#2240276) are SUSTAINED WITHOUT LEAVE TO AMEND.

The demurrer of 7-Eleven (Retailer Defendant) (R#2240281) and the demurrer of Target Corporation (Retailer Defendant) (R#2242040) are SUSTAINED WITHOUT LEAVE TO AMEND.

BACKGROUND

These are demurrers, so the court assumes "the truth of the properly pleaded factual allegations, facts that reasonably can be inferred from those expressly pleaded and matters of which judicial notice has been taken." (*Redfearn v. Trader Joe's Co.* (2018) 20 Cal.App.5th 989, 996.)

The court GRANTS all the requests for judicial notice. In other circumstances the court might not permit this expansive use of judicial notice because it has the effect of turning a demurrer into a de facto motion for summary judgment. (*Richtek USA, Inc. v. uPI Semiconductor Corporation* (2015) 242 Cal.App.4th 651, 660.) There were no objections to the requests for judicial notice. Furthermore, the issue presented is legal in nature and the evidence relevant to the legal issue is undisputed. The evidence is disputed regarding substantive issues, but the demurrers are not about the substantive issues.

Defendants manufacture, import, distribute, or sell the Products. (2AC, para 34.) The known carcinogen NDMA was in the Products when the consumers bought the products. Defendants know or should have known there was NDMA in the Products. (2AC, para 34, 43.)

In September 2019, there were recalls of the Products based on the presence of NDMA. (2AC, para 36.) Following the recalls, the FDA issued public alerts. (2AC, para 36.) Defendant

continued to sell the products after the recalls and public alerts without giving appropriate warmings. (2AC, para 37, 44.)

THE COMPLAINT

The 2AC assets a single cause of action against the Defendants under H&S 25249.6 alleging that they have intentionally exposed individuals to NDMA without first giving clear and reasonable warnings. (2AC, para 45.)

The demurrers are based on preemption and present the legal issue of whether the FDCA preempts the California Proposition 65 claim. The Brand Name Manufacturers, the Generic Manufacturers, and the Private Label Retailers argue impossibility preemption. Defendant Apotex is a Generic Manufacturer and also argues field preemption and mootness.

RELATED CASES

The court takes judicial notice of the existence of parallel mass tort proceedings concerning MDNA, ranitidine, and the Products. There is a Federal MDL in Florida, which concerns claims for personal injuries. There is a California JCCP that concerns claims for personal injuries. (*In re Ranitidine Cases*, JCCP 5150.)

PROPOSITION 65 – COMPLIANCE/LIABILITY AND REMEDY

H&S 25249.6 states: "No person in the course of doing business shall knowingly and intentionally expose any individual to a chemical known to the state to cause cancer or reproductive toxicity without first giving clear and reasonable warning to such individual, except as provided in Section 25249.10."

A defendant can comply with the law by ensuring that its products do not "expose any individual to a chemical known to the state to cause cancer or reproductive toxicity." This means keeping the chemical exposure below the "no significant risk" level. (H&S 25249.10(c).)

A defendant can comply with the law by providing a "clear and reasonable warning." The warning must have certain content. (27 CCR 25603.) The warning may be communicated through product labeling, point-of-sale signs, or public advertising. (*Dowhal v. SmithKline Beecham Consumer Healthcare* (2004) 32 Cal.4th 910, 918.) (See also 27 CCR 25601(c), 25602.)

If the court finds that a defendant is in violation of H&S 25249.6, then the court can order remedies in the form of injunctions and penalties. H&S 25249.7(a) states "A person who violates or threatens to violate Section 25249.5 or 25249.6 may be enjoined in any court of competent jurisdiction." H&S 25249.7(b) states "A person who has violated Section 25249.5 or 25249.6 is liable for a civil penalty."

For purposes of this motion, it is useful to distinguish between the compliance/liability provision (H&S 25249.6) and the remedy provision (H&S 25249.7).

A defendant can comply with Prop 65 and avoid liability by either providing a warning or ensuring that its products have chemical exposure below the "no significant risk" level. (H&S 25249.6 and 25249.6.10(c).) A lack of warning can result in liability.

Assuming a lack of compliance, which is liability, then the court can order a remedy. The court can order injunctions and penalties. (H&S 25249.7(a) and (b). The court can order a warning as a remedy.

The analysis in this order is focused on H&S 25249.10(a) and whether federal law governs warning in a manner that preempts state authority and thus defendants are not required

to comply with H&S 25249.6. The analysis in this order does not address or decide whether under the remedy provision of H&S 25249.7 the court could order a defendant to manufacture the products free of contaminants, to take greater care in storing the products, and to set expiration dates to require sale before the degradation of the products.

If the preemption analysis were a de facto inquiry into the scope of relief that the court can order under H&S 25249.7(a), then the court would permit the Attorney General to file an amicus brief and on that issue and to present evidence of any policies that might be relevant to statutory interpretation. (*Yamaha Corp. of America v. State Bd. of Equalization* (1998) 19 Cal.4th 1, 14-15.) The court does not do that because the preemption analysis is focused on compliance/liability under H&S 25249.6.

PROPOSITION 65 – SELF-EXEMPTION TO COMPLIANCE/LIABILITY WHERE THERE IS FEDERAL PREEMPTION OF WARNING.

Prop 65 states that there is an exemption to the compliance/liability provision when federal law governs warnings. H&S 25249.10(a) states: "Section 25249.6 [the compliance/liability provision] shall not apply to any of the following: (a) An exposure for which federal law governs warning in a manner that preempts state authority." This self-exception does more than state the obvious, which is that federal law preempts state law.

The self-exception states that if federal law for an exposure governs warning in a manner that preempts state authority, then there is no violation of the compliance/liability provision. This in turn means that if federal law on warning preempts state law on warning, then there is no liability for an exposure under H&S 25249.6, and thus the court cannot order any non-warning injunctive relief or award any penalties.

The self-exception is significant because it focuses the court on whether "federal law governs warning in a manner that preempts state authority." For purposes of these demurrers it is immaterial whether there was NDMA in the Products as a result of FDA approved design or manufacturing or as a result of manufacturing contamination, storage in high heat, or delay in sale to consumers. For purposes of these demurrers the court can assume that Defendants knowingly violated H&S 25249.6.

The FDCA has an express preemption provision for nonprescription drugs such as ranitidine. (21 USC 379r.) The FDCA's express preemption provision would preempt Proposition 65 as applied to nonprescription drugs, except that the provision has an express exception for any "State requirement adopted by a State public initiative or referendum enacted prior to September 1, 1997." (21 USC 379r(d)(2).) "Proposition 65 is the only state enactment that falls within the savings clause." (*Dowhal v. SmithKline Beecham Consumer Healthcare* (2004) 32 Cal.4th 910, 918.)

The FDCA's exclusion of Proposition 65 from the FDCA's express preemption clause does not exempt Proposition 65 from implied preemption. "[E]ven where the express preemption provision in [21 U.S.C. § 379r] is not applicable, implied preemption may arise … the savings clause does not foreclose the possibility that conflict preemption may arise from federal sources other than 21 U.S.C. § 379r.']. (*Trejo v. Johnson & Johnson* (2017) 13 Cal.App.5th 110, 150-151.)

Therefore, the court cannot determine whether the Proposition 65 express exemption (H&S 25249.10(a) applies unless the court goes through the analysis of implied preemption to determine whether "federal law governs warning in a manner that preempts state authority." H&S 25249.10(a) remains relevant because makes clear that if "federal law governs warning in a

manner that preempts state authority" then there is no liability and then there is no possibility of injunctive relief unrelated to warnings or of penalties.

The court notes, by way of observation, that the Proposition 65 self-exception under H&S 25249.6 is not part of other statutes. The effect of impossibility preemption operating through the Proposition 65 self-exception is different from impossibility preemption operating in isolation. There might be state law remedies other than Proposition 65 that are not preempted and that would apply if, as alleged, a drug manufacturer is selling, or had sold, drugs that comply with FDA labelling requirements but expose California consumers to hazardous chemicals because the drugs are contaminated, or improperly stored, or not timely sold.

PREEMPTION – GENERALLY.

The United States Congress has the power to preempt state law concerning matters that lie within its authority. (*Farm Raised Salmon Cases* (2008) 42 Cal.4th 1077, 1087.) Preemption of state law may be express or implied. Implied preemption occurs "'(i) when it is clear that Congress intended, by comprehensive legislation, to occupy the entire field of regulation, leaving no room for the states to supplement federal law [citation]; (ii) when compliance with both federal and state regulations is an impossibility [citation]; or (iii) when state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress. (*Solus Industrial Innovations, LLC v. Superior Court* (2018) 4 Cal.5th 316, 332.)

"[F]ederal preemption presents a pure question of law." (*Farm Raised Salmon Cases* (2008) 42 Cal.4th 1077, 1089 fn 10; *Coleman*, 223 Cal.App.4th at 422.) The court focuses on the intent of Congress. (*Spielholz v. Superior Court* (2001) 86 Cal.App.4th 1366, 1371.)

"Ordinarily, there is a presumption against preemption. (*Solus Industrial Innovations, LLC v. Superior Court* (2018) 4 Cal.5th 316, 332.) The strength of the presumption is heightened in areas where the subject matter has been the longstanding subject of state regulation in the first instance." (*Quesada v. Herb Thyme Farms, Inc.* (2015) 62 Cal.4th 298, 313.)

IMPOSSIBILITY PREMPTION - GENERALLY

"Federal preemption applies when state and federal laws directly conflict. … When it is impossible for a private party to comply with both state and federal requirements, a direct conflict exists. (*Teva Pharmaceuticals USA, Inc. v. Superior Court* (2013) 217 Cal.App.4th 96, 105.)

"A defendant cannot establish impossibility preemption "merely by demonstrating it is difficult or costly to comply. Rather, it must show using point of sale signs is a "physical impossibility." (*People v. Cotter & Co* (1997) 53 Cal.App.4th 1373, 1393-1394.)

FDA REGULATION – GENERALLY

A Brand Name Manufacturer must demonstrate to the FDA that a new drug is safe and effective. (21 U.S.C. 355(a), (b)(1); 21 C.F.R. 314.1–314.3, 314.50.) When a Brand Name Manufacturer seeks approval for an OTC version of a prescription medication, the manufacturer shows the FDA that the medication is appropriate for self-administration. (21 C.F.R. § 310.200(b); 21 U.S.C. §§ 353(b)(3), 355(c)–(d).)

The FDA approves the language in the labelling. The Brand Name Manufacturer must use the *exact* language approved by FDA in the labeling or packaging. (21 C.F.R. 214.70(b), (c), 314.71.)

The FDCA requires that OTC manufacturers provide *only* those warnings in OTC labeling approved by FDA in precisely the approved manner. (21 U.S.C. § 355.)

IMPOSSIBILITY PREMPTION – BRAND NAME MANUFACTURERS

The demurrer of Chattem and Sanofi-Aventis (Brand Name Defendant (R#2240283) is SUSTAINED WITH LEAVE TO AMEND.

The impossibility preemption demurrer of the Brand Name Defendants presents the issues of whether compliance with Proposition 65 was impossible given: (1) the ability of the Brand Name Defendants to change labelling under the Changes Being Effected process and (2) the ability of the Brand Name Defendants to provide Proposition 65 Warnings in the form of advertising.

THE CBE PROCESS

A Brand Name Defendant can change a label without FDA approval in certain limited circumstances. "Major changes" require FDA preapproval, while certain labeling changes separately defined as "moderate changes" do not. (21 CFR § 314.70(c)(6)(iii).)

A Brand Name Defendants can unilaterally make moderate changes, but those are limited to "changes … to reflect newly acquired information … [t]o add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter." (21 C.F.R. § 314.70(c)(6)(iii).) The CBE process only permits changes "add[ing] or strengthen[ing] a contraindication, warning, precaution, or adverse reaction" for a "clinically significant hazard"

for which there is "reasonable evidence of a causal association" with the drug. (21 C.F.R. 201.57.)

Wyeth v., Levine (2009) 555 US 555, addresses the CBE process and preemption. Procedurally, *Wyeth* was decided after trial. In *Wyeth*, a consumer sued the brand-name drug manufacturer for failure to provide an adequate warning on the drug's labeling. (555 US at 559-560). The Supreme Court held that the consumer's labeling claims were not pre-empted because the Changes Being Effected ("CBE") process permitted the brand-name drug manufacturer to "unilaterally strengthen" the warning on the labeling, without waiting for FDA approval. (555 US at 568-569.) The Court stated that it could not conclude that it was impossible for the brand-name drug manufacturer to comply with both its federal-law and state-law duties "absent clear evidence that the FDA would not have approved" a labeling change. (555 US at 571) The brand-name drug manufacturer "offered no such evidence," and the fact that the FDA had previously approved the labeling did "not establish that it would have prohibited such a change." (555 US at 572-573.)

To state a claim for failure-to-warn that is not preempted by the FDCA, a plaintiff must plead "a labeling deficiency that [Defendants] could have corrected using the CBE regulation." (*Gibbons v. Bristol-Myers Squibb Co.* (2nd Cir. 2019) 919 F.3d 699, 708.)

Turning to this case, the 2AC does not allege facts that would plausibly support an inference that the Brand Name Manufacturers could use the CBE process to present a Proposition 65 warning.

The CBE process requires Brand Name Manufacturers to demonstrate that there a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug. (21 C.F.R. 201.57.)

Proposition 65 applies unless a Brand Name Manufacturer can demonstrate that "the exposure poses no significant risk assuming lifetime exposure at the level in question for substances known to the state to cause cancer, and that the exposure will have no observable effect assuming exposure at one thousand (1,000) times the level in question for substances known to the state to cause reproductive toxicity. (H&S 25249.10(c).)

There is a gap where an exposure is above the level that arguably requires a Proposition 65 warning but below the level that might justify a CBE warning. If the NDMA exposure is in this gap, then federal law preempts Proposition 65. If the NDMA exposure is so high that it both requires a Proposition 65 warning and the manufacturer can use the CBE process, then there is no impossibility preemption because a defendant can comply with both state and federal law.

Plaintiff's may amend, if possible, to allege that the NDMA exposure presented a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug. (21 C.F.R. 201.57) and as a result the Brand Name Manufacturers could use the CBE process to unilaterally strengthen the warning on the labeling, without waiting for FDA approval.

LABELLING AND ADVERTISING

A Brand Name Defendant must provide information about non-prescription drugs to consumers through FDA approved labelling and can voluntarily provide additional information to consumers through advertising.

The labels and labelling of non-prescription drugs is highly regulated. The FDA must approve a manufacturer's labels and labelling. (21 USC 355.) "Label" is defined as "a display of written, printed, or graphic matter upon the immediate container of any article." (21 U.S.C. §

321(k).) There are regulations about what must be on a label on a container (21 CFR 201.66(c)), or, if the containers lacks space for the information, on accompanying printed material (21 CFR 201.66(c)(10).)

"Labeling" is more broadly defined to include "all labels and other written, printed, or graphic matter (1) upon any article or any article or any of its containers or wrappers, or (2) accompanying such article." (21 U.S.C. § 321(m).) There are no FDA regulations about point of sale or shelf disclosures for OTC drugs.

Advertising of OTC drugs is not regulated by the FCDA. Advertising of OTC drugs is regulated by the FTC (CEH RJN, Exh. 5, at 2; Brand Name Manufacturers RJN, Exh. F, at 13 n.25.)

Plaintiff argues that a defendant can a provide a Proposition 65 warning in an advertisement even if the defendant does not have FDA approval to provide a Proposition 65 warning in labelling. Plaintiff's argument can also be framed as the assertion that if a disclosure of information is not regulated as "labelling" under 21 CFR 201.66, then it must be "advertising" and therefore not regulated by the FDA.

The court decides that a Proposition 65 warning is by definition "labelling" both specifically because it fits within the FDCA definition of "labelling" and more generally because labelling is mandatory, advertising is voluntary, and plaintiff asserts that a Proposition 65 warning is mandatory.

Looking specifically at the FCDA, 21 USC 321(m) states: "(m) The term "labeling" means all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article."

21 USC 321(m) includes the phrase "accompanying such article." The Meat Inspection Act (MIA) includes the same phrase. In *American Meat Institute v. Leeman* (2009) 180 Cal.App.4th 728, the court held that for purposes of the MIA the phrase "accompanying such article" in the definition of labelling means that the MIA preempted Proposition 65's warning requirements.

Leeman cited to *Kordel v. United States* (1948) 335 US 345, for the proposition that 21 USC 321(m) in the FDCA defined "labeling" to include supplemental literature not attached to the product. Talking a detour from *Leeman*, in *Leeman* court quotes *Kordel*, 335 US at 350, which states:

> One article or thing is accompanied by another when it supplements or explains it, in the manner that a committee report of the Congress accompanies a bill. No physical attachment one to the other is necessary. It is the textual relationship that is significant. …
>
> The false and misleading literature in the present case was designed for use in the distribution and sale of the drug, and it was so used. The fact that it went in a different mail was wholly irrelevant whether we judge the transaction by purpose or result. …
>
> … The [FDCA] cannot be circumvented by the easy device of a 'sale' of the advertising matter where the advertising performs the function of labeling.

> Petitioner points out that in the evolution of the Act the ban on false advertising was eliminated, the control over it being transferred to the Federal Trade Commission. … We have searched the legislative history in vain, however, to find any indication that Congress had the purpose to eliminate from the Act advertising which performs the function of labeling. Every labeling is in a sense an advertisement. The advertising which we have here performs the same function as it would if it were on the article or on the containers or wrappers. As we have said, physical attachment or contiguity is unnecessary under s 201(m)(2).

[End of block quotation.] *Kordel* makes plain that a plaintiff cannot avoid federal preemption by characterizing labelling as advertising matter "where the advertising performs the function of labeling."

Leeman, 180 Cal.App.4th at 758, finds that *Chemical Specialties Mfrs. Ass'n, Inc. v. Allenby* (9th Cir., 1992) 958 F.2d 941, is not persuasive regarding the interpretation of "accompanying" in FIFRA and, if persuasive, the FIFRA analysis does not apply to the phrase "accompanying such article" as used in the MIA. *Leeman* arguably requires this court to find Allenby is not persuasive. (*Auto Equity Sales, Inc. v. Superior Court of Santa Clara County* (1962) 57 Cal.2d 450, 455.) This court independently does not find *Allenby* persuasive for the reasons stated in *Leeman*.

Leeman, 180 Cal.App.4th at 761, concludes, "Thus, because (1) point of sale warnings are "labeling" within the meaning of the FMIA, and (2) there is no dispute that the warnings required by Proposition 65 are "in addition to, or different than" the labeling required by the FMIA (21 U.S.C. § 678), we conclude that the trial court properly ruled that Proposition 65's

point of sale warning requirements with respect to meat are preempted by the FMIA." The MIA and the FDCA definitions of "labeling" both use the phrase "accompanying such article."

Leeman and *Kordel* compel the conclusion that any information that serves the purpose of labelling is "labelling" under the FDCA. Plaintiffs cannot avoid impossibility preemption by conflating labeling and advertising and suggesting that defendants can disclose the Proposition 65 warning in advertising.

Numerous lower federal courts have consistently held that FDA regulation of "labels" and "labelling" results in preemption of claims regarding any failure to communicate warnings through any communication channel. "While [California trial courts] are not bound by decisions of the lower federal courts, even on federal questions, they are persuasive and entitled to great weight. … where the decisions of the lower federal courts on a federal question are "both numerous and consistent," we should hesitate to reject their authority." (*Etcheverry v. Tri-Ag Service, Inc.* (2000) 22 Cal.4th 316, 320-321.) (*Fair v. BNSF Railway Co.* (2015) 238 Cal.App.4th 269, 287.)

Representative federal cases include:

1. *Strayhorn v. Wyeth Pharmaceuticals, Inc.* (6th Cir. 2013) 737 F.3d 378, 394 ["Because such advertising and promotional materials are considered labeling, and because labeling is limited by federal law to the information contained in the brand-name drug's labeling, all of the warranty claims against the Generic Manufacturers based on these materials are preempted under Mensing."]
2. *Guarino v. Wyeth* (11th Cir. 2013) 719 F.3d 1245, 1249 ["Guarino's attempt to elude Mensing by clothing her allegations as "failure-to-communicate" claims rather than failure-to-warn claims does not alter our analysis. No matter the garb in which she

attempts to present them, Guarino's claims are at bottom allegations regarding Teva's failure to warn her of the dangers of long-term metoclopramide use, and they therefore cannot escape Mensing's grasp."]

3. *Montero v. Teva Pharmaceuticals USA Inc.* (S.D. N.Y. 2020) 2020 WL 1862593 at *3 ["Plaintiff alleges inadequate warnings … in Defendants' communications with healthcare providers and advertisements to the public. The preemption of failure-to-warn claims extends to these latter types of communications as well."]
4. *In re Fosamax Products Liability Litigation* (S.D.N.Y 2013) 965 F.Supp.2d 413, 419 ["This Court joins the majority of other courts to consider this issue in holding that any claims stemming from the generic defendants' alleged failure to communicate additional warnings through some method other than their package inserts are preempted"]
5. *In re Yasmin and Yaz (Drospirenone) Marketing, Sales Practices And Products Liability Litigation* (S.D. IL. 2015) 2015 WL 7272766 *5 ["Plaintiff 's claims "are premised on misrepresentations or inadequacies in … labeling, promotions, and advertisements. As such, [generic manufacturer] could only avoid liability as to these claims by unilaterally strengthening their warning labels in violation of federal law or by leaving the marketplace altogether. Mensing and Bartlett establish that such challenges to … labeling are preempted."]

The specific definition of "labeling" in the FDCA is significant to the preemption analysis, as other federal statutes have other definitions and therefore have other scopes of preemption. The court focuses on the definition of labeling in 21 USC 321(m) and gives no weight to the analysis of preemption regarding statutes with other definitions or scopes.

One example of a different statute is the federal Hazardous Substances Act (FHSA), which has a preemption provision that applies to "cautionary labeling" (15 U.S.C. § 1261(b)(1)(A)) and defines "label" as "a display of written, printed, or graphic matter upon the immediate container of any substance" (15 USC 1261(n)). *People ex rel. Lungren v. Cotter & Co.* (1997) 53 Cal.App.4th 1373, held that the FHSA did not preempt Proposition 65 claims, noting that the preemption provision was expressly limited to information "upon the immediate container" or accompanying literature regarding instructions for use. (53 Cal.App.4th at 1387.)

Another example is the federal Alcohol Administration Act (AAA) (27 USC 201 et seq.) and Alcoholic Beverage Labeling Act. ("ABLA") (27 USC 213 et seq.) regulate "warnings or other information on alcoholic beverage containers," and the scope of preemption is limited to "statement[s] ... placed on any container of an alcoholic beverage, or on any box, carton, or other package." This court in *CEH v. GT Living Foods*, RG19-047748 [Order of 5/12/20], held that the AAA/ABLA did not preempt Proposition 65 regarding point of sale information because it was not on the places identified in the statute.

In addition to analysis focused on the FDC and its definition of "labeling," the court also considered on a general level the distinction between labelling and advertising. Federal, state or local authorities can mandate the existence, content, and form of labels and labelling on regulated products such as drugs for public health and safety interests as a condition of permitting sales to consumers. In contrast, private persons voluntarily decide to advertise their products. If a person decides to advertise, the existence, content, and form of advertising is generally at the discretion of the advertiser, with the limitation that advertising cannot be false or misleading.

This suggests a distinction that label on and labelling of a regulated product is required or compelled speech and advertising is voluntary speech. This distinction is subject to the exception that regulatory authorities can mandate that advertising include mandated disclosures "as long as disclosure requirements are reasonably related to the State's interest in preventing deception of consumers." (*National Ass'n of Manufacturers v. S.E.C.* (D.C. Cir. 2015) 800 F.3d 518, 519.) Regulatory authorities can require the dissemination of "purely factual and uncontroversial information." (*National Ass'n of Manufacturers*, 800 F.3d at 523.) Outside that context (commercial advertising), the "general rule" is "that the speaker has the right to tailor the speech" and that advertisers have First Amendment discretion regarding "expressions of value, opinion, or endorsement" and also "to statements of fact the speaker would rather avoid." (*National Ass'n of Manufacturers*, 800 F.3d at 523.)

This broad brush analysis of the distinction between mandated labelling and voluntary advertising suggests that as soon as a regulatory authority (or a person asserting a Proposition 65 case "in the public interest" under H&S 25249.7(d)) asserts that a warning is mandated then the warning becomes mandated "labelling" rather than voluntary "advertising." This is a broad brush analysis and the distinctions between "labelling" and "advertising" might vary based on the words of any given statute or the facts of any case.

When a party asserts a claim under Proposition 65, then the Proposition 65 warning is asserted to be mandatory. A Proposition 65 warning is therefore "labeling" for purposes of the claim and for the affirmative defense of preemption.

The court concludes that any mandated Proposition 65 warning fits within the FDCA's definition of "labeling." A Proposition 65 claim regarding a FDA regulated OTC drug under H&S 25249.6 concerns "labeling" as defined in 21 USC 321(m), which means that it concerns

"An exposure for which federal law governs warning in a manner that preempts state authority" under H&S 25249.10(a), which means that there is no claim for compliance/liability under H&S 25249.6.

IMPOSSIBILITY PREMPTION – GENERIC MANUFACTURERS

The demurrer of Apotex (Generic Manufacturer Defendant) (R#2240282) is SUSTAINED WITHOUT LEAVE TO AMEND. The demurrer of Perrigo (Generic Manufacturer Defendant) (R#2242700) is SUSTAINED WITHOUT LEAVE TO AMEND. The demurrer of Granules USA, Inc. (Generic Manufacturer Defendant) (R#2242703) is SUSTAINED WITHOUT LEAVE TO AMEND. The demurrer of Dr. Reddy's Laboratories, Inc. (Generic Manufacturer Defendant) (R#2240276) is SUSTAINED WITHOUT LEAVE TO AMEND.

The impossibility preemption demurrer of the Generic Manufacturer Defendants presents the issues of whether compliance with Proposition 65 was impossible given: (1) the obligation of the Generic Manufacturer Defendants to provide the same label and labelling information as the Brand Name Defendants (the "duty of sameness") and (2) the ability of the Brand Name Defendants to provide Proposition 65 Warnings in the form of advertising.

THE CBE PROCESS, DUTY OF SAMENESS, AND THE EXPIRATION DATE EXCEPTION

Generic drug manufacturers have an ongoing federal duty of sameness that requires "that the warning labels of a brand-name drug and its generic copy must always be the same." *PLIVA v. Mensing* (2011) 564 US 604, 613.)

An application for a generic drug (Abbreviated New Drug Application or ANDA), the applicant must provide information about the labeling. (21 USC 355(j)(2)(A)(i) and (G).)

The proposed labelling on warnings must be the same as the labelling on warnings for the original approval. An application for a generic drug must not "include a change to the "Warnings" section of the labeling." (21 USC 355(j)(10)(A)(iii).) The FDA may withdraw approval for a generic drug if it finds that the drug product's labeling "is no longer consistent with that for the listed drug." (21 C.F.R. 314.150(b)(10).)

The result is that unlike the holders of the original FDA approvals, the holder of generic approvals cannot use the CBE process. Generic drug manufacturers can use the CBE process only after the holder of the original FDA approval has used the CBE process. The CBE process allows "changes to generic drug labels only when a generic drug manufacturer changes its label to match an updated brand-name label or to follow the FDA's instructions." (*Mensing*, 564 U.S. at 614.)

PLIVA v. Mensing (2011) 564 US 604, and *Mutual Pharmaceutical v. Bartlett* (2013) 570 US 472, examine how the duty of sameness affects impossibility preemption.

In *Mensing*, consumers of generic drugs sued the generic drug manufacturers for failure to provide adequate warnings on the drugs' labeling. The Supreme Court held that the consumers' labeling claims were pre-empted because the generic drug manufacturers could not "independently" change the labeling while remaining in compliance with federal law. The generic drug manufacturers' "duty of 'sameness'" under federal law required them to use labeling identical to the labeling of the equivalent brand-name drug. Thus, the CBE process was unavailable to the generic drug manufacturers to change labeling absent a change to the brand-name drug's labeling. Because any change that the generic drug manufacturers made to the

drugs' labeling to comply with duties arising under state tort law would have violated federal law, the state tort claims were pre-empted.

In *Bartlett*, the Supreme Court expanded on *Mensing* and held that even though a generic drug manufacturer could in theory comply with both federal and state law by removing the drug from the market, that was "no solution." The Supreme Court reasoned pre-emption case law "presume[s] that an actor seeking to satisfy both his federal- and state-law obligations is not required to cease acting altogether in order to avoid liability." (570 US at 488.) The Supreme Court reasoned that this "stop-selling rationale would render impossibility pre-emption a dead letter and work a revolution in the Court's preemption case law. (570 US at 475, 488-490.) (See also *Trejo v. Johnson & Johnson* (2017) 13 Cal.App.5th 110,150-151 [discussing stop-selling as remedy].)

There is one arguably applicable specific exception to the duty of sameness and thus one arguably applicable exception to the impossibility preemption analysis of Mensing and Bartlett. Generic manufacturers have no duty under federal regulations to use the same expiration date on their drugs as the brand name equivalent.

When a Generic manufacturer submits an ANDA request for approval to the FDA, then 21 C.F.R. §314.94(a)(8) generally requires that the generic ANDA label have the same information as the brand name NDA label. The exception is that 21 C.F.R. §314.94(a)(8)(iv) states: "Labeling …proposed for the drug product must be the same as the labeling approved for the reference listed drug, except for changes required … because the drug product and the reference listed drug are produced or distributed by different manufacturers. Such differences between the applicant's proposed labeling and labeling approved for the reference listed drug may include differences in expiration date, …"

Addressing this specific exception, *in re Zantac (Ranitidine) Products Liability Litigation* (S.D. Fl., 2020) 2020 WL 7864213 at *5, states, "With limited exceptions, the FDA may approve the ANDA only if it finds that the generic drug and its proposed labeling are the same as the listed drug and the listed drug's labeling. … One such exception is that the generic drug's proposed labeling "may include differences in expiration date" from the listed drug."

The expiration date exception to the duty of sameness exists and affects impossibility preemption regarding expiration dates, but has no effect on the H&S 25249.10(a) self-exception analysis.

Turning to this case, as a matter of law the Generic Manufacturers cannot use the CBE process to present a Proposition 65 warning. If the Brand Name Manufacturers did not have a Proposition 65 warning on their labels or labelling, then the Generic Manufacturers cannot have a Proposition 65 warning on their labels or labelling. Impossibility preemption applies, which means the H&S 25249.10(a) self-exception applies.

The expiration date exception to the duty of sameness does not change the analysis. The H&S 25249.10(a) self-exception states that Proposition 65 does not apply to "An exposure for which federal law governs warning in a manner that preempts state authority." The FDCA governs warnings. An application for a generic drug must not "include a change to the "Warnings" section of the labeling." (21 USC 355(j)(10)(A)(iii).) Expiration dates are part of labels and labelling, but they are not warnings. As a result, the H&S 25249.10(a) self-exception applies to OTC drugs even though the duty of sameness and thus impossibility preemption does not apply to expiration dates.

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LABELLING AND ADVERTISING

A Generic Manufacturer must provide information about OTC drugs to consumers through FDA approved labelling but can voluntarily provide additional information to consumers through advertising.

As discussed above in the context of the Brand Name Manufacturers, the court concludes that any mandated Proposition 65 warning fits within the FDCA's definition of "labeling," which means that it concerns "An exposure for which federal law governs warning in a manner that preempts state authority" under H&S 25249.10(a), which means that there is no claim for compliance/liability under H&S 25249.6.

IMPOSSIBILITY PREMPTION - RETAILERS

The demurrer of 7-Eleven (Retailer Defendant) (R#2240281) is SUSTAINED WITHOUT LEAVE TO AMEND. The demurrer of Target Corporation (Retailer Defendant) (R#2242040) is SUSTAINED WITHOUT LEAVE TO AMEND.

The impossibility preemption demurrer of Target Corporation and 7-Eleven, Inc. ("Retailer Defendants") presents the issues of whether compliance with Proposition 65 was impossible given: (1) the Retailer Defendants have no approvals from the FDA to manufacture or market the Products and (2) the ability of the Retailer Defendants to provide Proposition 65 Warnings about the Products in the form of advertising.

THE CBE PROCESS AND DUTY OF SAMENESS

The Retailer Defendants do not hold any approvals from the FDA for the manufacture or labelling of the Products. (Retailer RJN ¶ 2, Ex. A.) The 2AC asserts that all defendant manufacture the Products, but "allegations in the pleading may be disregarded if they are contrary to facts judicially noticed." (Scott v. JPMorgan Chase Bank, N.A. (2013) 214 Cal.App.4th 743, 751.)

Because the Retailer Defendants do not hold any approvals from the FDA for the Products, the Retailers are not subject to any FDA oversight with respect to the Products. The Retailer Defendants are therefore analytically distinct from the Brand Drug manufacturers and the Generic Manufacturers.

The Retailer Defendants are not required by FDA approvals to provide any FDA approved label or labelling. In the absence of any obligation to provide any FDA approved labelling, it is immaterial whether the Retailer Defendants provided warnings that were the same the labelling that the FDA approved for the Brand Name Manufacturers or could have used the CBE process to provide different warnings.

LABELLING AND ADVERTISING

A Retailer Defendant can voluntarily provide information to consumers through advertising.

As discussed above in the context of the Brand Name Manufacturers, the court concludes that any mandated Proposition 65 warning fits within the FDCA's definition of "labeling," which means that it concerns "An exposure for which federal law governs warning in a manner that preempts state authority" under H&S 25249.10(a), which means that there is no claim for compliance/liability under H&S 25249.6.

FIELD PREEMPTION – APOTEX

Defendant Apotex is a Generic Manufacturer and argues field preemption. The field preemption argument has no merit.

Field preemption is "where the scheme of federal regulation is sufficiently comprehensive to make reasonable the inference that Congress "left no room" for supplementary state regulation." (*In re Jose C.* (2009) 45 Cal.4th 534, 551.)

Apotex makes what appears to be a novel argument. Apotex argues that the FDA has paid extensive attention to the Products in the time period after it was publicized that the Products contained NDMA and that this extensive attention in the discrete time period is field preemption.

The Apotex field preemption argument has no merit. The court starts with congressional intent. Congress intended through the FDCA to regulate drugs generally, not to regulate the Products specifically. There is no indication of Congressional intent to regulate the Products specifically, so there is no field preemption of the Products specifically. Assuming congressional intent focused on the Products, there is no indication that the regulation was sufficiently comprehensive to suggest that Congress "left no room" for supplementary state regulation." The Apotex argument suggests that there was no field preemption until September 2019 and that the FDA's attention in that discrete time frame then created field preemption in that discrete time frame.

Using the agrarian definition of field by analogy, Apotex argues that field preemption does not need to encompass the field and that under an appropriate set of facts there can be field

preemption for a small patch of grass that for purposes of a lawsuit can be defined as its own separate field. This is not the law.

MOOTNESS – APOTEX

Defendant Apotex is a Generic Manufacturer and argues mootness. The mootness argument has no merit.

"A case is considered moot when "the question addressed was at one time a live issue in the case," but has been deprived of life "because of events occurring after the judicial process was initiated."" (*Wilson & Wilson v. City Council of Redwood City* (2011) 191 Cal.App.4th 1559, 1574.)

Apotex argues that the case is moot because it has voluntarily recalled the Product. That does not make the claim moot.

Plaintiff could prove liability at trial by demonstrating that Apotex knowingly and intentionally exposed consumers to NDMA without first giving clear and reasonable warning. (H&S 25249.6.) The evidence might be that Apotex has for a long time known that contamination in its manufacturing process resulted in NDMA in the Product and that as a result of how the Product was stored and for how long it was stored the amount of NDMA in the product increase before sale to consumers.

Assuming liability, the court can order remedies in the form of injunctions and penalties. (H&S 25249.7(a).)

The court cannot determine at the inception of the case that injunctive relief will not be permissible and appropriate at the conclusion of the case. Assuming liability, the court will at the conclusion of the case determine whether Apotex is selling or has an intent to sell the

Products. (*Robinson v. U-Haul Company of California* (2016) 4 Cal.App.5th 304, 315-316 [need for injunctive relief is decided at trial].) The court will not presume that the factual landscape will remain unchanged from the filing of the complaint through the completion of trial. This is not a case like *Madrid v. Perot Systems Corp.* (2005) 130 Cal.App.4th 440, in which the court can determine at the pleading stage that there is no possible risk of continuing conduct.

The court cannot determine at the inception of the case that penalties will not be permissible and appropriate at the conclusion of the case. "An award of civil penalties under [Proposition 65] is a statutory punitive exaction … designed to deter misconduct and harm." (*DiPirro v. Bondo Corp.* (2007) 153 Cal.App.4th 150, 183.) Assuming Apotex knowingly and intentionally exposed consumers to NDMA, then penalties might be appropriate to deter similar actions in the future by Apotex and others.

ATTORNEYS' FEES – APOTEX

Defendant Apotex is a Generic Manufacturer and seeks to strike the prayer for attorneys' fees. Apotex points out that it recalled the Products before the Plaintiff filed this lawsuit and that plaintiff cannot prove a causal connection between the filing of the lawsuit and the recall.

Plaintiff could prevail at trial if plaintiff demonstrated that Apotex knowingly and intentionally exposed consumers to NDMA before September 2019 without first giving clear and reasonable warning. (H&S 25249.6.) For purposes of establishing liability, it is immaterial that Apotex no longer distributes the Product. The court could order penalties even if the court decided that injunctive relief was not appropriate.

In addition, it is immaterial whether the prayer for relief includes a request for attorneys' fees. If plaintiffs prevail at trial, then under CCP 1032 they can recover costs and under CCP

1033.5(a)(10 costs includes fees. (*Khavarian Enterprises, Inc. v. Commline, Inc.* (2013) 216 Cal.App.4th 310, 327.) (See also *Snatchko v. Westfield LLC* (2010) 187 Cal.App.4th 469, 497.)

FURTHER PROCEEDINGS

Plaintiff must file any third amended complaint on or before 5/28/21.

Dated: May __, 2021

Winifred Y. Smith
Judge of the Superior Court

Exhibit 44

SUPERIOR COURT OF THE STATE OF CALIFORNIA

IN AND FOR THE COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, et al, Plaintiffs/Petitioners, v. PERRIGO COMPANY, et al, Defendants/Respondents.	No. RG20-054985 ORDER SUSTAINING DEMURRERS WITH LEAVE TO AMEND. Date: 5/5/21 Time: 10:00 a.m. Dept.: 21

Several demurrers came on for hearing on 5/5/21, in Department 21 of this Court, the Honorable Winifred Y. Smith presiding. Counsel appeared on behalf of Plaintiff and on behalf of Defendant. After consideration of the points and authorities and the evidence, as well as the oral argument of counsel, IT IS ORDERED:

The demurrer of Chattem and Sanofi-Aventis (Brand Name Defendant (R#2240283) is SUSTAINED WITH LEAVE TO AMEND.

The demurrer of Apotex (Generic Manufacturer Defendant) (R#2240282), the demurrer of Perrigo (Generic Manufacturer Defendant) (R#2242700), the demurrer of Granules USA, Inc. (Generic Manufacturer Defendant) (R#2242703), and the demurrer of Dr. Reddy's Laboratories,

Inc. (Generic Manufacturer Defendant) (R#2240276) are SUSTAINED WITHOUT LEAVE TO AMEND.

The demurrer of 7-Eleven (Retailer Defendant) (R#2240281) and the demurrer of Target Corporation (Retailer Defendant) (R#2242040) are SUSTAINED WITHOUT LEAVE TO AMEND.

BACKGROUND

These are demurrers, so the court assumes "the truth of the properly pleaded factual allegations, facts that reasonably can be inferred from those expressly pleaded and matters of which judicial notice has been taken." (*Redfearn v. Trader Joe's Co.* (2018) 20 Cal.App.5th 989, 996.)

The court GRANTS all the requests for judicial notice. In other circumstances the court might not permit this expansive use of judicial notice because it has the effect of turning a demurrer into a de facto motion for summary judgment. (*Richtek USA, Inc. v. uPI Semiconductor Corporation* (2015) 242 Cal.App.4th 651, 660.) There were no objections to the requests for judicial notice. Furthermore, the issue presented is legal in nature and the evidence relevant to the legal issue is undisputed. The evidence is disputed regarding substantive issues, but the demurrers are not about the substantive issues.

THE COMPLAINT

Defendants manufacture, import, distribute, or sell the Products. (2AC, para 34.) The Products are non-prescription, or "over the counter ("OTC"), drugs The known carcinogen

NDMA was in the Products when the consumers bought the products. Defendants know or should have known there was NDMA in the Products. (2AC, para 34, 43.)

In September 2019, there were recalls of the Products based on the presence of NDMA. (2AC, para 36.) Following the recalls, the FDA issued public alerts. (2AC, para 36.) Defendant continued to sell the products after the recalls and public alerts without giving appropriate warmings. (2AC, para 37, 44.)

The 2AC assets a single cause of action against the Defendants under H&S 25249.6 alleging that they have intentionally exposed individuals to NDMA without first giving clear and reasonable warnings. (2AC, para 45.)

The demurrers are based on the related issues of H&S 25249.10(a) and preemption. The Brand Name Manufacturers, the Generic Manufacturers, and the Private Label Retailers argue impossibility preemption. Defendant Apotex is a Generic Manufacturer and also argues field preemption and mootness. For purposes of these demurrers the court can assume that defendants marketed and sold the Products knowing that there was NDMA in the Products, whether as a result of FDA approved design or manufacturing or as a result of manufacturing contamination, storage in high heat, or delay in sale to consumers.

RELATED CASES

The court takes judicial notice of the existence of parallel mass tort proceedings concerning MDNA, ranitidine, and the Products. There is a Federal MDL in Florida, which concerns claims for personal injuries. There is a California JCCP that concerns claims for personal injuries. (*In re Ranitidine Cases*, JCCP 5150.)

PROPOSITION 65 – COMPLIANCE/LIABILITY AND REMEDY

H&S 25249.6 states: "No person in the course of doing business shall knowingly and intentionally expose any individual to a chemical known to the state to cause cancer or reproductive toxicity without first giving clear and reasonable warning to such individual, except as provided in Section 25249.10."

A defendant can comply with the law by ensuring that its products do not "expose any individual to a chemical known to the state to cause cancer or reproductive toxicity." This means keeping the chemical exposure below the "no significant risk" level. (H&S 25249.10(c).)

A defendant can comply with the law by providing a "clear and reasonable warning." The warning must have certain content. (27 CCR 25603.) The content of the warning may be transmitted through product labeling, point-of-sale signs, or public advertising. (*Dowhal v. SmithKline Beecham Consumer Healthcare* (2004) 32 Cal.4th 910, 918.) (See also 27 CCR 25601(c), 25602.)

If the court finds that a defendant is in violation of H&S 25249.6, then the court can order remedies in the form of injunctions and penalties. H&S 25249.7(a) states "A person who violates or threatens to violate Section 25249.5 or 25249.6 may be enjoined in any court of competent jurisdiction." H&S 25249.7(b) states "A person who has violated Section 25249.5 or 25249.6 is liable for a civil penalty."

For purposes of this motion, it is useful to distinguish between the compliance/liability provision (H&S 25249.6) and the remedy provision (H&S 25249.7).

A defendant can comply with Prop 65 and avoid liability by either providing a warning or ensuring that its products have chemical exposure below the "no significant risk" level. (H&S 25249.6 and 25249.6.10(c).) A lack of warning can result in liability.

Assuming a lack of compliance, which is liability, then the court can order a remedy. The court can order injunctions and penalties. (H&S 25249.7(a) and (b). The court can order a warning as a remedy.

The analysis in this order is focused on the liability provision, H&S 25249.6, which is limited by the exemption provision, H&S 25249.10(a), which states that there is no Proposition 65 liability for "an exposure for which federal law governs warning in a manner that preempts state authority." The analysis in this order does not address or decide whether under the remedy provision of H&S 25249.7 the court could order a defendant to manufacture the products free of contaminants, to take greater care in storing the products, and to set expiration dates to require sale before the degradation of the products.

If the preemption analysis were a de facto inquiry into the scope of relief that the court can order under H&S 25249.7(a), then the court would permit the Attorney General to file an amicus brief and on that issue and to present evidence of any policies that might be relevant to statutory interpretation. (*Yamaha Corp. of America v. State Bd. of Equalization* (1998) 19 Cal.4th 1, 14-15.) The court does not do that because the preemption analysis is focused on compliance/liability under H&S 25249.6.

PROPOSITION 65 – SELF-EXEMPTION TO COMPLIANCE/LIABILITY WHERE THERE IS FEDERAL PREEMPTION OF WARNING.

Prop 65 states that there is an exemption to the compliance/liability provision when federal law governs warnings. H&S 25249.10(a) states: "Section 25249.6 [the compliance/liability provision] shall not apply to any of the following: (a) An exposure for which

federal law governs warning in a manner that preempts state authority." This self-exception does more than state the obvious, which is that federal law preempts state law.

The self-exception states that if federal law for an exposure governs warning in a manner that preempts state authority, then there is no violation of the compliance/liability provision. This in turn means that if federal law on warning preempts state law on warning, then there is no liability for an exposure under H&S 25249.6, whether based on either lack of warning or knowing exposure to chemicals, and thus the court cannot order any non-warning injunctive relief or award any penalties.

Plaintiff argues that this is an improper reading of H&S 25249.10(a) because it limits Proposition 65 more than the direct application of federal preemption. The court is giving effect to the plain words in the statute. Proposition 65 is focused on providing warnings and reasonably does not apply to "An exposure for which federal law governs warning in a manner that preempts state authority."

The FDCA has an express preemption provision for non-prescription ("OTC") drugs such as ranitidine. (21 USC 379r.) The express preemption provision has wide scope and includes "any requirement relating to public information or any other form of public communication relating to a warning of any kind for a drug." (21 USC 379r(c)(2).) The FDCA's express preemption provision would preempt Proposition 65 as applied to OTC drugs, except that the provision has an express exception for any "State requirement adopted by a State public initiative or referendum enacted prior to September 1, 1997." (21 USC 379r(d)(2).) "Proposition 65 is the only state enactment that falls within the savings clause." (*Dowhal v. SmithKline Beecham Consumer Healthcare* (2004) 32 Cal.4th 910, 918.)

The FDCA's exclusion of Proposition 65 from the FDCA's express preemption clause does not exempt Proposition 65 from implied preemption. "[E]ven where the express preemption provision in [21 U.S.C. § 379r] is not applicable, implied preemption may arise … the savings clause does not foreclose the possibility that conflict preemption may arise from federal sources other than 21 U.S.C. § 379r.']. (*Trejo v. Johnson & Johnson* (2017) 13 Cal.App.5th 110, 150-151.) Therefore, the court cannot determine whether the Proposition 65 express exemption (H&S 25249.10(a) applies unless the court goes through the analysis of implied preemption to determine whether "federal law governs warning in a manner that preempts state authority."

The court notes, by way of observation, that the Proposition 65 self-exception under H&S 25249.6 is not part of other statutes. The effect of impossibility preemption operating through the Proposition 65 self-exception is different from impossibility preemption operating in isolation. There might be state law remedies other than Proposition 65 that are not preempted and that would apply if, as alleged, a drug manufacturer is selling, or had sold, drugs that comply with FDA labelling requirements but expose California consumers to hazardous chemicals because the drugs are contaminated, or improperly stored, or not timely sold.

PREEMPTION – GENERALLY.

The United States Congress has the power to preempt state law concerning matters that lie within its authority. (*Farm Raised Salmon Cases* (2008) 42 Cal.4th 1077, 1087.) Preemption of state law may be express or implied. Implied preemption occurs "'(i) when it is clear that Congress intended, by comprehensive legislation, to occupy the entire field of regulation, leaving no room for the states to supplement federal law [citation]; (ii) when compliance with both

federal and state regulations is an impossibility [citation]; or (iii) when state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress. (*Solus Industrial Innovations, LLC v. Superior Court* (2018) 4 Cal.5th 316, 332.)

"[F]ederal preemption presents a pure question of law." (*Farm Raised Salmon Cases* (2008) 42 Cal.4th 1077, 1089 fn 10; *Coleman*, 223 Cal.App.4th at 422.) The court focuses on the intent of Congress. (*Spielholz v. Superior Court* (2001) 86 Cal.App.4th 1366, 1371.)

"Ordinarily, there is a presumption against preemption. (*Solus Industrial Innovations, LLC v. Superior Court* (2018) 4 Cal.5th 316, 332.) The strength of the presumption is heightened in areas where the subject matter has been the longstanding subject of state regulation in the first instance." (*Quesada v. Herb Thyme Farms, Inc.* (2015) 62 Cal.4th 298, 313.)

IMPOSSIBILITY PREMPTION - GENERALLY

"Federal preemption applies when state and federal laws directly conflict. … When it is impossible for a private party to comply with both state and federal requirements, a direct conflict exists. (*Teva Pharmaceuticals USA, Inc. v. Superior Court* (2013) 217 Cal.App.4th 96, 105.) "A defendant cannot establish impossibility preemption "merely by demonstrating it is difficult or costly to comply. Rather, it must show using point of sale signs is a "physical impossibility." (*People v. Cotter & Co* (1997) 53 Cal.App.4th 1373, 1393-1394.)

FDA REGULATION – GENERALLY

A Brand Name Manufacturer must demonstrate to the FDA that a new drug is safe and effective. (21 U.S.C. 355(a), (b)(1); 21 C.F.R. 314.1–314.3, 314.50.) When a Brand Name Manufacturer seeks approval for an OTC version of a prescription medication, the manufacturer

shows the FDA that the medication is appropriate for self-administration. (21 C.F.R. § 310.200(b); 21 U.S.C. §§ 353(b)(3), 355(c)–(d).)

The FDA approves the language in the labelling. The Brand Name Manufacturer must use the *exact* language approved by FDA in the labeling or packaging. (21 C.F.R. 214.70(b), (c), 314.71.)

The FDCA requires that OTC manufacturers provide *only* those warnings in OTC labeling approved by FDA in precisely the approved manner. (21 U.S.C. § 355.)

IMPOSSIBILITY PREMPTION – BRAND NAME MANUFACTURERS

The demurrer of Chattem and Sanofi-Aventis (Brand Name Defendant (R#2240283) is SUSTAINED WITH LEAVE TO AMEND.

The impossibility preemption demurrer of the Brand Name Defendants presents the issues of whether compliance with Proposition 65 was impossible given: (1) the ability of the Brand Name Defendants to change labelling under the Changes Being Effected process and (2) the ability of the Brand Name Defendants to add a Proposition 65 warning to the FDA approved warnings.

THE CBE PROCESS

A Brand Name Defendant can change a label without FDA approval in certain limited circumstances. "Major changes" require FDA preapproval, while certain labeling changes separately defined as "moderate changes" do not. (21 CFR 314.70(c)(6)(iii).)

A Brand Name Defendants can unilaterally make moderate changes, but those are limited to "changes … to reflect newly acquired information … [t]o add or strengthen a contraindication,

warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter." (21 CFR 314.70(c)(6)(iii).) The CBE process only permits changes "add[ing] or strengthen[ing] a contraindication, warning, precaution, or adverse reaction" for a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug. (21 CFR 201.57.)

Wyeth v., Levine (2009) 555 US 555, addresses the CBE process and preemption. Procedurally, *Wyeth* was decided after trial. In *Wyeth*, a consumer sued the brand-name drug manufacturer for failure to provide an adequate warning on the drug's labeling. (555 US at 559-560). The Supreme Court held that the consumer's labeling claims were not pre-empted because the Changes Being Effected ("CBE") process permitted the brand-name drug manufacturer to "unilaterally strengthen" the warning on the labeling, without waiting for FDA approval. (555 US at 568-569.) The Court stated that it could not conclude that it was impossible for the brand-name drug manufacturer to comply with both its federal-law and state-law duties "absent clear evidence that the FDA would not have approved" a labeling change. (555 US at 571) The brand-name drug manufacturer "offered no such evidence," and the fact that the FDA had previously approved the labeling did "not establish that it would have prohibited such a change." (555 US at 572-573.)

To state a claim for failure-to-warn that is not preempted by the FDCA, a plaintiff must plead "a labeling deficiency that [Defendants] could have corrected using the CBE regulation." (*Gibbons v. Bristol-Myers Squibb Co.* (2nd Cir. 2019) 919 F.3d 699, 708.)

Turning to this case, the 2AC does not allege that the Brand Name Manufacturers could use the CBE process to present a Proposition 65 warning.

The CBE process requires Brand Name Manufacturers to demonstrate that there a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug. (21 C.F.R. 201.57.)

Proposition 65 applies unless a Brand Name Manufacturer can demonstrate that "the exposure poses no significant risk assuming lifetime exposure at the level in question for substances known to the state to cause cancer, and that the exposure will have no observable effect assuming exposure at one thousand (1,000) times the level in question for substances known to the state to cause reproductive toxicity. (H&S 25249.10(c).)

There is a gap where an exposure is above the level that arguably requires a Proposition 65 warning but below the level that permit a Brand Name Manufacturer to "unilaterally strengthen" the labelling by adding a CBE warning. If the NDMA exposure is in this gap, then federal law preempts Proposition 65. If the NDMA exposure is so high that it both requires a Proposition 65 warning and the manufacturer can use the CBE process, then there is no impossibility preemption because a defendant can comply with both state and federal law.

Plaintiff's may amend, if possible, to allege that the NDMA exposure presented a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug. (21 C.F.R. 201.57) and as a result the Brand Name Manufacturers could use the CBE process to unilaterally strengthen the warning on the labeling without waiting for FDA approval. Plaintiff is not required to allege evidentiary facts to support this allegation. "[A] complaint ordinarily is sufficient if it alleges ultimate rather than evidentiary facts." (*Doe v. City of Los Angeles* (2007) 42 Cal.4th 531, 550.) Furthermore, preemption is an affirmative defense and a plaintiff is not required to anticipate and "plead around" a defendant's affirmative

defenses. (*Stowe v. Fritzie Hotels, Inc.* (1955) 44 Cal.2d 416, 422.) That said, pleadings that define the issues clearly are important for framing discovery, summary judgment, and trial.

WARNINGS

The Brand Name (and Generic) Manufacturers argue that the FDCA regulates warnings for OTC drugs, that Proposition 65 warnings are a form of warning, it is impossible to comply with both federal and state law requirements for warnings, and that impossibility preemption applies. Plaintiff argues that the FDCA does not regulate warnings in the advertising of OTC drugs, that Proposition 65 warnings can be provided through advertising, it is possible to comply with both federal and state law requirements, and that impossibility preemption does not apply. Counsel for plaintiff succinctly summarized the argument at the hearing on 5/5/21 with the phase "That which is possible is not impossible." The court concludes that impossibility preemption applies to warnings.

The court starts with Proposition 65. H&S 25249.10(a) states that Proposition 65 does not apply if "federal law governs warning in a manner that preempts state authority." A warning is defined by the substantive content. (27 CCR 25603.) A warning can be transmitted through various mechanisms. (H&S 25249.11(f) [warning "may be provided by general methods such as labels, …, posting of notices, placing notices in public news media, and the like"]; 22 CCR 3202 [warnings can be delivered through signs, notices, or newspapers].) The Proposition 65 regulations repeatedly distinguish between "Warnings-Content" and "Warnings-Methods of Transmission." (27 CCR 25601 et seq.)

The court turns to the FDCA. The FDA must approve a manufacturer's warnings as they appear on a drug's labels and labelling. (21 USC 355(b)(1)(A)(6), (d).) The FDA must similarly

approve warnings in a generic manufacturer's labels and labelling. (21 USC 355(j)(2)(A)(i) and (v), (j)(4)(G) and (H).) A generic manufacturer cannot change the content or form of the "warnings" section of the labelling. (21 USC 355(j)(10)(A)(2).))

The FDCA regulations state that "warning" is part of "content." (21 CFR 201.66(c)(5).) The FDCA regulations state the format for disclosing the warnings. (21 CFR 201.66(d)(10).) The location for the warning is on "The outside container or wrapper of the retail package, or the immediate container label if there is no outside container or wrapper." (21 CFR 201.66(c).) "Label" is defined as "a display of written, printed, or graphic matter upon the immediate container of any article." (21 U.S.C. § 321(k).) There are regulations about what must be on a label on a container (21 CFR 201.66(c)), or, if the containers lacks space for the information, on accompanying printed material (21 CFR 201.66(c)(10).) "Labeling" is more broadly defined to include "all labels and other written, printed, or graphic matter (1) upon any article or any article or any of its containers or wrappers, or (2) accompanying such article." (21 U.S.C. § 321(m).) There are no FDA regulations about point of sale or shelf disclosures for OTC drugs.

The FDCA does not regulate the advertising of OTC drugs. The FTC regulates the advertising of OTC drugs. (CEH RJN, Exh. 5, at 2; Brand Name Manufacturers RJN, Exh. F, at 13 n.25.)

The court's focus is on the word "warning" and the substantive content of the information in the communication. A Proposition 65 warning is a warning. A Proposition 65 warning on a "label" (21 U.S.C. 321(k)) does not become less of a warning if it is on "labelling" (21 U.S.C. 321(m)) and does not cease to be a warning when it is in "advertising."

A Proposition 65 warning is a "warning" within the definition of the FDCA definition of "warning" used in the FDCA regulations on "Format and content requirements for over-the-

counter (OTC) drug product labeling." (21 CFR 201.66(c)(5).) The FDCA approves "warnings" for OTC drugs, the Brand Name Manufacturers must use the FDA approved "warnings," it is impossible for the Brand Name Manufacturers to deviate from the approved warnings, so there is impossibility preemption, so the H&S 25249.10(a) self-exception applies. Proposition 65 does not apply to exposures in the OTC drugs. This ends the analysis.

LABELS, LABELLING, AND ADVERTISING

Much of the briefing and analysis was based on the assumption or argument that the scope of FDCA regulation of the Content of "warnings" was defined by the Methods of Transmission of the warnings. (27 CCR 25601 et seq. [Distinguishing between "Warnings-Content" and "Warnings-Methods of Transmission"].) This is reasonable. The FDCA regulation of "warnings" is very specific regarding labels, is less specific regarding labelling, and is non-existent regarding advertising. In the interest of thoroughness, the court covers three issues related to the means of transmitting the warnings: (1) the definition of labelling under the FDCA and (2) the voluntary nature of advertising, and (3) plaintiff's argument that "That which is possible is not impossible."

LABELS, LABELLING, AND ADVERTISING THE FDCA

Plaintiff argues that the Brand Name Manufacturers does not prevent them from transmitting Proposition 65 warnings to consumers through advertising and that therefore it is possible to continues to transmit only FDCA approved warnings in labels and labelling while transmitting California required Proposition 65 warning in advertising. This argument fails because "labelling" under the FDCA includes all means of transmitting warnings.

The FCDA at 21 USC 321(m) states: "(m) The term "labeling" means all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) *accompanying such article*." (Emphasis added.)

The Meat Inspection Act (MIA) also includes the phrase "accompanying such article." In *American Meat Institute v. Leeman* (2009) 180 Cal.App.4th 728, the court held that for purposes of the MIA the phrase "accompanying such article" in the definition of labelling means that the MIA preempted Proposition 65's warning requirements. *Leeman* cited to *Kordel v. United States* (1948) 335 US 345, for the proposition that 21 USC 321(m) in the FDCA defined "labeling" to include supplemental literature not attached to the product.

Talking a detour from *Leeman*, in *Leeman* the court quotes *Kordel*, 335 US at 350, which states:

> One article or thing is accompanied by another when it supplements or explains it, in the manner that a committee report of the Congress accompanies a bill. No physical attachment one to the other is necessary. It is the textual relationship that is significant. ...
>
> The false and misleading literature in the present case was designed for use in the distribution and sale of the drug, and it was so used. The fact that it went in a different mail was wholly irrelevant whether we judge the transaction by purpose or result. ...
>
> ... The [FDCA] cannot be circumvented by the easy device of a 'sale' of the advertising matter where the advertising performs the function of labeling.

> Petitioner points out that in the evolution of the Act the ban on false advertising was eliminated, the control over it being transferred to the Federal Trade Commission. ... We have searched the legislative history in vain, however, to find any indication that Congress had the purpose to eliminate from the Act advertising which performs the function of labeling. Every labeling is in a sense an advertisement. The advertising which we have here performs the same function as it would if it were on the article or on the containers or wrappers. As we have said, physical attachment or contiguity is unnecessary under s 201(m)(2).

Kordel makes plain that a plaintiff cannot avoid federal preemption by characterizing labelling as advertising matter "where the advertising performs the function of labeling."

Leeman, 180 Cal.App.4th at 758, finds that *Chemical Specialties Mfrs. Ass'n, Inc. v. Allenby* (9th Cir., 1992) 958 F.2d 941, is not persuasive regarding the interpretation of "accompanying" in FIFRA and, if persuasive, the FIFRA analysis does not apply to the phrase "accompanying such article" as used in the MIA. *Leeman* arguably requires this court to find Allenby is not persuasive. (*Auto Equity Sales, Inc. v. Superior Court of Santa Clara County* (1962) 57 Cal.2d 450, 455.) This court independently does not find *Allenby* persuasive for the reasons stated in *Leeman*.

Leeman, 180 Cal.App.4th at 761, concludes, "Thus, because (1) point of sale warnings are "labeling" within the meaning of the FMIA, and (2) there is no dispute that the warnings required by Proposition 65 are "in addition to, or different than" the labeling required by the FMIA (21 U.S.C. § 678), we conclude that the trial court properly ruled that Proposition 65's

point of sale warning requirements with respect to meat are preempted by the FMIA." The MIA and the FDCA definitions of "labeling" both use the phrase "accompanying such article."

Also relevant are the FDCA regulations at 21 CFR 202.1(l) which distinguish "advertisements" from "labeling" by the target audience. For purposes of prescription drugs, "advertisements" advertisements directed to the general public whereas "labeling" is "Brochures, booklets, mailing pieces, detailing pieces, ... for use by medical practitioners, pharmacists, or nurses." (*In re Lipitor* (D. S.C., 2016) 185 F.Supp.3d 761, 772 ["advertising to the general public, as opposed to materials for use by medical professionals, is not considered labeling and, thus, can be changed without the need to invoke the CBE regulation."].) Where prescription drugs are involved, "medical practitioners, pharmacists, or nurses" are the persons who make those decisions and "the duty to warn runs to the physician, not to the patient." (*Carlin v. Superior Court* (1996) 13 Cal.4th 1104, 1116.) When the target audience is defined, 21 CFR 202.1(l) supports a reading of "labelling" to include any information transmitted to the person who makes the decision whether the drug is appropriate. With OTC drugs, the target audience is the general public, so all content transmitted to the general public is arguably "labelling."

Leeman, Kordel, and 21 CFR 202.1(l) compel the conclusion that any information that is transmitted to the person who makes the drug use decision serves the purpose of labelling and is "labelling" under the FDCA. Plaintiffs cannot avoid impossibility preemption by conflating labeling and advertising and suggesting that defendants can transmit the Proposition 65 warning in advertising.

Numerous lower federal courts have consistently held that FDA regulation of "labels" and "labelling" results in preemption of claims regarding any failure to transmit warnings through any communication channel. "While [California trial courts] are not bound by decisions

of the lower federal courts, even on federal questions, they are persuasive and entitled to great weight. … where the decisions of the lower federal courts on a federal question are "both numerous and consistent," we should hesitate to reject their authority." (*Etcheverry v. Tri-Ag Service, Inc.* (2000) 22 Cal.4th 316, 320-321.) (*Fair v. BNSF Railway Co.* (2015) 238 Cal.App.4th 269, 287.)

Representative federal cases include:

1. *Strayhorn v. Wyeth Pharmaceuticals, Inc.* (6th Cir. 2013) 737 F.3d 378, 394 ["Because such advertising and promotional materials are considered labeling, and because labeling is limited by federal law to the information contained in the brand-name drug's labeling, all of the warranty claims against the Generic Manufacturers based on these materials are preempted under *Mensing*."]
2. *Guarino v. Wyeth* (11th Cir. 2013) 719 F.3d 1245, 1249 ["Guarino's attempt to elude *Mensing* by clothing her allegations as "failure-to-communicate" claims rather than failure-to-warn claims does not alter our analysis. No matter the garb in which she attempts to present them, Guarino's claims are at bottom allegations regarding Teva's failure to warn her of the dangers of long-term metoclopramide use, and they therefore cannot escape *Mensing*'s grasp."]
3. *Montero v. Teva Pharmaceuticals USA Inc.* (S.D. N.Y. 2020) 2020 WL 1862593 at *3 ["Plaintiff alleges inadequate warnings … in Defendants' communications with healthcare providers and advertisements to the public. The preemption of failure-to-warn claims extends to these latter types of communications as well."]
4. *In re Fosamax Products Liability Litigation* (S.D.N.Y 2013) 965 F.Supp.2d 413, 419 ["This Court joins the majority of other courts to consider this issue in holding that any

claims stemming from the generic defendants' alleged failure to communicate additional warnings through some method other than their package inserts are preempted"]

5. *In re Yasmin and Yaz (Drospirenone) Marketing, Sales Practices And Products Liability Litigation* (S.D. IL. 2015) 2015 WL 7272766 *5 ["Plaintiff 's claims "are premised on misrepresentations or inadequacies in … labeling, promotions, and advertisements. As such, [generic manufacturer] could only avoid liability as to these claims by unilaterally strengthening their warning labels in violation of federal law or by leaving the marketplace altogether. *Mensing* and *Bartlett* establish that such challenges to … labeling are preempted."]

The specific definition of "labeling" in the FDCA is significant to the preemption analysis, as other federal statutes have other definitions and therefore have other scopes of preemption. The court focuses on the definition of labeling in 21 USC 321(m) and gives no weight to the analysis of preemption regarding statutes with other definitions or scopes.

One example of a different statute is the federal Hazardous Substances Act (FHSA), which has a preemption provision that applies to "cautionary labeling" (15 U.S.C. § 1261(b)(1)(A)) and defines "label" as "a display of written, printed, or graphic matter upon the immediate container of any substance" (15 USC 1261(n)). *People ex rel. Lungren v. Cotter & Co.* (1997) 53 Cal.App.4th 1373, held that the FHSA did not preempt Proposition 65 claims, noting that the preemption provision was expressly limited to information "upon the immediate container" or accompanying literature regarding instructions for use. (53 Cal.App.4th at 1387.)

Another example is the federal Alcohol Administration Act (AAA) (27 USC 201 et seq.) and Alcoholic Beverage Labeling Act. ("ABLA") (27 USC 213 et seq.), which regulate

"warnings or other information on alcoholic beverage containers," and the scope of preemption is limited to "statement[s] ... placed on any container of an alcoholic beverage, or on any box, carton, or other package." This court in *CEH v. GT Living Foods*, RG19-047748 [Order of 5/12/20], held that the AAA/ABLA did not preempt Proposition 65 regarding point of sale information because it was not on the places identified in the statute.

THE VOLUNTARY NATURE OF ADVERTISING

Plaintiff's argument that the Brand Name Manufacturers can transmit warnings through advertisement that they cannot transmit though the current FDA approved labels and labelling suggests some conceptual distinction between labelling and advertising. The court sua sponte considered this issue in the tentative decision and it was the subject of discussion at the 5/5/21 hearing. The court concludes that "advertising" is by definition voluntary in nature, which means that if Proposition 65 is compelling a manufacturer to transmit a warning then the transmittal is by definition not through "advertising," which means that it is through "labelling" as defined in and regulated under the FDCA.

Federal, state or local authorities can mandate the transmittal of information to consumers for public health and safety interests as a condition of permitting sales to consumers. The FDA requires certain information about drug on labels and in labelling (21 CFR 201.1 et seq), the FDA requires warnings on packs of cigarettes (21 CFR 1141.5), and California requires warnings when there is exposure to a chemical known to the state to cause cancer or reproductive toxicity (H&S 25249.6). In contrast, private persons voluntarily decide to advertise their products. If a person decides to advertise, the existence, content, and form of advertising is generally at the discretion of the advertiser.

This suggests a distinction between required or compelled speech and voluntary speech. This distinction is subject to two exceptions. Voluntary speech cannot be false to misleading. Voluntary speech can also be conditioned on mandated disclosures "as long as disclosure requirements are reasonably related to the State's interest in preventing deception of consumers." (*National Ass'n of Manufacturers v. S.E.C.* (D.C. Cir. 2015) 800 F.3d 518, 519.) Regulatory authorities can require the transmittal of "purely factual and uncontroversial information." (*National Ass'n of Manufacturers*, 800 F.3d at 523.) For example, the FDA requires the Brand Name Manufacturers to transmit certain information as a condition of the approval to sell the Products. Putting aside restrictions on false and misleading information and mandated disclosures, the "general rule" is "that the speaker has the right to tailor the speech" and that advertisers have First Amendment discretion regarding "expressions of value, opinion, or endorsement" and also "to statements of fact the speaker would rather avoid." (*National Ass'n of Manufacturers*, 800 F.3d at 523.)

At the hearing on 5/5/21, plaintiff noted that in *Consumers Union of U.S., Inc. v. Alta-Dena Certified Dairy* (1992) 4 Cal.App.4th 963, 973-974, the Court of Appeal affirmed a trial court's ability to order affirmative disclosure of information as a remedy for previous consumer deception and argued that this shows that compelled speech can be "advertising." *Alta-Dena* used the word "advertising" to describe the defendant's prior misrepresentations. Regarding the remedy of compelled speech, the Court of Appeal referred to "the court's authority to order the placement of warnings on its consumer products" and "the placement of a warning on products sold in the future." (4 Cal.App.4th at 974, 975 and fn 6.)

This broad-brush analysis of the distinction between compelled speech and voluntary speech suggests that as soon as a regulatory authority (or Proposition 65 plaintiff) asserts that a

warning is mandated then the warning is no longer voluntary "advertising." Under this analysis, when a party asserts that the Proposition 65 warning is mandatory then the obligation to provide a warning cannot be categorized as "advertising" under the FDCA and is more properly categorized as "labeling" under 21 USC 321(m). If it its "labeling," then impossibility preemption applies and the H&S 25249.10(a) self-exclusion applies.

PROPOSITION 65 WARNINGS ARE POSSIBLE, SO THEY ARE NOT IMPOSSIBLE

At the hearing on 5/5/21, plaintiff noted that the FDCA does not prevent defendant from transmitting Proposition 65 warnings in advertising, advanced the maxim of "That which is possible is not impossible," and argued that the impossibility preemption does not apply.

The "not impossible" argument finds plausible support in *Leipart v. Guardian Industries, Inc.* (9th Cir., 2000) 234 F.3d 1063, 1070-1071, where the court held it was "not impossible" for a glass door to have both the Consumer Product Safety Act ("CSPA") mandated label and also a different state common law tort based warning. *Leipart* is distinguishable because although federal law mandated a federal label on the glass door and provided a labelling "floor," the manufacturer's responsibility to provide the mandated CPSA federal warning does not prevent the manufacturer from providing additional warnings to meet the California tort duty to warn.

The "not impossible" argument also finds plausible support in *Clark v. Citizens of Humanity, LLC* (S.D. Cal., 2015) 97 F.Supp.3d 1199, 1205-1206, where the court held it was "not impossible" for defendants to comply with the federal standard for using a "Made in the U.S.A." label and the different California standard for the same label. The court reasoned that defendant could sell the clothes with no label or could or use a distinct label for clothing sold in California. *Clark* is distinguishable because the "Made in the U.S.A." label was in the nature of

voluntary advertising. In this case, in contrast, the FDCA prevents the sale of the Products unless they have the FDA approved labels and labelling.

The "not impossible" argument calls attention to the distinctions between federal laws that prohibit actions, that mandate actions, that mandate actions as a condition of otherwise voluntary actions, and that permit actions. In *Leipert*, federal law permitted additional state warnings. In *Clark*, federal law permitted federal and state labels, but did not require either as a condition of selling the product. With OTC drugs, the FDCA mandates the use of the FDA approved labels and labelling as a condition of marketing and sales. Unlike *Leipert*, the federal labelling for OTC drugs is not a labelling "floor" and instead determines the content and the means of transmission for warnings about OTC drugs.

The "not impossible" argument fails because although the FDCA might not prevent the defendants from voluntarily putting Proposition 65 warnings in advertisements for the Products, the FDCA's regulation of warnings on labels and in labelling means that "federal law governs warning in a manner that preempts state authority", which means that the H&S 25249.10(a) self-exception applies.

IMPOSSIBILITY PREMPTION – GENERIC MANUFACTURERS

The demurrer of Apotex (Generic Manufacturer Defendant) (R#2240282) is SUSTAINED WITHOUT LEAVE TO AMEND. The demurrer of Perrigo (Generic Manufacturer Defendant) (R#2242700) is SUSTAINED WITHOUT LEAVE TO AMEND. The demurrer of Granules USA, Inc. (Generic Manufacturer Defendant) (R#2242703) is SUSTAINED WITHOUT LEAVE TO AMEND. The demurrer of Dr. Reddy's Laboratories,

Inc. (Generic Manufacturer Defendant) (R#2240276) is SUSTAINED WITHOUT LEAVE TO AMEND.

The impossibility preemption demurrer of the Generic Manufacturer Defendants presents the issues of whether compliance with Proposition 65 was impossible given: (1) the obligation of the Generic Manufacturer Defendants to provide the same label and labelling information as the Brand Name Defendants (the "duty of sameness") and (2) the ability of the Brand Name Defendants to provide Proposition 65 Warnings in the form of advertising.

THE CBE PROCESS, DUTY OF SAMENESS, AND THE EXPIRATION DATE EXCEPTION

Generic drug manufacturers have an ongoing federal duty of sameness that requires "that the warning labels of a brand-name drug and its generic copy must always be the same." (*PLIVA v. Mensing* (2011) 564 US 604, 613.)

An application for a generic drug (Abbreviated New Drug Application or ANDA), the applicant must provide information about the labeling. (21 USC 355(j)(2)(A)(i) and (G).)

The proposed labelling on warnings must be the same as the labelling on warnings for the original approval. An application for a generic drug must not "include a change to the "Warnings" section of the labeling." (21 USC 355(j)(10)(A)(iii).) The FDA may withdraw approval for a generic drug if it finds that the drug product's labeling "is no longer consistent with that for the listed drug." (21 C.F.R. 314.150(b)(10).)

The result is that unlike the holders of the original FDA approvals, the holder of generic approvals cannot use the CBE process. Generic drug manufacturers can use the CBE process only after the holder of the original FDA approval has used the CBE process. The CBE process allows "changes to generic drug labels only when a generic drug manufacturer changes its label

to match an updated brand-name label or to follow the FDA's instructions." (*Mensing*, 564 U.S. at 614.)

PLIVA v. Mensing (2011) 564 US 604, and *Mutual Pharmaceutical v. Bartlett* (2013) 570 US 472, examines how the duty of sameness affects impossibility preemption.

In *Mensing*, consumers of generic drugs sued the generic drug manufacturers for failure to provide adequate warnings on the drugs' labeling. The Supreme Court held that the consumers' labeling claims were pre-empted because the generic drug manufacturers could not "independently" change the labeling while remaining in compliance with federal law. The generic drug manufacturers' "duty of 'sameness'" under federal law required them to use labeling identical to the labeling of the equivalent brand-name drug. Thus, the CBE process was unavailable to the generic drug manufacturers to change labeling absent a change to the brand-name drug's labeling. Because any change that the generic drug manufacturers made to the drugs' labeling to comply with duties arising under state tort law would have violated federal law, the state tort claims were pre-empted.

In *Bartlett*, the Supreme Court expanded on *Mensing* and held that even though a generic drug manufacturer could in theory comply with both federal and state law by removing the drug from the market, that was "no solution." The Supreme Court reasoned pre-emption case law "presume[s] that an actor seeking to satisfy both his federal- and state-law obligations is not required to cease acting altogether in order to avoid liability." (570 US at 488.) The Supreme Court reasoned that this "stop-selling rationale would render impossibility pre-emption a dead letter and work a revolution in the Court's preemption case law. (570 US at 475, 488-490.) (See also *Trejo v. Johnson & Johnson* (2017) 13 Cal.App.5th 110,150-151 [discussing stop-selling as remedy].)

There is one arguably applicable specific exception to the duty of sameness and thus one arguably applicable exception to the impossibility preemption analysis of *Mensing* and *Bartlett*. Generic manufacturers have no duty under federal regulations to use the same expiration date on their drugs as the brand name equivalent.

When a Generic manufacturer submits an ANDA request for approval to the FDA, then 21 C.F.R. 314.94(a)(8) generally requires that the generic ANDA label have the same information as the brand name NDA label. The exception is that 21 C.F.R. 314.94(a)(8)(iv) states: "Labeling …proposed for the drug product must be the same as the labeling approved for the reference listed drug, except for changes required … because the drug product and the reference listed drug are produced or distributed by different manufacturers. Such differences between the applicant's proposed labeling and labeling approved for the reference listed drug may include differences in expiration date, …"

Addressing this specific exception, *in re Zantac (Ranitidine) Products Liability Litigation* (S.D. Fl., 2020) 2020 WL 7864213 at *5, states, "With limited exceptions, the FDA may approve the ANDA only if it finds that the generic drug and its proposed labeling are the same as the listed drug and the listed drug's labeling. … One such exception is that the generic drug's proposed labeling "may include differences in expiration date" from the listed drug."

Turning to this case, as a matter of law the Generic Manufacturers cannot use the CBE process to present a Proposition 65 warning. If the Brand Name Manufacturers did not have a Proposition 65 warning on their labels or labelling, then the Generic Manufacturers cannot have a Proposition 65 warning on their labels or labelling. Impossibility preemption applies, which means the H&S 25249.10(a) self-exception applies.

The expiration date exception to the duty of sameness exists and affects impossibility preemption regarding expiration dates, but has no effect on the H&S 25249.10(a) self-exception analysis. The H&S 25249.10(a) self-exception states that Proposition 65 does not apply to "An exposure for which federal law governs warning in a manner that preempts state authority." The FDCA governs warnings. An application for a generic drug must not "include a change to the "Warnings" section of the labeling." (21 USC 355(j)(10)(A)(iii).) Expiration dates are part of labels and labelling, but they are not warnings. As a result, the H&S 25249.10(a) self-exception applies to OTC drugs even though the duty of sameness and thus impossibility preemption does not apply to expiration dates.

LABELLING AND ADVERTISING

A Generic Manufacturer must provide information about OTC drugs to consumers through FDA approved labelling but can voluntarily provide additional information to consumers through advertising.

As discussed above in the context of the Brand Name Manufacturers, the court concludes that any mandated Proposition 65 warning fits within the FDCA's definition of "labeling," which means that it concerns "An exposure for which federal law governs warning in a manner that preempts state authority" under H&S 25249.10(a).

IMPOSSIBILITY PREMPTION - RETAILERS

The demurrer of 7-Eleven (Retailer Defendant) (R#2240281) is SUSTAINED WITHOUT LEAVE TO AMEND. The demurrer of Target Corporation (Retailer Defendant) (R#2242040) is SUSTAINED WITHOUT LEAVE TO AMEND.

The impossibility preemption demurrer of Target Corporation and 7-Eleven, Inc. ("Retailer Defendants") presents the issues of whether compliance with Proposition 65 was impossible given: (1) the Retailer Defendants have no approvals from the FDA to manufacture or market the Products and (2) the ability of the Retailer Defendants to provide Proposition 65 Warnings about the Products in the form of advertising.

THE CBE PROCESS AND DUTY OF SAMENESS

The Retailer Defendants do not hold any approvals from the FDA for the manufacture or labelling of the Products. (Retailer RJN ¶ 2, Ex. A.) The 2AC asserts that all defendant manufacture the Products, but "allegations in the pleading may be disregarded if they are contrary to facts judicially noticed." (*Scott v. JPMorgan Chase Bank, N.A.* (2013) 214 Cal.App.4th 743, 751.)

Because the Retailer Defendants do not hold any approvals from the FDA for the Products, the Retailers are not subject to any FDA oversight with respect to the Products. The Retailer Defendants are therefore analytically distinct from the Brand Drug manufacturers and the Generic Manufacturers.

The Retailer Defendants are not required by FDA approvals to provide any FDA approved label or labelling. In the absence of any obligation to provide any FDA approved labelling, it is immaterial whether the Retailer Defendants provided warnings that were the same as the labelling that the FDA approved for the Brand Name Manufacturers or could have used the CBE process to provide different warnings.

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LABELLING AND ADVERTISING

A Retailer Defendant can voluntarily provide information to consumers through advertising.

As discussed above in the context of the Brand Name Manufacturers, the court concludes that any mandated Proposition 65 warning fits within the FDCA's definition of "labeling," which means that it concerns "An exposure for which federal law governs warning in a manner that preempts state authority" under H&S 25249.10(a).

FIELD PREEMPTION – APOTEX

Defendant Apotex is a Generic Manufacturer and argues field preemption. The field preemption argument has no merit.

Field preemption is "where the scheme of federal regulation is sufficiently comprehensive to make reasonable the inference that Congress "left no room" for supplementary state regulation." (*In re Jose C.* (2009) 45 Cal.4th 534, 551.)

Apotex makes what appears to be a novel argument. Apotex argues that the FDA has paid extensive attention to the Products in the time period after it was publicized that the Products contained NDMA and that this extensive attention in this discrete time period is field preemption.

The Apotex field preemption argument has no merit. The court starts with congressional intent. Congress intended through the FDCA to regulate drugs generally, not to regulate the Products specifically. There is no indication of Congressional intent to regulate the Products specifically, so there is no field preemption of the Products specifically. Assuming congressional intent focused on the Products, there is no indication that the regulation was

sufficiently comprehensive to suggest that Congress "left no room" for supplementary state regulation." The Apotex argument suggests that there was no field preemption until September 2019 and that the FDA's attention in that discrete time frame then created field preemption in that discrete time frame.

Using the agrarian definition of field by analogy, Apotex argues that field preemption does not need to encompass the field and that under an appropriate set of facts there can be field preemption for a small patch of grass that for purposes of a lawsuit can be defined as its own separate field. This is not the law.

MOOTNESS – APOTEX

Defendant Apotex is a Generic Manufacturer and argues mootness. The mootness argument has no merit.

"A case is considered moot when "the question addressed was at one time a live issue in the case," but has been deprived of life "because of events occurring after the judicial process was initiated."" (*Wilson & Wilson v. City Council of Redwood City* (2011) 191 Cal.App.4th 1559, 1574.)

Apotex argues that the case is moot because it has voluntarily recalled the Product. That does not make the claim moot.

Plaintiff could prove liability at trial by demonstrating that Apotex knowingly and intentionally exposed consumers to NDMA without first giving clear and reasonable warning. (H&S 25249.6.) The evidence might be that Apotex has for a long time known that contamination in its manufacturing process resulted in NDMA in the Product and that as a result

of how the Product was stored and for how long it was stored the amount of NDMA in the product increase before sale to consumers.

Assuming liability, the court can order remedies in the form of injunctions and penalties. (H&S 25249.7(a).)

The court cannot determine at the inception of the case that injunctive relief will not be permissible and appropriate at the conclusion of the case. Assuming liability, the court will at the conclusion of the case determine whether Apotex is selling or has an intent to sell the Products. (*Robinson v. U-Haul Company of California* (2016) 4 Cal.App.5th 304, 315-316 [need for injunctive relief is decided at trial].) The court will not presume that the factual landscape will remain unchanged from the filing of the complaint through the completion of trial. This is not a case like *Madrid v. Perot Systems Corp.* (2005) 130 Cal.App.4th 440, in which the court can determine at the pleading stage that there is no possible risk of continuing conduct.

The court cannot determine at the inception of the case that penalties will not be permissible and appropriate at the conclusion of the case. "An award of civil penalties under [Proposition 65] is a statutory punitive exaction … designed to deter misconduct and harm." (*DiPirro v. Bondo Corp.* (2007) 153 Cal.App.4th 150, 183.) Assuming Apotex knowingly and intentionally exposed consumers to NDMA, then penalties might be appropriate to deter similar actions in the future by Apotex and others.

ATTORNEYS' FEES – APOTEX

Defendant Apotex is a Generic Manufacturer and seeks to strike the prayer for attorneys' fees. Apotex points out that it recalled the Products before the Plaintiff filed this lawsuit and

asserts that plaintiff cannot prove a causal connection between the filing of the lawsuit and the recall.

Plaintiff could prevail at trial if plaintiff demonstrated that Apotex knowingly and intentionally exposed consumers to NDMA before September 2019 without first giving clear and reasonable warning. (H&S 25249.6.) For purposes of establishing liability, it is immaterial that Apotex no longer distributes the Product. The court could order penalties even if the court decided that injunctive relief was not appropriate.

In addition, it is immaterial whether the prayer for relief includes a request for attorneys' fees. If plaintiffs prevail at trial, then under CCP 1032 they can recover costs and under CCP 1033.5(a)(10 costs includes fees. (*Khavarian Enterprises, Inc. v. Commline, Inc.* (2013) 216 Cal.App.4th 310, 327.) (See also *Snatchko v. Westfield LLC* (2010) 187 Cal.App.4th 469, 497.)

FURTHER PROCEEDINGS

Plaintiff must file any third amended complaint on or before 6/4/21.

Dated: May 7, 2021

Winifred Y. Smith
Judge of the Superior Court

Superior Court of California, County of Alameda
Department 21, Administration Building

Case Number: RG20054985
Case Name: Center for Environmental Health vs. Perrigo Company

RE: ORDER SUSTAINING DEMURRERS WITH LEAVE TO AMEND

DECLARATION OF SERVICE BY MAIL

I certify that I am not a party to this cause and that a true and correct copy of the foregoing document was mailed first class, postage prepaid, in a sealed envelope, addressed as shown at the bottom of this document, and that the mailing of the foregoing and execution of this certificate occurred at 1221 Oak Street, Oakland, California.

Executed on May 11, 2021

Executive Officer/Clerk of the Superior Court

By *Belinda Mercado*
Deputy Clerk

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Exhibit 45

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Attorneys for Plaintiff
CENTER FOR ENVIRONMENTAL HEALTH

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

Case No. RG 20-054985

THIRD AMENDED COMPLAINT FOR INJUNCTIVE RELIEF AND CIVIL PENALTIES

Health & Safety Code § 25249.6, *et seq.*

(Other)

Plaintiff Center for Environmental Health, in the public interest, based on information and belief and investigation of counsel, except for information based on knowledge, hereby makes the following allegations:

INTRODUCTION

1. This Complaint seeks to remedy Defendants' continuing failure to warn individuals in California that they are being exposed to n-nitrosodimethylamine ("NDMA"), a chemical known to the State of California to cause cancer. Such exposures have occurred, and continue to occur, through the manufacture, distribution, sale, and use of over-the-counter acid reducing medications containing ranitidine (the "Products"). Individuals in California are exposed to NDMA when they use the Products.

2. Under California's Proposition 65, Health & Safety Code § 25249.5, *et seq.*, it is unlawful for businesses to knowingly and intentionally expose individuals in California to chemicals known to the State to cause cancer without providing clear and reasonable warnings to such individuals. Defendants introduce Products containing significant quantities of NDMA into the California marketplace, thereby exposing users of their Products to NDMA.

3. Despite the fact that Defendants expose individuals to NDMA, Defendants provide no clear and reasonable warnings about the carcinogenic hazards associated with NDMA exposure. Defendants' conduct thus violates the warning provision of Proposition 65, Health & Safety Code § 25249.6.

PARTIES

4. Plaintiff CENTER FOR ENVIRONMENTAL HEALTH ("CEH") is a non-profit corporation dedicated to protecting the public from environmental health hazards and toxic exposures. CEH is based in Oakland, California and incorporated under the laws of the State of California. CEH is a "person" within the meaning of Health & Safety Code § 25249.11(a) and brings this enforcement action in the public interest pursuant to Health & Safety Code § 25249.7(d). CEH is a nationally recognized non-profit environmental advocacy group that has prosecuted a large number of Proposition 65 cases in the public interest. These cases have resulted in significant public benefit, including the reformulation of thousands of products to

remove toxic chemicals and to make them safer. CEH also provides information to Californians about the health risks associated with exposure to hazardous substances, where manufacturers and other responsible parties fail to do so.

5. Defendant SANOFI-AVENTIS U.S. LLC is a person in the course of doing business within the meaning of Health & Safety Code § 25249.11. Defendant SANOFI-AVENTIS U.S. LLC manufactures, distributes, and/or sells the Products for sale and use in California.

6. Defendant CHATTEM INC. is a person in the course of doing business within the meaning of Health & Safety Code § 25249.11. Defendant CHATTEM INC. manufactures, distributes, and/or sells the Products for sale and use in California.

7. DOES 1 through 20 are each a person in the course of doing business within the meaning of Health & Safety Code § 25249.11. DOES 1 through 20 manufacture, distribute, and/or sell the Products for sale and use in California. Defendants SANOFI-AVENTIS U.S. LLC; CHATTEM INC.; and DOES 1 through 20 are collectively referred to herein as "Defendants."

8. The true names of DOES 1 through 20 are either unknown to CEH at this time or the applicable time period before which CEH may file a Proposition 65 action has not run. When their identities are ascertained or the applicable time period before which CEH may file a Proposition 65 action has run, the Complaint shall be amended to reflect their true names.

JURISDICTION AND VENUE

9. The Court has jurisdiction over this action pursuant to Health & Safety Code § 25249.7, which allows enforcement in any court of competent jurisdiction, and pursuant to California Constitution Article VI, Section 10, because this case is a cause not given by statute to other trial courts.

10. This Court has jurisdiction over Defendants because each is a business entity that does sufficient business, has sufficient minimum contacts in California, or otherwise intentionally avails itself of the California market through the sale, marketing, or use of the Products in California and/or by having such other contacts with California so as to render the exercise of

jurisdiction over it by the California courts consistent with traditional notions of fair play and substantial justice.

11. Venue is proper in Alameda County Superior Court because one or more of the violations arise in the County of Alameda.

BACKGROUND FACTS

12. The People of the State of California have declared by initiative under Proposition 65 their right "[t]o be informed about exposures to chemicals that cause cancer, birth defects, or other reproductive harm." Proposition 65, § 1(b).

13. To effectuate this goal, Proposition 65 prohibits exposing people to chemicals listed by the State of California as known to cause cancer, birth defects, or other reproductive harm above certain levels without a "clear and reasonable warning" unless the business responsible for the exposure can prove that it fits within a statutory exemption. Under Proposition 65 and its implementing regulations, no warning is required for exposures below the "No Significant Risk Level" for listed chemicals, which is defined as the highest level of exposure that would result in not more than one excess case of cancer in 100,000 individuals exposed to the chemical over a 70-year lifetime. Health and Safety Code § 25249.10(c), 27 Cal. Code Regs. ("C.C.R.") § 25721(a), (b). Health & Safety Code § 25249.6 states, in pertinent part:

> No person in the course of doing business shall knowingly and intentionally expose any individual to a chemical known to the state to cause cancer or reproductive toxicity without first giving clear and reasonable warning to such individual . . . .

14. On October 1, 1987, the State of California officially listed NDMA as a chemical known to cause cancer. 27 C.C.R. § 27001(b). On October 1, 1988, one year after it was listed as a chemical known to cause cancer, NDMA became subject to the clear and reasonable warning requirement regarding carcinogens under Proposition 65. 27 C.C.R. § 27001(b); Health & Safety Code § 25249.10(b).

15. NDMA is a nitrosamine, a class of chemical compounds that form when nitrates and amino acids combine. NDMA is used in laboratory research to induce tumors in

experimental animals. Nitrosamines such as NDMA can also form during the manufacturing process of certain drug products, such as those containing ranitidine.

16. Scholarly articles published as early as 1983 have suggested a link between NDMA and ranitidine. Numerous published studies since then have confirmed that levels of NDMA in ranitidine are significant and increase over time, especially when exposed to temperatures higher than room temperature.

17. The U.S. Food and Drug Administration ("FDA") performed a root cause analysis to determine how and why nitrosamines, including NDMA, form in ranitidine and other drug products. FDA's analysis determined that NDMA formation can occur in ranitidine through the use of contaminated materials and ingredients, the application of inferior drug manufacturing processes, and improper drug storage after manufacture. Thus, Defendants can reduce or eliminate NDMA from the Products by using cleaner ingredients and manufacturing processes and more careful storage techniques.

18. Defendants' Products contain sufficient quantities of NDMA such that individuals are exposed to NDMA through the average use of the Products. The primary route of exposure is through ingestion when individuals use the Products. The Products are designed to be ingested, and persons who ingest Products have an increased likelihood of developing cancer. These exposures occur everywhere throughout California where the Products are used.

19. No clear and reasonable warning is provided with the Products regarding the carcinogenic hazards of NDMA.

20. The Products are popular over-the-counter ("OTC") medications for treatment of heartburn. They are part of a class of acid reducing products known as H2 blockers, because they block the formation of acid in the stomach. There are a number of other H2 blockers available for OTC sale that do not contain ranitidine. The failure to provide warnings regarding the carcinogenicity of NDMA in Products is of particular concern in light of evidence that ingestion of NDMA causes cancer and the alternative products on the market that do not contain NDMA.

21. The incredible popularity of the Products is due, in part, to the widespread and robust advertising campaign employed by Defendants for the Products. This campaign included

all forms of public advertising, including television, print, and online media. None of these advertisements were required to have or had FDA approval. None of these advertisements included a clear and reasonable warning regarding the hazards of NDMA.

22. On or about September 9, 2019, Valisure LLC and ValisureRX LLC (collectively, "Valisure") – an independent third-party accredited analytical laboratory and online pharmacy – filed a formal citizen petition with the FDA to report that it had detected high levels of NDMA in ranitidine products that were already made available for sale to consumers. These high levels of NDMA were found in every lot tested by Valisure, including Products made and sold specifically by Defendants. In light of the substantial risk to public safety presented by the cancer risk of consuming such ranitidine products, Valisure urged the FDA to suspend all sales of ranitidine across the United States and to instruct users to dispose of any ranitidine still in their possession. In support of its petition, Valisure cited to scientific studies finding an affirmative link between ranitidine consumption and increased incidence of cancer.

23. On or about September 13, 2019, based on the Valisure petition, the FDA publicly issued a safety information bulletin reporting that the agency had learned that NDMA had been found in ranitidine. Prior to the Valisure testing and petition, the FDA was not aware that the Products contained NDMA. Thus, despite their own knowledge of the contamination, Defendants never informed the FDA of this hazard.

24. On or about November 1, 2019, FDA publicly issued a summary of laboratory testing performed by the agency on ranitidine products that were already made available for sale to consumers. NDMA was found at varying levels in every item of ranitidine tested, including Products made and sold by Defendants. The FDA instructed companies selling Products to perform their own testing for NDMA in Products, and advised such companies to recall their Products if testing confirmed the presence of NDMA above certain federal levels established to reduce cancer risks.

25. On or about April 1, 2020, the FDA contacted all of the manufacturers of Products sold to the U.S. market, including Defendants, formally requesting that these entities withdraw all prescription and OTC ranitidine from the market immediately. This request was based on further

testing by the FDA showing that NDMA is present in many Products at unacceptable levels that exceed the agency's safety thresholds for cancer. The FDA further advised consumers to stop taking any Products in their possession, to dispose of them and to not buy more, and to consider using alternative medications that do not pose cancer risks.

26. The FDA has promulgated regulations that specify certain changes to safety warnings on labels of FDA-approved drugs that may be made without prior FDA approval. According to those regulations, the labeling of such a drug "must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitely established." 21 C.F.R. § 201.57(c)(6)(i). The FDA views a "clinically significant hazard" as one that affects therapeutic decision-making, such as whether or not to ingest a given drug.

27. Congress has expressly exempted Proposition 65 from the provisions of the federal Food, Drug, and Cosmetic Act governing "National Uniformity for Nonprescription Drugs," which otherwise disallow states from "establish[ing] or continu[ing] in effect any requirement … that is different from or in addition to, or that is otherwise not identical with, a requirement under this Act." 21 U.S.C. § 379r(a) & (d)(2). In so legislating, Congress has determined that Proposition 65 warnings are consistent with warnings on federally regulated OTC drug products. As to cancer, Congress has therefore determined that the Proposition 65 risk standard for requiring a cancer warning – *i.e.*, the "No Significant Risk Level" for exposures under a 1-in-100,000 cases threshold – constitutes a "clinically significant hazard."

28. Defendants could have added a clear and reasonable Proposition 65 warning to the label of their Products, or to other materials accompanying their Products, regarding the carcinogenic hazards of NDMA under the FDA's regulation without seeking agency approval. The cancer risk from consuming ranitidine or Products containing NDMA presents a "clinically significant hazard" for which "there is reasonable evidence of a causal association" with these drugs. The FDA has determined that no one should ingest Products because of the causal association between taking Products containing NDMA and an increased risk of developing cancer. Moreover, the FDA has never stated that there would be a conflict between Proposition

65 cancer warnings on Products and any federal standard, or otherwise indicated that adding such warnings would be inconsistent with the agency's views on drug warnings generally or the cancer risks of NDMA specifically.

29. Many OTC drugs regulated by the FDA contain Proposition 65 warnings on their labels or their labeling. In fact, California courts have approved Proposition 65 settlements mandating that OTC manufacturers of such drugs place Proposition 65 cancer warnings on the front of the label. Defendants themselves manufacture, distribute, or sell OTC drug products for which Proposition 65 cancer warnings are provided on third-party websites that sell these products. The fact that FDA allows these warnings further demonstrates that providing Proposition 65 cancer warnings on OTC drug products does not conflict with any federal laws.

30. Although the FDA has promulgated a regulation governing certain aspects of the content of the label of an OTC drug (such as the contents of the familiar "Drug Facts" section of drug labels), nothing in this regulation precludes such a drug from containing additional language elsewhere on the label or in any associated labeling materials. *See* 21 C.F.R. § 201.66. For example, Products sold by Defendants often contain additional statements that are not contemplated by the FDA's regulations – such as "tips" for reducing heartburn symptoms or statements about drug safety – on the drug's label, packaging, or inserted pamphlets, without objection from the FDA.

31. When the FDA does not agree that a Proposition 65 warning on an OTC drug is appropriate, it clearly and publicly states its position. For example, it has affirmatively rejected the inclusion of a Proposition 65 warning on OTC nicotine replacement products and has filed amicus briefs explicitly stating its opposition to the inclusion of any Proposition 65 warnings on those products. Moreover, when California was considering listing acetaminophen as a carcinogen under Proposition 65, the FDA formally weighed in, stating its belief that a cancer warning for acetaminophen products would be misleading and that it would issue a preemptive regulation if California went ahead with the listing (it did not). Conversely, the FDA has never expressed any concern over a Proposition 65 warning regarding NDMA in the Products.

32. Defendants could also have provided clear and reasonable Proposition 65 cancer warnings in the form of public advertising. The FDA does not regulate the advertising of OTC drugs at all. Consequently, in response to the FDA's initial report in September 2019 regarding NDMA in ranitidine, Defendants voluntarily issued an announcement posted on the FDA's public website stating that Defendants were recalling all of their Products from the U.S. market because the Products may contain NDMA, which Defendants described as a probable human carcinogen. This was not a valid Proposition 65 warning, but does show that Defendants broadly communicate information about cancer risks associated with their drugs to the public without FDA approval.

33. Any person acting in the public interest has standing to enforce violations of Proposition 65 provided that such person has supplied the requisite public enforcers with a valid 60-Day Notice of Violation and such public enforcers are not diligently prosecuting the action within such time. Health & Safety Code § 25249.7(d).

34. More than sixty days prior to naming each Defendant in this lawsuit, CEH provided a 60-Day "Notice of Violation of Proposition 65" to the California Attorney General, to the District Attorneys of every county in California, to the City Attorneys of every California city with a population greater than 750,000, and to each of the named Defendants. In compliance with Health & Safety Code § 25249.7(d) and 27 C.C.R. § 25903(b), each Notice included the following information: (1) the name and address of each violator; (2) the statute violated; (3) the time period during which violations occurred; (4) specific descriptions of the violations, including (a) the routes of exposure to NDMA from the Products, and (b) the specific type of Products sold and used in violation of Proposition 65; and (5) the name of the specific Proposition 65-listed chemical that is the subject of the violations described in each Notice.

35. CEH also sent a Certificate of Merit for each Notice to the California Attorney General, to the District Attorneys of every county in California, to the City Attorneys of every California city with a population greater than 750,000, and to each of the named Defendants. In compliance with Health & Safety Code § 25249.7(d) and 11 C.C.R. § 3101, each Certificate certified that CEH's counsel: (1) has consulted with one or more persons with relevant and

appropriate experience or expertise who reviewed facts, studies, or other data regarding the exposures to NDMA alleged in each Notice; and (2) based on the information obtained through such consultations, believes that there is a reasonable and meritorious case for a citizen enforcement action based on the facts alleged in each Notice. In compliance with Health & Safety Code § 25249.7(d) and 11 C.C.R. § 3102, each Certificate served on the Attorney General included factual information – provided on a confidential basis – sufficient to establish the basis for the Certificate, including the identity of the person(s) consulted by CEH's counsel and the facts, studies, or other data reviewed by such persons.

36. None of the public prosecutors with the authority to prosecute violations of Proposition 65 has commenced and/or is diligently prosecuting a cause of action against Defendants under Health & Safety Code § 25249.5, *et seq.*, based on the claims asserted in each of CEH's Notices.

37. Defendants both know and intend that individuals will use the Products, thus exposing them to NDMA.

38. Under Proposition 65, an exposure is "knowing" where the party responsible for such exposure has:

> knowledge of the fact that a[n] . . . exposure to a chemical listed pursuant to [Health & Safety Code § 25249.8(a)] is occurring. No knowledge that the . . . exposure is unlawful is required.

27 C.C.R. § 25102(n). This knowledge may be either actual or constructive. *See, e.g.*, Final Statement of Reasons Revised (November 4, 1988) (pursuant to former 22 C.C.R. Division 2, § 12601).

39. As companies that manufacture, import, distribute, and/or sell the Products for use in the California marketplace, Defendants know or should know that the Products contain NDMA and that individuals who use the Products will be exposed to NDMA. Indeed, the link between ranitidine and NDMA was known as far back as 1983. The fact that Valisure, an independent third party, was able to determine that the Products contain NDMA provides additional support for the fact that Defendants have likely always known that the Products contain NDMA. The

NDMA exposures to individuals who use the Products are a natural and foreseeable consequence of Defendants' placing the Products into the stream of commerce.

40. Defendants have also been informed of the NDMA exposures caused by their Products pursuant to the 60-Day Notice of Violation and accompanying Certificate of Merit served on them by CEH.

41. Defendants have also been informed of the NDMA exposures caused by their Products by the FDA's widely-publicized reporting on NDMA in Products and subsequent withdrawal of all Products from the national marketplace due to the presence of NDMA.

42. Nevertheless, Defendants continued to expose individuals to NDMA without prior clear and reasonable warnings regarding the carcinogenic hazards of NDMA even after the publicity and recalls.

43. CEH has engaged in good-faith efforts to resolve the claims alleged herein prior to filing this Complaint.

44. Any person "violating or threatening to violate" Proposition 65 may be enjoined in any court of competent jurisdiction. Health & Safety Code § 25249.7. "Threaten to violate" is defined to mean "to create a condition in which there is a substantial probability that a violation will occur." Health & Safety Code § 25249.11(e). Proposition 65 provides for civil penalties not to exceed $2,500 per day for each violation of Proposition 65.

FIRST CAUSE OF ACTION
(Violations of Health & Safety Code § 25249.6)

45. CEH realleges and incorporates by reference as if specifically set forth herein Paragraphs 1 through 44, inclusive.

46. By placing the Products into the stream of commerce, Defendants are each a person in the course of doing business within the meaning of Health & Safety Code § 25249.11.

47. NDMA is a chemical listed by the State of California as known to cause cancer.

48. Defendants know that ordinary use of the Products will expose users of their Products to NDMA. Defendants intend that the Products be used in a manner that results in exposures to NDMA.

49. Defendants have failed, and continue to fail, to provide clear and reasonable warnings regarding the carcinogenicity of NDMA to users of the Products.

50. By committing the acts alleged above, Defendants have at all times relevant to this Complaint violated Proposition 65 by knowingly and intentionally exposing individuals to NDMA without first giving clear and reasonable warnings to such individuals regarding the carcinogenicity of NDMA.

PRAYER FOR RELIEF

Wherefore, CEH prays for judgment against Defendants as follows:

1. That the Court, pursuant to Health & Safety Code § 25249.7(a), preliminarily and permanently enjoin Defendants from offering Products for sale in California without providing prior clear and reasonable warnings, as CEH shall specify in further application to the Court;

2. That the Court, pursuant to Health & Safety Code § 25249.7(a), order Defendants to take action to stop ongoing unwarned exposures to NDMA resulting from use of Products sold by Defendants by either: (a) reducing or eliminating NDMA exposures resulting from ingestion of the Products such that no warning is required; or (b) providing clear and reasonable warnings for the Products by means of a label, shelf-sign, public advertising, or other method designed to provide users with warnings prior to their use of the Products, as CEH shall specify in further application to the Court;

3. That the Court, pursuant to Health & Safety Code § 25249.7(b), assess civil penalties against each of the Defendants in the amount of $2,500 per day for each violation of Proposition 65 according to proof;

4. That the Court, pursuant to Code of Civil Procedure § 1021.5 or any other applicable theory, grant CEH its reasonable attorneys' fees and costs of suit; and

5. That the Court grant such other and further relief as may be just and proper.

Dated: June 4, 2021

Respectfully submitted,

LEXINGTON LAW GROUP

Mark N. Todzo
Attorneys for Plaintiff
CENTER FOR ENVIRONMENTAL HEALTH

PROOF OF SERVICE

I, Owen Sutter, declare:

I am a citizen of the United States and employed in the County of San Francisco, State of California. I am over the age of eighteen (18) years and not a party to this action. My business address is 503 Divisadero Street, San Francisco, CA 94117 and my email address is osutter@lexlawgroup.com.

On June 4, 2021, I served the following document(s) on all interested parties in this action by placing a true copy thereof in the manner and at the addresses indicated below:

THIRD AMENDED COMPLAINT FOR INJUNCTIVE RELIEF AND CIVIL PENALTIES

☐ **BY MAIL**: I am readily familiar with the firm's practice for collecting and processing mail with the United States Postal Service ("USPS"). Under that practice, mail would be deposited with USPS that same day with postage thereon fully prepaid at San Francisco, California in the ordinary course of business. On this date, I placed sealed envelopes containing the above mentioned documents for collection and mailing following my firm's ordinary business practices.

☐ **BY FACSIMILE**: I caused all pages of the document(s) listed above to be transmitted via facsimile to the fax number(s) as indicated and said transmission was reported as complete and without error.

☒ **BY ELECTRONIC MAIL**: I transmitted a PDF version of the document(s) listed above via email to the email address(es) indicated on the attached service list [or noted above] before 5 p.m. on the date executed.

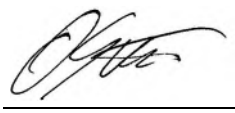
Please see attached service list

☐ **BY PERSONAL DELIVERY**: I placed all pages of the document(s) listed above in a sealed envelope addressed to the party(ies) listed above, and caused such envelope to be delivered by hand to the addressee(s) as indicated.

☐ **BY OVERNIGHT DELIVERY**: I deposited such document(s) in a box or other facility regularly maintained by FedEx, or delivered such document(s) to a courier or driver authorized by FedEx, with delivery fees paid or provided for, and addressed to the person(s) being served below.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed on June 4, 2021 at San Francisco, California.



Owen Sutter

SERVICE LIST
CEH v. Perrigo Company, et al.
RG 20-054985

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Exhibit 46

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CHATTEM, INC. and SANOFI-AVENTIS U.S. LLC

ENDORSED
FILED
ALAMEDA COUNTY
JUL 21 2021
CLERK OF THE SUPERIOR COURT
By _____ Deputy

COPY

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

CASE NO. RG20054985

ASSIGNED FOR ALL PURPOSES TO:
HON. WINIFRED Y. SMITH
DEPT. 21

DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S NOTICE OF DEMURRER AND DEMURRER TO PLAINTIFF'S THIRD AMENDED COMPLAINT; MEMORANDUM OF POINTS AND AUTHORITIES

Date: September 15, 2021
Time: 10:00 a.m.
Dept.: 21
Judge: Hon. Winifred Y. Smith

Reservation Nos.: R-2277974
R-2277975

TAC Filed: June 9, 2021

TO ALL PARTIES AND TO THEIR ATTORNEYS OF RECORD HEREIN:

PLEASE TAKE NOTICE THAT on September 15, 2021, at 10:00 a.m., or as soon thereafter as this matter may be heard, in Department 21 of the above-titled court, located at 1221 Oak Street, Oakland, CA 94612, Defendants Chattem, Inc. and Sanofi-Aventis U.S. LLC (collectively "Defendants") will and hereby do demur to the Third Amended Complaint filed in this action by Plaintiff Center for Environmental Health.

Under Code of Civil Procedure §430.10(e), Plaintiff has failed to state facts sufficient to constitute the cause of action for violations of the Safe Drinking Water and Toxic Enforcement Act, Cal. Health & Safety Code § 25249.6 (first cause of action).

This demurrer is based on this Notice of Demurrer and Demurrer, the Memorandum of Points and Authorities, the Declaration of Sean Newland, the Request for Judicial Notice, the papers and records on file in this action, and such further oral and documentary evidence as may be presented at the hearing on this motion.

Dated: July 21, 2021

DLA PIPER LLP (US)

By: _____

George J. Gigounas
Gregory G. Sperla
Sean A. Newland
Attorneys for Defendants
CHATTEM, INC. and SANOFI-AVENTIS U.S. LLC

DEFENDANTS' DEMURRER TO THIRD AMENDED COMPLAINT

Defendants Chattem, Inc. and Sanofi-Aventis U.S. LLC demur to Plaintiff Center for Environmental Health's Third Amended Complaint under Code of Civil Procedure § 430.10(e) because Plaintiff failed to state facts sufficient to constitute a cause of action for violations of the Safe Drinking Water and Toxic Enforcement Act, Health & Safety Code § 25249.6 (first cause of action).

Demurrer to First Cause of Action for Violations of Safe Drinking Water and Toxic Enforcement Act

1. Defendants jointly demur to the first cause of action on the grounds that the Complaint does not state facts sufficient to constitute a cause of action for violations of the Safe Drinking Water and Toxic Enforcement Act, Health & Safety Code § 25249.6.

Dated: July 21, 2021

DLA PIPER LLP (US)

By: _____

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I. INTRODUCTION

In its May 5, 2021 Order granting Defendants' demurrer, the Court held Plaintiff must "plead 'a labeling deficiency that [Defendants] could have corrected using the CBE regulation'" to avoid preemption. Order Sustaining Demurrers ("Order") at 10. The Court granted Plaintiff leave to file a Third Amended Complaint ("TAC") *if* Plaintiff could "allege that the NDMA exposure presented a 'clinically significant hazard' for which there is 'reasonable evidence of a causal association' with the drug[] (21 C.F.R. 201.57) and as a result [Defendants] could use the CBE process to unilaterally strengthen the warning on the labeling without waiting for FDA approval." Order at 11.

A. Plaintiff Has Not Alleged What the Court Required

The TAC incants the words "clinically significant hazard" and "reasonable evidence of a causal association," but that is not enough as a matter of law. These are not loose, general standards, as courts have confirmed. Plaintiff generally alleges the FDA views a "clinically significant hazard" as "one that affects therapeutic decision-making, such as whether or not to ingest a given drug" (TAC at ¶ 26), but the CBE standards require more than that, as detailed below. And under the correct standards, the TAC allegations fail on their face to adequately allege a "clinically significant hazard" or "reasonable evidence of a causal association" sufficient to open the CBE process to Defendants. Plaintiff cites three categories of information trying to link its bald assertions to evidence that would meet the CBE standard, but each is inadequate to meet its pleading burden.

***Conclusory statements do not suffice*:** Plaintiff alleges "NDMA is used in laboratory research to induce tumors in experimental animals" and "[t]he Products are designed to be ingested, and persons who ingest Products have an increased likelihood of developing cancer[,]" TAC at ¶¶ 16, 18. These conclusory statements are not "reasonable evidence of a casual association."

***Second-hand assertions in a citizen petition do not suffice*:** "In support of its petition, Valisure cited to scientific studies finding an affirmative link between ranitidine consumption and increased incidence of cancer." *Id.* at ¶ 22. This one-off statement elliptically referring to a third-party assertion in a citizen's petition does not meet the high standards for triggering the CBE.

***Incomplete citations to public FDA statements do not suffice*:** Plaintiff cannot establish a

"clinically significant hazard" and "reasonable evidence of a causal association" based on selective citation to three of four FDA public statements about ranitidine that mischaracterize the entirety of FDA's public statements.[1] TAC ¶¶ 23-25. The TAC omits critical, judicially noticeable statements that contradict Plaintiff's assertions. For instance, it fails to include from the FDA's September 13, 2019 statement: "*[a]lthough NDMA may cause harm in large amounts, the levels the FDA is finding in ranitidine from preliminary tests barely exceed amounts you might expect to find in common foods;*" or, from the FDA's most recent July 2, 2021 statement: "*the amounts of NDMA contained in ranitidine products were 3,000-fold lower than those reported in the citizen petition,*" and "*[FDA research] found no evidence of elevated NDMA content in the urine of participants … [and] found that ranitidine did not increase NDMA in blood plasma*…." Because Plaintiff invokes selections from the FDA statements to support its allegations, this Court may review the full statements to assess whether the TAC's allegations adequately allege "reasonable evidence of a causal association." When the TAC's excerpts are put in context, they clearly fall short of that standard.

B. A Proposition 65 Warning is, In Any Event, Improper Under the CBE Regulations

The Court did not need to reach the issue on Defendants' prior demurrer, but it remains true that the CBE and OTC warning regulations are not compatible with a Proposition 65 warning. First, a Proposition 65 warning cannot, as a matter of law, "add or strengthen a contraindication, warning, precaution, or adverse reaction" in the way the CBE regulations require. *See* 21 C.F.R. § 314.70, § 201.57. A warning just stating the possible presence of a carcinogenic compound in Zantac is not labeling information that can be added unilaterally under the narrow CBE process. Second, Defendants could not include a non-clinical, non-therapeutic Proposition 65 warning without violating OTC drug content and formatting regulations. 21 C.F.R. § 201.66(d). OTC regulations only permit specific categories of OTC drug label warnings, not including a Proposition 65 warning of NDMA exposure. *Id.* § 201.66(c)(5). FDA regulations specify mandatory content and formatting requirements incompatible with the warning required by Proposition 65. 27 C.C.R. §§ 25601, *et seq.*

[1] As discussed *infra*, only one of those FDA statements could even arguably constitute "reasonable evidence" (though it does not) because the others were issued after Zantac was withdrawn from the market. *See infra*, § III(A).

The Supremacy Clause of the U.S. Constitution preempts state laws in conflict with federal law, and California's Proposition 65 exempts chemical exposure warnings governed by federal law. Defendants cannot comply with both federal law and Plaintiff's view of Proposition 65. Thus, state and federal law bar this action and this Court should sustain Defendants' demurrer with prejudice.

II. BACKGROUND

A. This Court Sustained Demurrers to the Second Amended Complaint ("SAC")

Defendants' demurrer to the SAC argued federal law preempted the alleged Proposition 65 violations because: (1) putting a Proposition 65 warning on Zantac violates 21 C.F.R. § 201.66; and (2) the CBE regulation preempted any requirement to add that warning. The Court's Order granting Defendants' demurrer focused on Proposition 65's "liability provision, H&S 25249.6, which is limited by the exemption provision, H&S 25249.10(a), which states that there is no Proposition 65 liability for 'an exposure for which federal law governs warning in a manner that preempts state authority.'" Order at 5. The Court found that where federal law governs, "there is no liability for an exposure under H&S 25249.6, whether based on lack of warning or knowing exposure to chemicals, and thus the court cannot order any non-warning injunctive relief or award any penalties." *Id.* at 6.

First**,** the Court addressed the CBE process. The Court stated Plaintiff "must plead 'a labeling deficiency that [Defendants] could have corrected'" through this process to avoid preemption, and found Plaintiff did not because it failed to allege NDMA exposure from taking ranitidine "presented a 'clinically significant hazard' for which there is 'reasonable evidence of a causal association' with the drug[] (21 C.F.R. 201.57)" such that Defendants "could use the CBE process to unilaterally strengthen the warning on the labeling without waiting for FDA approval." Order at 10-11. The Court granted Plaintiff leave to amend its complaint, "if possible," to make that allegation. *Id.* at 11.

Next, the Court addressed Defendants' arguments that (a) the FDCA regulates warnings for OTC drugs, (b) "Proposition 65 warnings are a form of warning," (c) manufacturers cannot "comply with both federal and state [warning] requirements …," and (d) "impossibility preemption applies." *See* Order at 12. Plaintiff argued the contrary, specifically suggesting that Proposition 65 warnings can be provided through advertising. The Court rejected Plaintiff's arguments, finding:

> A Proposition 65 warning is a "warning" within the… definition of "warning" used in the FDCA regulations on "Format and content requirements for over-the-counter (OTC) drug product labeling." (21 CFR 201.66(c)(5).) The FDCA approves "warnings" for OTC drugs, the [Defendants] must use the FDA approved "warnings," it is impossible for the [Defendants] to deviate from the approved warnings, so there is impossibility preemption, so the H&S 25249.10(a) self-exception applies. Proposition 65 does not apply to exposures in the OTC drugs. This ends the analysis. Order at 13-14.

Finally, the Court covered "three issues related to the means of transmitting the warnings: (1) the definition of labeling under the FDCA, (2) the voluntary nature of advertising, and (3) plaintiff's argument '[t]hat which is possible is not impossible.'" Order at 15. As to (1), Plaintiff argued Defendants could circumvent the CBE process by "transmitting Proposition 65 warnings to consumers through advertising" and not changing product labeling. Order at 14. The Court rejected that argument because "'labeling' under the FDCA includes all means of transmitting warnings." *Id*. The Court found "a plaintiff cannot avoid federal preemption by characterizing labeling as advertising matter 'where the advertising performs the function of labeling,'" *id*. at 16 (citing *Kordel v. United States*, 335 U.S. 345 (1948)), and "any information … transmitted to the person who makes the drug use decision serves the purpose of labeling and is 'labeling' under the FDCA. *Plaintiffs cannot avoid impossibility preemption by conflating labeling and advertising and suggesting that defendants can transmit the Proposition 65 warning in advertising*." *Id*. at 17 (emphasis supplied).

As for (2), the Court found advertising is "voluntary in nature," so if Proposition 65 compels "a manufacturer to transmit a warning," that transmittal is "by definition not through 'advertising,' which means that it is through 'labeling' as defined in and regulated under the FDCA." *Id*.

As for (3), the Court found Defendants cannot transmit Proposition 65 warnings in advertising because "although the FDCA might not prevent defendants from voluntarily putting Proposition 65 warnings in advertisement for the Products, the FDCA's regulation of warnings on labels and in labeling means that 'federal law governs warning in a manner that preempts state authority', which means that the H&S 25249.10(a) self-exemption applies." *Id*. at 22-23.

B. Plaintiff's New Allegations in the TAC Fail to Trigger CBE Conditions

On June 4, 2021, Plaintiff filed its TAC with new allegations intended to fix the deficiencies the Court identified in the SAC, falling into several categories.

1. Attempts to allege a "clinically significant hazard" and "reasonable evidence of a causal association"

Plaintiff's TAC attempts to allege a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with use of Zantac in three ways.

First, Plaintiff added two conclusory statements about NDMA and cancer:

- "NDMA is used in laboratory research to induce tumors in experimental animals." TAC at ¶ 16.
- "The Products are designed to be ingested, and persons who ingest Products have an increased likelihood of developing cancer." *Id.* at ¶ 18.

Second, Plaintiff added an allegation alluding to a citation in a citizen's petition by a third party that was part of the genesis of the current FDA inquiry into ranitidine products:

- "In support of its petition, Valisure cited to scientific studies finding an affirmative link between ranitidine consumption and increased incidence of cancer." *Id.* at ¶ 22.

Third, Plaintiff selectively cited or characterized three of the four primary public statements that the FDA has issued regarding NDMA in ranitidine products, alleging:

- On September 13, 2019 the FDA issued "a safety information bulletin reporting that the agency had learned that NDMA had been found in ranitidine." *Id.* at ¶ 23.[2]
- On November 1, 2019 the FDA issued a summary of its testing on ranitidine products. NDMA was found at varying levels in every item of ranitidine tested, including products made and sold by Defendants. The FDA instructed companies selling ranitidine products to perform their own testing for NDMA and advised such companies to recall their products if testing confirmed the presence of NDMA above federal levels established to reduce cancer risks. *Id.* at ¶ 24.[3]
- On April 1, 2020 FDA contacted manufacturers to request the withdrawal of ranitidine from the market. This request was based on FDA testing showing "NDMA is present in many Products at unacceptable levels that exceed the agency's safety thresholds for cancer." The FDA "advised

[2] *See* Declaration of Sean Newland ISO Demurrer to Third Amended Complaint ("Newland Decl."), ¶ 4, Exh. A. The Court took judicial notice of this document on Defendants' prior demurrer. *See* Order at 2; Request for Judicial Notice ISO Demurrer to Third Amended Complaint ("RJN").

[3] *See* Newland Decl., ¶ 5, Exh. B. Plaintiff attached this document as Exhibit 6 to Plaintiff's Opposition to Defendants' Demurrer to the SAC. The Court took judicial notice of it in its Order granting the demurrer. *See* Order at 2; RJN.

consumers to stop taking any Products in their possession, to dispose of them and to not buy more, and to consider using alternative medications that do not pose cancer risks." *Id.* at ¶ 25.[4]

2. Attempts to Fit Proposition 65 Warnings Into CBE Regulations

Plaintiff also alleged Defendant could have used the CBE regulation to put Proposition 65 warnings about NDMA on Zantac without prior FDA approval and not thereby violate FDA labeling requirements. *See id.*, ¶¶ 26-28, 30-31. Plaintiff alleges "many OTC drugs" have "Proposition 65 warnings on their labels," California courts have approved Proposition 65 settlements that require warnings on OTC drugs labels, and Proposition 65 warnings are "provided on third-party websites that sell" Zantac products. *See id.*, ¶ 29. Plaintiff provides no examples of these alleged warnings.

3. Attempts to Characterize Warnings as Advertisements

Finally, although the Court rejected the argument that warnings for Proposition 65 can be provided through advertising, Plaintiff adds allegations about Defendants' "widespread and robust advertising campaign" for Zantac that did not require FDA approval or add "a clear and reasonable warning regarding the hazards of NDMA" (i*d.*, ¶ 20), and alleges Defendants could have "provided clear and reasonable Proposition 65 cancer warnings in the form of public advertising" (*id.*, ¶ 32).

C. <u>What the FDA Statements Actually Say</u>

Plaintiff's TAC selectively characterized judicially noticeable FDA statements. Viewing those statements as a whole, it is apparent they do not satisfy the high standards required to utilize the CBE process. And Plaintiff's reliance on these statements is damaged further by the FDA's July 2, 2021 update, which eviscerates the science behind the citizen petition.

***September 13, 2019*.** The TAC alleges the FDA "issued a safety information bulletin" after the citizen petition but does not summarize its contents. The bulletin did nothing more than alert the public that the FDA was investigating whether "the low levels of NDMA in ranitidine"—which "preliminary tests" showed "barely exceed amounts found in common foods"—"pose a risk to patients." The FDA advised that it was "not calling for individuals to stop taking ranitidine…"

October 18, 2019--Sanofi Withdraws Zantac. Defendants voluntarily withdrew all Zantac

[4] *See* Newland Decl., ¶ 6, Exh. C. The Court took judicial notice of this document in connection with Defendants' prior demurrer. *See* Order at 2; RJN.

products from the market on October 18, 2019; nearly six months before the FDA's recall request and 31 days before Plaintiff filed the Proposition 65 Notice of Violation related to this action.[5]

November 1, 2019. This statement summarized test results on ranitidine products and indicated recalls would be "recommend[ed]" to companies with products with NDMA levels above federal limits, but it also reiterated "that the levels of NDMA in ranitidine … are similar to the levels you would expect to be exposed to if you ate common foods like grilled or smoked meats."

April 1, 2020. The FDA requested a recall as the "latest step in an ongoing investigation of [NDMA] in ranitidine medications" and clarified its focus was on the age and storage conditions of ranitidine drugs, not ranitidine itself. Contrary to Plaintiff's allegation that the FDA found "NDMA is present in many Products at unacceptable levels that exceed the agency's safety thresholds for cancer," Janet Woodcock, M.D. (Director of the FDA's Center for Drug Evaluation and Research ("CDER")) said: "We didn't observe unacceptable levels of NDMA in many of the samples that we tested. However, since we don't know how or for how long the product might have been stored, we decided that it should not be available to consumers and patients unless its quality can be assured[.]"

July 2, 2021. This recent statement summarizing CDER research findings about NDMA and ranitidine refutes many of the claims asserted in the Valisure Citizen Petition. The FDA found:

- The procedures used to quantify NDMA were inappropriate to assess its presence in ranitidine, because of the "high temperatures that could convert ranitidine to NDMA during that analysis."
- Although some elevated levels were found, CDER's low-temperature methods determined the NDMA in ranitidine was "3,000-fold lower than those reported in the citizen petition[.]"
- "Multiple limitations" in a study the petition referenced. CDER's own "rigorous" testing "found no evidence of elevated NDMA content in the urine of participants over the 24 hours after they took ranitidine, regardless of diet," and found "ranitidine did not increase NDMA in blood plasma and did not increase dimethylamine (DMA) (proposed … to be the precursor to NDMA generated from ranitidine) in plasma or urine."

[5] *See* Newland Decl., ¶ 7, Exh. D. Plaintiff attached this document as Exhibit 7 to its Opposition to Defendants' Demurrer to the SAC. The Court granted judicial notice of this document in its Order granting the demurrer. *See* Order at 2; RJN.

- Ranitidine *did not* produce NDMA in simulated gastric fluid "unless nitrite was 50-fold greater than the upper range of physiologic gastric nitrite concentration in acidic conditions."[6]

In sum, CDER's clinical trial and experiments did "not support the conclusion that ranitidine is converted to NDMA in humans." Indeed, the "findings suggested that prior reports had detected falsely high levels of NDMA in ranitidine drug products and human biological fluids." The FDA closed by noting that while ranitidine was recalled, "the product approvals were not withdrawn, and the FDA may consider allowing ranitidine products back on the market if they are proven to be stable, with low, acceptable amounts of NDMA that do not increase over time during storage."

D. California's Prop 65 and FDA's Exclusive Framework for Drug Labeling

Proposition 65 requires that Californians receive a "clear and reasonable warning" before exposure to chemicals "known to the State to cause cancer." H&S §§ 25249.6; 25249.10(b); 25601. To ensure a warning is "clear and reasonable," the only real option is to provide a regulatory "safe harbor" warning. *See* 27 C.C.R. §§ 25601, *et seq.*; *Nat'l Ass'n of Wheat Growers v. Becerra*, 468 F. Supp. 3d 1247, 1261 (E.D. Cal. 2020) (rejecting argument that Proposition 65 only requires "clear and reasonable" warnings, "not the particular language of the safe harbor warning").[7]

Proposition 65 exempts warning compliance when federal law governs warnings. H&S § 25249.10(a). "[I]f federal law for an exposure governs warning in a matter that preempts state authority, then there is no violation of the compliance/liability provision. This in turn means that if federal law on warning preempts state law on warning, then there is no liability for an exposure under H&S 25249.6, whether based on lack of warning or knowing exposure to chemicals, and thus the court cannot order any non-warning injunctive relief or award any penalties." Order at 6.

Where, as with Zantac, a manufacturer seeks OTC approval for a prescription drug (which required a new drug application ("NDA") subjected to rigorous FDA review), the NDA's data must show that the drug is appropriate to self-administer. 21 C.F.R. § 310.200(b); 21 U.S.C. §§ 353(b)(3),

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[6] *See* Newland Decl., ¶ 8, Exh. E; RJN.

[7] A Zantac NDMA safe harbor warning would say:

> ⚠**WARNING:** This product can expose you to chemicals including n-Nitrosodimethylamine, which is known to the State of California to cause cancer. For more information go to www.P65Warnings.ca.gov.

355(c)–(d). This may include studies showing that labeling can be understood and followed without guidance from a health care provider. James T. O'Reilly and Katharine A. Van Tassel, *Prescription Drug to OTC Drug Switches*, Food and Drug Admin. § 13:37 (4th ed. 2020).

NDA approval requires that the *exact* language FDA approved in the marketing application appear on the labeling or packaging. *See* 21 C.F.R. §§ 314.70(b), (c), 314.71. "Labeling" embraces all "advertising or descriptive matter that goes with the package in which the articles are transported" and things "accompanying such article." 21 U.S.C. § 321(m). An article is accompanied by another if it supplements or explains it—"no physical attachment one to the other is necessary." *Kordel v. United States*, 335 U.S. 345, 349-50 (1948). Stated plainly, federal law *broadly* defines "labeling" and requires consistency with FDA approved labeling. *Strayhorn v. Wyeth Pharms., Inc.*, 737 F.3d 378, 394 (6th Cir. 2013) (citing 21 C.F.R. §§ 202.1(l)(2), 201.100(d)(1), 202.1(e)(4)).

III. ARGUMENT

Federal law is "the Supreme Law of the Land." U.S. Const. art. VI, cl. 2. State law in conflict with federal law "is without effect." *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 516 (1992). "Impossibility" preemption arises (i) where a private party cannot comply with both state and federal requirements (*PLIVA, Inc. v. Mensing*, 564 U.S. 604, 618 (2011)), and (ii) where a party "cannot comply with state law without first obtaining the approval of a federal regulatory agency" (*Gustavsen v. Alcon Laboratories*, 903 F.3d 1, 9-10 (lst Cir. 2018)).

A. Plaintiff's Amendments to the TAC Fail to Plead A "Clinically Significant Hazard" and "Reasonable Evidence Of A Causal Association" Between Taking Zantac And Developing Cancer

Because the CBE process is the only way that Plaintiff could argue Proposition 65 warnings could be applied without FDA approval, this Court authorized an amended complaint if Plaintiff could allege the CBE process's threshold requirements, *i.e.*, a "clinically significant hazard," and "reasonable evidence of a casual association" between Zantac and an increased risk of cancer. The TAC tries to do so with conclusory statements, reference to Valisure's Citizen Petition, and selective references to three FDA statements about NDMA and ranitidine between September 13, 2019 and April 1, 2020. *See* TAC, ¶¶ 16, 22-25. On their face, none of Plaintiff's new allegations suffice.

"Reasonable evidence of a casual association" is evidence "on the basis of which experts

qualified by scientific training and experience can reasonably conclude that the hazard is associated with the drug." *O'Neal v. Smithkline Beecham Corp.*, 551 F. Supp. 2d 993, 995 n.2 (E.D. Cal. 2008) (quoting 44 Fed. Reg. 37434, 37447 (June 26, 1979)). It cannot be based upon "an indeterminate or inconclusive relationship," it must be "scientifically reliable" and not "'rooted in conjecture or hypothesis," and "'it must conclusively establish, by scientifically valid measurable and statistically significant data, that the different or increased risks are actual and real.'" *Silverstein v. Boehringer Ingelheim Pharms., Inc.*, 2020 WL 6110909, at *8 (S.D. Fla. Oct. 7, 2020) (citation omitted); *Seufert v. Merck Sharp & Dohme Corp.*, 187 F. Supp. 3d 1163, 1175 (S.D. Cal. 2016) (citation omitted).[8]

And, even though weighing evidence is generally not appropriate on demurrer, this Court must probe Plaintiff's allegations purporting to establish "reasonable evidence" against the full picture of what Plaintiff cites. "[W]here scientific studies are cited and thus incorporated into the complaint, and where those studies simply do not support the allegations," it is appropriate to consider whether the deficiencies make allegations of "reasonable evidence" infirm as a matter of law. *See Sabol v. Bayer Healthcare Pharm., Inc.*, 439 F. Supp. 3d 131, 148 (S.D.N.Y. 2020).

Critically, not just the existence of "reasonable evidence" opens the CBE regulation to manufacturers. An OTC manufacturer must have knowledge of the alleged association. *See O'Neal*, 551 F. Supp. 2d at 1007 (no reasonable evidence supported adding a warning about suicidality risks in *pediatric* patients prescribed SSRI's before February 1997 because the data then available showed increased risk in *adult* patients). "[T]he CBE provision is an integral means for a manufacturer to maintain adequate product labeling," but "only when a submission is supported by sufficient scientific data." *Id.* at 1176. And the FDA cautions that "[e]xaggeration of risk, or inclusion of speculative or hypothetical risks, could discourage appropriate use of a beneficial drug ... or decrease the usefulness and accessibility of important information by diluting or obscuring it." Supp. Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices,

[8] *See also In re Incretin-Based Therapies Prod. Liab. Litig.*, 2021 WL 880316, at *14 (S.D. Cal. Mar. 9, 2021) (insufficient evidence of causal association between pancreatic cancer and incretin mimetics); *Ridings v. Maurice*, 444 F. Supp. 3d 973, 992 (W.D. Mo. 2020) (studies finding "that it 'remains unknown' whether a drug is linked" to an adverse reaction or risk "or that 'further studies are required to address possible clinical consequences'" do not suffice).

73 Fed. Reg. 2848, 2851 (Jan. 16, 2008). Labeling with "theoretical hazards not well-grounded in scientific evidence can cause meaningful risk information to lose its significance"; and thus "the CBE regulation requires that there be sufficient evidence of a causal association between the drug and the information sought to be added." *Utts v. Bristol-Myers Squibb Co.*, 251 F.Supp.3d 644, 659 (S.D.N.Y. 2017) (citations omitted).

1. "Reasonable Evidence" Before Zantac Withdrawal

Plaintiff relies on three pre-withdrawal allegations to try to satisfy the Court's instruction.

***First*,** Plaintiff added two bald statements regarding NDMA and cancer: "NDMA is used in laboratory research to induce tumors in experimental animals[,]" and "[t]he Products are designed to be ingested, and persons who ingest Products have an increased likelihood of developing cancer." TAC at ¶¶ 16, 18. These conclusory allegations neither satisfy California's pleading standards nor show "reasonable evidence" to support use of the CBE process. *Rossberg v. Bank of Am., N.A.*, 219 Cal. App. 4th 1481, 1500 (2013) (conclusory allegations are insufficient to state a claim).

***Second*,** Plaintiff points to the September 9, 2019 citizen petition that alleged high levels of NDMA in ranitidine products and encouraged the FDA to order a recall. TAC ¶ 22. This is not the "reasonable evidence" federal law requires, or reasonable evidence of any clinical hazard. If it were, any citizen could immediately force changes to carefully vetted labeling. The FDA, not Valisure, is the final arbiter of citizen petition claims. *O'Neal*, 551 F.Supp.2d at 998 (FDA denies petitions about Prozac, finding "no 'reasonable evidence of an association between … Prozac and suicidality'").

Third, Plaintiff cites the FDA's September 13, 2019 statement that it had "learned that some ranitidine medicines … contain [NDMA] at low levels." TAC, ¶ 23. That is the very definition of "indeterminate or inconclusive," and far from evidence "conclusively establish[ed], by scientifically valid measurable and statistically significant data" on which "experts qualified by scientific training and experience can reasonably conclude that the hazard is associated with the drug." *Silverstein*, 2020 WL 6110909, at *8; *Seufert*, 187 F. Supp. 3d at 1175; *O'Neal*, 551 F. Supp. 2d at 995 n.2. And the statement walks back any suggestion that the citizen petition is reasonable evidence: "*The FDA is evaluating whether the low levels of NDMA in ranitidine pose a risk to patients [and] will post that information when it is available*"; "*NDMA may cause harm in large amounts, [but] the levels*

the FDA is finding in ranitidine from preliminary tests barely exceed amounts you might expect to find in common foods"; and "*The FDA is not calling for individuals to stop taking ranitidine*[.]"

2. "Reasonable Evidence" After Zantac Withdrawal

Plaintiff acknowledged Defendants voluntarily withdrew Zantac from the market on October 18, 2019. The CBE process thus could have not been triggered by the "evidence" Plaintiff cites after that date because there was no product label in the marketplace to change. Even still, these FDA statements cannot, as a matter of law, comprise "reasonable evidence of a causal association."

November 1, 2019. The FDA released test results on ranitidine products. TAC, ¶ 24. The November statement did not say taking Zantac increases cancer risks. The FDA found "the levels of NDMA in ranitidine … are similar to the levels you would expect to be exposed to if you ate common foods like grilled or smoked meats." But since samples exhibited a range of levels, the FDA recommended recalls of products above the acceptable daily intake limit while studies continued. This November 1 statement was, on its face, "indeterminate or inconclusive," and not the caliber of evidence demanded by federal law to trigger access to CBE labeling changes.

April 1, 2020. The FDA requested manufacturers withdraw ranitidine drugs, noting its action was part of an "ongoing investigation" and reiterated that initial laboratory tests found NDMA in such products at low levels that "would not be expected to lead to an increase in the risk of cancer," but found NDMA "in some ranitidine products increases over time and when stored at higher than room temperatures and may result in consumer exposure to unacceptable levels of [NDMA]." In the April statement, the Director of the FDA's CDER confirmed it "didn't observe unacceptable levels of NDMA in many of the samples … tested. However, since [the FDA] d[id]n't know how or for how long the product might have been stored, [it] decided that is should not be available to consumers and patients unless its quality can be assured[.]"

The FDA's April statement is *not* "reasonable evidence of a causal association." The FDA suggested old products and certain storage conditions "*may* raise the level of NDMA in … ranitidine … above the acceptable daily intake limit." At most, that suggests an "indeterminate or inconclusive relationship" that does not support using the CBE process. *See Seufert*, 187 F.Supp.3d at 1175. And as explained *supra*, the April Statement was made nearly *six months* after Defendants withdrew

Zantac from the market, and thus could not have led to labeling changes under the CBE regulation

July 2, 2021. The July 2 statement conclusively refutes the notion that the statements in the TAC from FDA or Valisure established "a clinically significant hazard" with "reasonable evidence of a causal association" sufficient to allow Defendants to open the CBE label-revision process. That statement of CDER research findings powerfully rebuts the claims in the citizen petition by finding (detailed above) that (i) Valisure's testing for NDMA was invalid, (ii) FDA's valid method yielded NDMA levels "3,000-fold lower," (iii) no formation of NDMA in vivo, and (iv) "no evidence" of elevated NDMA in urine or blood plasma after taking ranitidine. The "findings suggested that prior reports had detected falsely high levels of NDMA in ranitidine drug products and human biological fluids."[9] The FDA closed by noting that while ranitidine was recalled, "the product approvals were not withdrawn," and ranitidine products may be allowed "back on the market if they are proven to be stable, with low, acceptable amounts of NDMA that do not increase over time during storage."

3. Other OTC Products or Other Parties' Alleged Actions Are Irrelevant

Plaintiff argues Zantac's labeling should have a Proposition 65 warning because "[m]any OTC drugs" have such warnings, California courts have approved Proposition 65 settlements that permit such warnings on OTC drug labeling, and third-party websites selling Defendants' OTC products have included such warnings online. *See* TAC at ¶ 29. None of those allegations suggest *Defendants* put Proposition 65 warnings on any OTC product, and none address the propriety of the warnings. Whether or not such warnings exist (Plaintiff offers no examples) the question is not whether or why other parties violated CBE rules to put Proposition 65 warnings on OTC products, but whether Defendants could have put a Proposition 65 warning on Zantac. They could not have.

B. <u>A Proposition 65 Warning on Zantac Would Violate 21 C.F.R. § 201.66</u>

A Proposition 65 NDMA exposure warning is not the type of information FDA allows on OTC drug labels. The content and format requirements for OTC drug labels are codified in 21 C.F.R. § 201.66, and labels violating these requirements "are subject to regulatory action." *Id*., § 201.66(g).

[9] The FDA's statement noted that, after CDER published its results, "the prior clinical study that had reported a 400-fold increase in NDMA urinary excretion after ingestion of ranitidine was retracted by the authors, citing that an analytical artifact may have contributed to their results."

In contrast to Proposition 65, FDA warnings about drug contents or ingredients provide necessary, potentially life-saving therapeutic information, *e.g.*, disclosing magnesium, potassium, and calcium content to avoid "serious toxicity in people with impaired renal function." 69 Fed. Reg. at 13725.

While Proposition 65 concerns "warnings" in the vernacular sense, the content is distinct from the disclaimers and disclosures permitted under OTC drug labeling regulations, which do not authorize anything resembling what Plaintiff seeks here. The only other warnings permitted under 21 C.F.R. § 201.66 are limited categories of clinical, not theoretical, information: allergic reaction warnings, liver or stomach issues, flammability, sexually transmitted diseases, serious contraindications ("Do not use"), preexisting conditions ("Ask a doctor before use if you have"), serious side effects ("Stop use and ask a doctor if"), and pregnancy information.

Proposition 65 would require disclosure of the *mere presence* of a potentially carcinogenic substance without regard to drug risks and benefits, or whether that substance causes harm. That is incompatible with the specific, therapeutic, clinically focused information about the *entire* drug, not constituents, FDA permits on OTC labels. Consistent with the FDA's goal of ensuring consumers can make "reasoned decisions" about drug products, none of the categories of permissible warnings bear any relation to the NDMA exposure disclaimer Plaintiff would require on Zantac.

Not only are federal regulations laser-precise about the *content* of OTC warning labels, they provide the *formatting* for warnings down to the specific font size and style, several of which contradict Proposition 65 regulations. *See, e.g.*, § 201.66(d). First, FDA prohibits graphical images to "interrupt" labeling content, including the triangle hazard symbol required by California's safe harbor regulations. *Compare* 27 C.C.R. § 25603(a)(1) *with* § 201.66(d)(7). Additionally, under California law, a Proposition 65 warning is not "clear and reasonable" unless it is "prominently displayed with such conspicuousness as compared with other words, statements, designs or devices on the label, labeling, or sign, as to render the warning likely to be seen, read, and understood by an ordinary individual under customary conditions of purchase or use." 27 C.C.R. § 25601(c). That means California requires that a Proposition 65 warning receive a place of prominence in relation to specifically approved, FDA-required statements critical to consumer safety. Yet the FDA requires that no single warning be given priority over others—indeed, the elevation of a Proposition 65

NDMA content warning devoid of any clinical information is precisely what the FDA sought to avoid for OTC labels and § 201.66 expressly prohibits it. *See* OTC Rule, 65 FR 81082-01.

Further, a Proposition 65 warning is not a "contraindication, warning, precaution, or adverse reaction" associated with a "clinically significant hazard"—the only information a manufacturer can unilaterally add using the CBE process. 21 C.F.R. § 314.70(b)(2)(v)(A) (requiring preapproval of changes to labeling not authorized by 21 C.F.R. § 314.70(c)(6)(iii)). A Proposition 65 Zantac warning merely citing possible exposure to NDMA is not a change permitted by the regulation.

To comply with Plaintiff's version of Proposition 65's requirements, Defendants would need to do the impossible: unilaterally add a warning on Zantac not contained in preapproved labeling or authorized by the CBE regulation, in violation of 21 U.S.C. § 355 and C.F.R. § 314.70(b)(2)(v)(A). Defendants cannot do this, nor may the Court require it.

IV. CONCLUSION

Defendants could not have complied and cannot comply with the requirements of California law that the TAC seeks to enforce without violating federal law. Under the Supremacy Clause, such state law requirements are preempted and unenforceable as a matter of law. For these reasons, the TAC must be dismissed with prejudice.

Dated: July 21, 2021

DLA PIPER LLP (US)

By: _____

George J. Gigounas
Gregory G. Sperla
Sean A. Newland
Attorneys for Defendants
CHATTEM, INC. and SANOFI-AVENTIS U.S. LLC

Exhibit 47

COPY

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ENDORSED
FILED
ALAMEDA COUNTY

JUL 21 2021

CLERK OF THE SUPERIOR COURT
By _____ Deputy
Jessica Flores

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

CASE NO. RG20054985

ASSIGNED FOR ALL PURPOSES TO:
HON. WINIFRED Y. SMITH
DEPT. 21

DECLARATION OF SEAN NEWLAND IN SUPPORT OF DEFENDANTS' DEMURRER TO PLAINTIFF'S THIRD AMENDED COMPLAINT

Date: September 15, 2021
Time: 10:00 a.m.
Dept.: 21
Judge: Hon. Winifred Y. Smith

Reservation Nos.: R-2277974
R-2277975

TAC Filed: June 9, 2021

I, Sean Newland, declare as follows:

1. I am an attorney at law authorized to practice before courts of the State of California, and an associate of DLA Piper LLP (US), counsel for Defendants Chattem, Inc. and Sanofi-Aventis U.S. LLC ("Defendants").

2. I submit this declaration in support of Defendants' Demurrer to Plaintiff Center for Environmental Health's ("CEH") Third Amended Complaint ("Demurrer") and Defendants' Request for Judicial Notice in Support of Demurrer. The matters declared herein are based upon my personal knowledge, and if called to testify I could and would testify competently thereto.

3. My colleague George Gigounas and I met and conferred with Mark N. Todzo of the Lexington Law Group, counsel for CEH, telephonically on Friday, July 9, 2021, more than five days in advance of the deadline for Defendants' responsive pleading pursuant to California Code of Civil Procedure § 430.10 *et seq*. Mr. Gigounas, Mr. Todzo, and I discussed the grounds for Defendants' Demurrer and whether any agreement may be reached to resolve the grounds to be raised. Ultimately no agreement was reached.

4. A true and correct copy of the FDA's September 13, 2019 statement advising patients and health care professionals of NDMA found in samples of ranitidine is attached hereto as **Exhibit A** and is publicly available on the FDA's website at https://www.fda.gov/news-events/press-announcements/statement-alerting-patients-and-health-care-professionals-ndma-found-samples-ranitidine.

5. A true and correct copy of the FDA's November 1, 2019 release titled "Laboratory Tests | Ranitidine" is attached hereto as **Exhibit B** and is publicly available on the FDA's website at https://www.fda.gov/drugs/drug-safety-and-availability/laboratory-tests-ranitidine.

6. A true and correct copy of the FDA's April 1, 2020 release requesting removal of all ranitidine products from the market is attached hereto as **Exhibit C** and is publicly available on the FDA's website at https://www.fda.gov/news-events/press-announcements/fda-requests-removal-all-ranitidine-products-zantac-market.

7. A true and correct copy of Defendants' "Company Announcement" published by the FDA on October 23, 2019 ("Sanofi Provides Update on Precautionary Voluntary Recall of Zantac

OTC in U.S.") noting Defendants' October 18, 2019 voluntary withdrawal of Zantac from the U.S. market is attached as **Exhibit D** and is publicly available on the FDA's website at https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/sanofi-provides-update-precautionary-voluntary-recall-zantac-otc-us.

8. A true and correct copy of the FDA's July 2, 2021 release titled "Ensuring the Rigor of Regulatory Science: CDER Conducts Laboratory and Clinical Studies to Investigate Reports of NDMA Production from Ingested Ranitidine Products" is attached hereto as **Exhibit E** and is publicly available on the FDA's website at https://www.fda.gov/drugs/news-events-human-drugs/ensuring-rigor-regulatory-science-cder-conducts-laboratory-and-clinical-studies-investigate-reports.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct. Executed this 21st day of July, 2021 in Tiburon, California.

SEAN NEWLAND

EXHIBIT A

FDA STATEMENT

Statement alerting patients and health care professionals of NDMA found in samples of ranitidine

For Immediate Release:

September 13, 2019

Statement From:

Acting Commissioner of Food and Drugs - Food and Drug Administration
Janet Woodcock M.D.

Español (/news-events/press-announcements/declaracion-de-la-dra-janet-woodcock-directora-del-centro-de-evaluacion-e-investigacion-de)

The U.S. Food and Drug Administration has learned that some ranitidine medicines, including some products commonly known as the brand-name drug Zantac, contain a nitrosamine impurity called N-nitrosodimethylamine (NDMA) at low levels. NDMA is classified as a probable human carcinogen (a substance that could cause cancer) based on results from laboratory tests. NDMA is a known environmental contaminant and found in water and foods, including meats, dairy products, and vegetables.

The FDA has been investigating NDMA and other nitrosamine impurities in blood pressure and heart failure medicines called Angiotensin II Receptor Blockers (ARBs) since last year. In the case of ARBs, the FDA has recommended numerous recalls as it discovered unacceptable levels of nitrosamines.

When the agency identifies a problem, it takes appropriate action quickly to protect patients. The FDA is evaluating whether the low levels of NDMA in ranitidine pose a risk to patients. FDA will post that information when it is available.

Patients should be able to trust that their medicines are as safe as they can be and that the benefits of taking them outweigh any risk to their health. Although NDMA may cause harm in large amounts, the levels the FDA is finding in ranitidine from preliminary tests barely exceed amounts you might expect to find in common foods.

Ranitidine is an over-the-counter (OTC) and prescription drug. Ranitidine is an H2 (histamine-2) blocker, which decreases the amount of acid created by the stomach. Over-the-counter ranitidine is approved to prevent and relieve heartburn associated with acid ingestion and sour stomach. Prescription ranitidine is approved for multiple indications, including treatment and prevention of ulcers of the stomach and intestines and treatment of gastroesophageal reflux disease.

The agency is working with international regulators and industry partners to determine the source of this impurity in ranitidine. The agency is examining levels of NDMA in ranitidine and evaluating any possible risk to patients. The FDA will take appropriate measures based on the results of the ongoing investigation. The agency will provide more information as it becomes available.

The FDA is not calling for individuals to stop taking ranitidine at this time; however, patients taking prescription ranitidine who wish to discontinue use should talk to their health care professional about other treatment options. People taking OTC ranitidine could consider using other OTC medicines approved for their condition. There are multiple drugs on the market that are approved for the same or similar uses as ranitidine.

Consumers and health care professionals should report any adverse reactions with ranitidine to the FDA's MedWatch program (/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program) to help the agency better understand the scope of the problem:

- Complete and submit the report online at www.fda.gov/medwatch/report.htm (https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home)
- Download and complete the appropriate form, then submit it via fax at 1-800-FDA-0178

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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Inquiries

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Consumer:

888-INFO-FDA

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EXHIBIT B

Laboratory Tests | Ranitidine

Laboratory analysis of ranitidine and nizatidine products

FDA continues to investigate the presence of the N-Nitrosodimethylamine (NDMA) impurity in ranitidine and is now aware of NDMA in nizatidine, which is chemically similar to ranitidine. Both medicines are H2 blockers which decrease the amount of acid in the stomach. FDA has identified NDMA in ranitidine and nizatidine active pharmaceutical ingredient (API) and finished drugs.

FDA is posting its laboratory results in the table below showing NDMA levels in all ranitidine and nizatidine samples it tested, including API and finished drug which included tablets and syrup. NDMA was present in all samples tested. Testing of ranitidine for injection is still ongoing.

For reference, consuming up to 0.096 micrograms or 0.32 parts per million (ppm) of NDMA per day is considered reasonably safe for human ingestion based on lifetime exposure. FDA has set the acceptable daily intake limit for NDMA at 0.096 micrograms or 0.32 ppm for ranitidine. Although many manufacturers have already recalled ranitidine voluntarily, FDA will recommend recalls to manufacturers with NDMA levels above the acceptable daily intake limit.

The methods FDA used in the laboratory testing are available here (/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine).

FDA also developed a simulated gastric fluid (SGF) model to be used with the LC-MS testing method (/media/131868/download) to estimate the biological significance of in vitro findings. The SGF and simulated intestinal fluid (SIF) models are intended to detect the formation of NDMA in systems that approximate the stomach and intestinal fluids, respectively. The results of these tests showed no additional NDMA generated in the stomach.

NDMA ESTIMATED RISK:

FDA has determined that the levels of NDMA in ranitidine and nizatidine are similar to the levels you would expect to be exposed to if you ate common foods like grilled or smoked meats.

Company	Product	Lots Tested	NDMA level ppm	NDMA level (micrograms-mcg/tablet or oral dose)
Sanofi Pharmaceutical	OTC Ranitidine 150mg	19E413M, 19D554, 19A432U, 19C540, 19D431I, 19D442N, 19D423M, 19D464M,	0.07-2.38	0.01-0.36
Sanofi Pharmaceutical	OTC Ranitidine 75mg	18L012U, 9A003U, 19B006M, 18M025M, 18N023U, 19B005N, 19A002U, 18N026U	0.10-0.55	0.01-0.04
Cardinal Health	OTC Ranitidine 150mg	9FE2953	1.02	0.15
Watson	Rx Nizatidine 150mg	1350798M	0.05	0.01
Watson	Rx Nizatidine 300mg	1333973A	0.04	0.01
Strides Shasun Ltd	Rx Nizatidine 150mg	7704758A	0.11	0.02
Strides Shasun Ltd	Rx Nizatidine 300mg	7704022A	0.09	0.03
Novitium	Rx Ranitidine 300mg	S18038B	2.85	0.86
Dr Reddy's	Rx Ranitidine 300mg	C805265	0.68	0.20
Strides Shasun Ltd	Rx Ranitidine 300mg	7702255A	0.11	0.03
Sandoz	Rx Ranitidine 300mg	HU2207	0.82	0.25
Strides Shasun Ltd	Rx Ranitidine 300mg	7704537A	0.02	0.00
Aurobindo	Rx Ranitidine 300mg	RA3019001-A	1.86	0.56
Ajanta Pharma USA Inc	Rx Ranitidine 300mg	PA1229B	0.23	0.07
Silarx Pharma	Ranitidine 150mg Syrup	3652081-02661	1.37	0.20

Company	Product	Lots Tested	NDMA level ppm	NDMA level (micrograms-mcg/tablet or oral dose)
Pharma Associates	Ranitidine 150mg Syrup	BE00, BF75, BF77, BF78, BDFF, COAC	0.03-0.07	0.004-0.012
Amneal Pharmaceuticals	Ranitidine 300mg	AR181795A, AR190878A, AR190876A, AR191177A, HB05819, HB06119, HL08718	0.52-2.17	0.16-0.65
Sanofi Pharmaceutical	Ranitidine 150mg	19D570, 19D428U, 19E408M	0.08-2.17	0.01-0.33

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EXHIBIT C

FDA NEWS RELEASE

FDA Requests Removal of All Ranitidine Products (Zantac) from the Market

FDA Advises Consumers, Patients and Health Care Professionals After New FDA Studies Show Risk to Public Health

For Immediate Release:

April 01, 2020

Español (/news-events/press-announcements/la-fda-solicita-el-retiro-del-mercado-de-todos-los-productos-hechos-base-de-ranitidina-zantac)

The U.S. Food and Drug Administration today announced it is requesting manufacturers withdraw all prescription and over-the-counter (OTC) ranitidine drugs from the market immediately. This is the latest step in an ongoing investigation (/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine) of a contaminant known as N-Nitrosodimethylamine (NDMA) in ranitidine medications (commonly known by the brand name Zantac). The agency has determined that the impurity in some ranitidine products increases over time and when stored at higher than room temperatures and may result in consumer exposure to unacceptable levels of this impurity. As a result of this immediate market withdrawal request, ranitidine products will not be available for new or existing prescriptions or OTC use in the U.S.

"The FDA is committed to ensuring that the medicines Americans take are safe and effective. We make every effort to investigate potential health risks and provide our recommendations to the public based on the best available science. We didn't observe unacceptable levels of NDMA in many of the samples that we tested. However, since we don't know how or for how long the product might have been stored, we decided that it should not be available to consumers and patients unless its quality can be assured," said Janet Woodcock, M.D., director of the FDA's Center for Drug Evaluation and Research. "The FDA will continue our efforts to ensure impurities in other drugs do not exceed acceptable limits so that patients can continue taking medicines without concern."

NDMA is a probable human carcinogen (a substance that could cause cancer). In the summer of 2019, the FDA became aware of independent laboratory testing that found NDMA in ranitidine. Low levels of NDMA are commonly ingested in the diet, for example NDMA is present in foods and in water. These low levels would not be expected to lead to an increase in the risk of cancer. However, sustained higher levels of exposure may increase the risk of cancer in humans. The FDA conducted thorough laboratory tests and found NDMA in ranitidine at low levels. At the time, the agency did not have enough scientific evidence to recommend whether individuals should continue or stop taking ranitidine medicines, and continued its investigation and warned the public in September 2019 (/news-events/press-announcements/statement-new-testing-results-including-low-levels-impurities-ranitidine-drugs) of the potential risks and to consider alternative OTC and prescription treatments.

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New FDA testing and evaluation prompted by information from third-party laboratories confirmed that NDMA levels increase in ranitidine even under normal storage conditions, and NDMA has been found to increase significantly in samples stored at higher temperatures, including temperatures the product may be exposed to during distribution and handling by consumers. The testing also showed that the older a ranitidine product is, or the longer the length of time since it was manufactured, the greater the level of NDMA. These conditions may raise the level of NDMA in the ranitidine product above the acceptable daily intake limit.

With today's announcement, the FDA is sending letters to all manufacturers of ranitidine requesting they withdraw their products from the market. The FDA is also advising consumers taking OTC ranitidine to stop taking any tablets or liquid they currently have, dispose of them properly and not buy more; for those who wish to continue treating their condition, they should consider using other approved OTC products. Patients taking prescription ranitidine should speak with their health care professional about other treatment options before stopping the medicine, as there are multiple drugs approved for the same or similar uses as ranitidine that do not carry the same risks from NDMA. To date, the FDA's testing has not found NDMA in famotidine (Pepcid), cimetidine (Tagamet), esomeprazole (Nexium), lansoprazole (Prevacid) or omeprazole (Prilosec).

In light of the current COVID-19 pandemic, the FDA recommends patients and consumers not take their medicines to a drug take-back location but follow the specific disposal instructions in the medication guide or package insert (/drugs/drug-safety-and-availability/medication-guides) or follow the agency's recommended steps (/drugs/safe-disposal-medicines/disposal-unused-medicines-what-you-should-know), which include ways to safely dispose of these medications at home.

The FDA continues its ongoing review, surveillance, compliance and pharmaceutical quality efforts across every product area, and will continue to work with drug manufacturers to ensure safe, effective and high-quality drugs for the American public.

The FDA encourages health care professionals and patients to report adverse reactions or quality problems with any human drugs to the agency's MedWatch Adverse Event Reporting (https://www.fda.gov/about-fda/forms/medwatch-fda-safety-information-and-adverse-event-reporting-program-mandatory-html) program:

- Complete and submit the report online at www.fda.gov/medwatch/report.htm (https://www.fda.gov/about-fda/forms/medwatch-fda-safety-information-and-adverse-event-reporting-program-mandatory-html); or
- Download and complete the form, then submit it via fax at 1-800-FDA-0178.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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Consumer:

888-INFO-FDA

Related Information

- Questions and Answers: NDMA impurities in ranitidine (commonly known as Zantac) (/drugs/drug-safety-and-availability/questions-and-answers-ndma-impurities-ranitidine-commonly-known-zantac)
- What to Know and Do About Possible Nitrosamines in Your Medication (/consumers/consumer-updates/what-know-and-do-about-possible-nitrosamines-your-medication)
- Information about Nitrosamine Impurities in Medications (/drugs/drug-safety-and-availability/information-about-nitrosamine-impurities-medications)

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EXHIBIT D

COMPANY ANNOUNCEMENT

Sanofi Provides Update on Precautionary Voluntary Recall of Zantac OTC in U.S.

Summary

Company Announcement Date:

October 22, 2019

FDA Publish Date:

October 23, 2019

Product Type:

Drugs

Reason for Announcement:

May Contain N-Nitrosodimethylamine (NDMA)

Company Name:

Sanofi

Brand Name:

Sanofi

Product Description:

Zantac 150, Zantac 150 Cool Mint, Zantac 75 (OTC Products)

Company Announcement

As a precautionary measure, Sanofi on Friday, October 18, intiated a voluntary recall of all Zantac OTC (over-the-counter) in the United States. This includes Zantac 150®, Zantac 150® Cool Mint, and Zantac 75®. Zantac tablets are an oral, over-the-counter product to prevent and relieve heartburn associated with acid ingestion and sour stomach.

On September 13, 2019, the U.S Food and Drug Administration issued a public statement

alerting that some ranitidine medicines, including Zantac OTC, could contain NDMA at low levels and asked manufacturers to conduct testing.

Evaluations are ongoing on both drug substance (active ingredient) and finished drug product. Due to inconsistencies in preliminary test results of the active ingredient used in the U.S. products, Sanofi has made the decision to conduct the voluntary recall as the investigation continues.

Active ingredients used in Sanofi's ranitidine products outside of the U.S. and Canada are sourced from different suppliers. Sanofi has also issued a voluntary recall in Canada. The company is committed to transparency and will continue to communicate results with health authorities from the ongoing testing, and work with them to make informed decisions based on available data and evidence.

Risk Statement: NDMA is classified as a probable human carcinogen (a substance that could cause cancer) based on results from laboratory tests. NDMA is a known environmental contaminant and found in water and foods, including meats, dairy products, and vegetables.

Sanofi will be notifying its distributors and customers via email and via the Sanofi web site, and will arrange for return of all recalled products. Wholesalers (direct customers) will be asked to immediately stop distribution and return any stock to Sanofi, and contact the retail outlets in their group to do the same. Retailers will be asked to immediately stop dispensing Zantac tablets and return remaining stock to Sanofi by contacting INMAR at 877-275-0993 (option 1) or via fax at 336-499-8145 or email at zantacrecall@inmar.com (mailto:zantacrecall@inmar.com). Consumers are asked to speak to their physician or pharmacist about alternate heartburn relief options.

Adverse reactions or quality problems experienced with the use of this product may be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax.

- Complete and submit the report Online (/node/360543)
- Regular Mail or Fax: Download form (/node/360547) or call 1- 800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

This recall is being conducted with the knowledge of the U.S. Food and Drug Administration

Company Contact Information

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zantacrecall@inmar.com (mailto:zantacrecall@inmar.com)

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More Recalls, Market Withdrawals, & Safety Alerts (/safety/recalls-market-withdrawals-safety-alerts)

EXHIBIT E

Ensuring the Rigor of Regulatory Science: CDER Conducts Laboratory and Clinical Studies to Investigate Reports of NDMA Production from Ingested Ranitidine Products

Ranitidine, which blocks histamine-induced acid secretion in the stomach, was approved in 1983. It became widely used over the ensuing decades as a prescription and over-the-counter product. In 2019, the FDA received a citizen petition (http://www.regulations.gov/document/FDA-2019-P-4281-0001) indicating that high levels of N-nitrosodimethylamine (NDMA), a probable human carcinogen, were detected in specific ranitidine products. The petitioner also proposed that ranitidine could convert to NDMA in humans. In response, the FDA immediately alerted the public (https://www.fda.gov/news-events/press-announcements/statement-alerting-patients-and-health-care-professionals-ndma-found-samples-ranitidine), and CDER scientists worked quickly to mobilize specialized FDA laboratory and clinical research capabilities.

CDER's initial research focused on assessing the amount of NDMA in ranitidine drug products. CDER researchers found that the procedures previously used to quantify NDMA were not appropriate for assessing its presence in ranitidine, owing to the use of high temperatures that could convert ranitidine to NDMA during that analysis. CDER researchers therefore developed and validated low-temperature analytical methods (https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-ranitidine-zantac) and found that the amounts of NDMA (https://www.fda.gov/drugs/drug-safety-and-availability/laboratory-tests-ranitidine) contained in ranitidine products were 3,000-fold lower than those reported in the citizen petition; however, these lower amounts of NDMA were still above the FDA-acceptable level, corresponding to a daily intake limit of 96 ng NMDA per day, in many of the ranitidine lots tested. CDER scientists further observed that the amounts of NDMA in ranitidine samples could increase over time, prompting the FDA to request the market withdrawal of ranitidine products (https://www.fda.gov/news-events/press-announcements/fda-requests-removal-all-ranitidine-products-zantac-market). The agency noted, however, that if ranitidine products could be manufactured to control NDMA amounts, they could be allowed back on the market—but additional information would first be needed to understand whether NDMA could form in vivo from ranitidine in humans.

Assessing the Potential for Ranitidine to Convert to NDMA in Humans

The citizen petition referenced in vitro studies suggesting ranitidine could convert to NDMA in simulated gastric fluid (with high levels of supplemental nitrite) and a prior clinical study (https://dx.doi.org/10.1093/carcin/bgw034) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) with 10 participants. The referenced clinical study reported an approximate 400-fold increase in NDMA excreted in urine over 24-hours after oral ranitidine 150 mg. However, there were multiple limitations to the referenced study, including the lack of placebo-controlled randomization; the lack of information concerning environmental or dietary exposure of study participants to NDMA or the reactants that may contribute to NDMA production; and a lack of detail about biological sample handling and validation of analytical methods.

To better address the possibility of NDMA production from ranitidine in humans, CDER scientists conducted a more rigorous, randomized, double-blinded, placebo-controlled clinical trial, published in JAMA: Journal of the American Medical Association (https://jamanetwork.com/journals/jama/fullarticle/10.1001/jama.2021.9199?utm_campaign=articlePDF%26utm_medium=articlePDFlink%26utm_source=articlePDF%26utm_content=jama.2021.9199) (http://www.fda.gov/about-fda/website-policies/website-disclaimer). The study included 18 participants who each received ranitidine (300 mg) and placebo on two different diets, the second of which was designed to contain higher amounts of nitrites, nitrates, and NDMA from foods such as cured meats. The study used rigorous procedures for handling urine and blood samples and validated low-temperature analytical methods for measuring NDMA. The CDER researchers found no evidence of elevated NDMA content in the urine of participants over the 24 hours after they took ranitidine, regardless of diet. CDER's clinical trial further found that ranitidine did not increase NDMA in blood plasma and did not increase dimethylamine (DMA) (proposed in the citizen petition to be the precursor to NDMA generated from ranitidine) in plasma or urine.

In addition, CDER researchers conducted an in vitro study, also published by the JAMA network (https://jama.jamanetwork.com/article.aspx?doi=10.1001/jamanetworkopen.2021.18253&utm_campaign=articlePDF%26utm_medium=articlePDFlink%26utm_source=articlePDF%26utm_content (http://www.fda.gov/about-fda/website-policies/website-disclaimer), on the potential for ranitidine to convert to NDMA in simulated gastric fluid. Importantly, CDER researchers performed an assessment of the range of physiologic gastric nitrite concentrations from prior clinical studies, which had not been done in a recent prior study published in the same journal. CDER researchers found that ranitidine did not produce NDMA in simulated gastric fluid unless nitrite was 50-fold greater than the upper range of physiologic gastric nitrite concentration in acidic conditions. The combined findings from CDER's in vivo clinical trial and in vitro experiments do not support the conclusion that ranitidine is converted to NDMA in humans.

Broader Context of CDER's Research Findings

After CDER completed its clinical trial and submitted the results for publication, the prior clinical study that had reported a 400-fold increase in NDMA urinary excretion after ingestion of ranitidine was retracted (https://dx.doi.org/10.1093/carcin/bgab029) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) by the authors, citing that an analytical artifact may have contributed to their results. In addition, as summarized in the reports that CDER investigators published in JAMA (https://jamanetwork.com/journals/jama/fullarticle/10.1001/jama.2021.9199?utm_campaign=articlePDF%26utm_medium=articlePDFlink%26utm_source=articlePDF%26utm_content=jama.2021.9199) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) and JAMA Network Open (https://jama.jamanetwork.com/article.aspx?

doi=10.1001/jamanetworkopen.2021.18253&utm_campaign=articlePDF%26utm_medium=articlePDFlink%26utm_source=articlePDF%26utm_content (http://www.fda.gov/about-fda/website-policies/website-disclaimer), other reports of nonclinical results (https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775727) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) (or commentaries on nonclinical studies (https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775725) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)) had described in vitro findings without properly contextualizing the physiological relevance of their test conditions. Indeed, the CDER in vitro analysis demonstrates that proper investigation into the potential for drugs to lead to NDMA formation in humans should include physiologically relevant conditions.

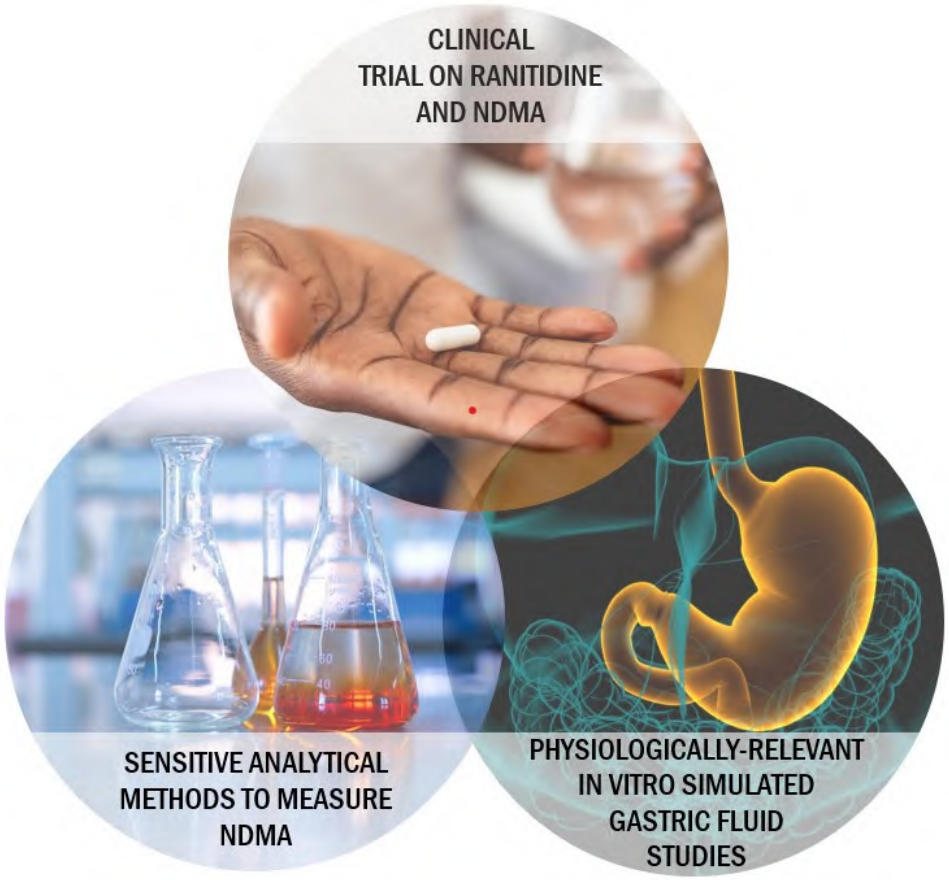
As noted above and elsewhere (https://jamanetwork.com/journals/jama/fullarticle/10.1001/jama.2021.9199?utm_campaign=articlePDF%26utm_medium=articlePDFlink%26utm_source=articlePDF%26utm_content=jama.2021.9199) (http://www.fda.gov/about-fda/website-policies/website-disclaimer), ranitidine products were removed from the US market in April 2020, owing to unacceptable amounts of NDMA in ranitidine products that could increase over time; however, the product approvals were not withdrawn, and the FDA may consider allowing ranitidine products back on the market if they are proven to be stable, with low, acceptable amounts of NDMA that do not increase over time during storage. All FDA-approved drug products must meet FDA standards for safety, effectiveness, and quality before they are allowed on the market. In addition, it may be assuring to patients and health care professionals to consider in proper context the potential risk posed by products that may contain NDMA amounts at the acceptable daily limit (https://www.fda.gov/media/141720/download); the cancer risk for an average individual with a mass of 50 kg and consuming 96 ng of NDMA daily for 70 years is 1 in 100,000.

CDER Research to Address Emergent Regulatory and Public Health Questions

CDER's research capabilities and activities empower the agency to respond rapidly to emergent regulatory and public health questions regarding the products it regulates. In the case discussed above, CDER developed new analytical methods for measuring NDMA in drug products and in biological fluids, and then conducted rigorous laboratory (https://jama.jamanetwork.com/article.aspx?doi=10.1001/jamanetworkopen.2021.18253&utm_campaign=articlePDF%26utm_medium=articlePDFlink%26utm_source=articlePDF%26utm_content (http://www.fda.gov/about-fda/website-policies/website-disclaimer) and clinical (https://jamanetwork.com/journals/jama/fullarticle/10.1001/jama.2021.9199?utm_campaign=articlePDF%26utm_medium=articlePDFlink%26utm_source=articlePDF%26utm_content=jama.2021.9199) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) studies. The findings suggested that prior reports had detected falsely high levels of NDMA in ranitidine drug products and human biological fluids.

In another case, pertaining to sunscreens (also a type of widely used over-the-counter product), historical assumptions had posited that the active ingredients in sunscreens were not absorbed; however, the studies necessary for addressing this absorption issue (https://jamanetwork.com/journals/jama/fullarticle/2733084) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) were not pursued until CDER regulatory science initiatives led the way. CDER scientists conducted both laboratory and clinical research, including 2 clinical trial reports published in JAMA (report 1 (https://jamanetwork.com/journals/jama/fullarticle/2733085) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) and report 2 (https://jamanetwork.com/journals/jama/fullarticle/2759002) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)), that demonstrated that sunscreen active ingredients in fact can be absorbed, revealing the need for further studies by industry.

In these and many other cases (see, for example, CDER's Impact Stories (https://www.fda.gov/drugs/regulatory-science-action/impact-stories) or the CDER Division of Applied Regulatory Science annual report (https://www.fda.gov/media/147239/download)), CDER scientists play a unique role in moving new science into the drug regulatory review process and addressing emergent regulatory and public health questions.



To inform science-based regulatory decisions, CDER scientists employed a multidisciplinary, translational research approach to investigate whether ranitidine converts to NDMA in humans.

The Spotlight series presents generalized perspectives on ongoing research- and science-based activities within CDER. Spotlight articles should not be construed to represent FDA's views or policies.

References to Published CDER Investigations

Florian J, Matta MK, DePalma R, Gershuny V, Patel V, Hsiao CH, Zusterzeel R, Rouse R, Prentice K, Nalepinski CG, Kim I, Yi S, Zhao L, Yoon M, Selaya S, Keire D, Korvick J, Strauss DG. Effect of Oral Ranitidine on Urinary Excretion of N-Nitrosodimethylamine (NDMA): A Randomized Clinical Trial. JAMA. 2021 Jun 28. doi: 10.1001/jama.2021.9199.

Gao Z, Karfunkle M, Ye W, Marzan TA, Yang J, Lex T, Sommers C, Rodriguez JD, Han X, Florian J, Strauss DG, Keire DA. In Vitro Analysis of N-Nitrosodimethylamine (NDMA) Formation From Ranitidine Under Simulated Gastrointestinal Conditions. JAMA Netw Open. 2021 Jun 1;4(6):e2118253. doi: 10.1001/jamanetworkopen.2021.18253.

Exhibit 48

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

CASE NO. RG20054985

ASSIGNED FOR ALL PURPOSES TO:
HON. WINIFRED Y. SMITH
DEPT. 21

REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S DEMURRER TO PLAINTIFF'S THIRD AMENDED COMPLAINT

Date: September 15, 2021
Time: 10:00 a.m.
Dept.: 21
Judge: Hon. Winifred Y. Smith

Reservation Nos.: R-2277974
R-2277975

TAC Filed: June 9, 2021

Under California Evidence Code §§ 450 *et seq.*, Defendants Sanofi-Aventis U.S. LLC and Chattem, Inc. submit this Request for Judicial Notice (this "RJN") in Support of their Demurrer to Plaintiff's Third Amended Complaint.

I. This Court Has Already Granted Judicial Notice of Exhibits Submitted in Support of Defendants' Demurrer to Plaintiff's Third Amended Complaint

In its May 5, 2021 Order granting Defendants' demurrer to the Second Amended Complaint, the Court granted judicial notice of 20 exhibits, pursuant to Defendants' and Plaintiff's Requests for Judicial Notice. *See* Order at 2.[1] Four of these exhibits are attached as **Exhibits A through D** to the Declaration of Sean Newland in Support of Defendants' Demurrer to the Third Amended Complaint ("Newland Declaration"):

A. September 13, 2019 FDA "Statement alerting patients and health care professionals of NDMA found in samples of ranitidine";

B. November 1, 2019 FDA release entitled "Laboratory Tests ı Ranitidine";

C. April 1, 2020 FDA release entitled "FDA Requests Removal of All Ranitidine Products (Zantac) from the Market"; and

D. Defendants' "Company Announcement" published by the FDA on October 23, 2019.

With reference to this Court's prior Order granting judicial notice of the foregoing exhibits, Defendants request judicial notice of the same documents in connection with their Demurrer to the Third Amended Complaint, filed concurrently with this RJN. As noted in the prior requests—and as discussed more fully below with respect to Exhibit E—granting judicial notice of these exhibits is proper under California Evidence Code §§ 452(c) and (h).

[1] Defendants submitted a "Request for Judicial Notice in Support of Defendants' Chattem, Inc. and Sanofi-Aventis U.S. LLC's Demurrer to Plaintiff's Second Amended Complaint" seeking judicial notice of 13 exhibits attached to the "Declaration of Greg G. Sperla in Support of Defendants' Demurrer to Plaintiff's Second Amended Complaint." Plaintiff submitted "Plaintiff's Request for Judicial Notice in Support of Omnibus Opposition to Defendants' Demurrers" seeking judicial notice of 7 exhibits attached to the "Declaration of Mark N. Todzo in Support of Plaintiff's Omnibus Opposition to Defendants' Demurrers."

II. This Court Can Take Judicial Notice of the Additional Exhibit Submitted in Support of Defendants' Demurrer to Plaintiff's Third Amended Complaint

This RJN requests that the Court take judicial notice of the additional document summarized below, which is attached as **Exhibit E** to the Newland Declaration and, like the exhibits this Court has already noticed, is a publicly available release on the FDA's website.

This Court is authorized to take judicial notice of official records of the U.S. Food and Drug Administration ("FDA"). *See* Cal Evid. Code § 452(c) (permitting judicial notice of "[o]fficial acts of the legislative, executive, and judicial departments of the United States"). Judicial notice is also appropriate under California Evidence Code § 452(h) where "[f]acts and propositions" to be noticed "are not reasonably subject to dispute and are capable of immediate and accurate determination by resort to courses of reasonable accuracy." Defendants thus request that the Court take judicial notice of the following exhibit attached to the Newland Declaration, which is an official record of the FDA not reasonably subject to dispute and immediately and accurately verifiable on the FDA's website.

Exhibit E: July 2, 2021 online statement by FDA entitled "Ensuring the Rigor of Regulatory Science: CDER Conducts Laboratory and Clinical Studies to Investigate Reports of NDMA Production from Ingested Ranitidine Products."

Dated: July 21, 2021

DLA PIPER LLP (US)

By: _____

George J. Gigounas
Gregory G. Sperla
Sean A. Newland
Attorneys for Defendants CHATTEM, INC. and SANOFI-AVENTIS U.S. LLC

Exhibit 49

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Attorneys for Defendants
CHATTEM, INC. and SANOFI-AVENTIS U.S. LLC

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

CASE NO. RG20054985

ASSIGNED FOR ALL PURPOSES TO:
HON. WINIFRED Y. SMITH
DEPT. 21

[PROPOSED] ORDER SUSTAINING DEMURRER TO THIRD AMENDED COMPLAINT

[PROPOSED] ORDER

Defendants Chattem, Inc. and Sanofi-Aventis U.S. LLC ("Defendants") Demurrer to Plaintiff Center for Environmental Health's ("Plaintiff") Third Amended Complaint, came on regularly for hearing before the Honorable Winifred Y. Smith on September 15, 2021, at 10:00 a.m., in Department 21 of the Superior Court of the County of Alameda. Counsel from the Lexington Law Group appeared for Plaintiff, and counsel from DLA Piper LLP (US) appeared for Defendants.

Having considered the papers filed in support of and in opposition to the Demurrer, having heard the arguments of counsel, and with good cause appearing, **IT IS HEREBY ORDERED** that:

1. Defendants' Demurrer to Plaintiff's Third Amended Complaint is **SUSTAINED WITHOUT LEAVE TO AMEND.**

2. Defendants to give notice.

Dated:_____

_____
Honorable Winifred Y. Smith
Alameda County Superior Court Judge

Exhibit 50

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Attorneys for Defendants
CHATTEM, INC. and SANOFI-AVENTIS U.S. LLC

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

CASE NO. RG20054985

ASSIGNED FOR ALL PURPOSES TO:
HON. WINIFRED Y. SMITH
DEPT. 21

PROOF OF SERVICE

Date: September 15, 2021
Time: 10:00 a.m.
Dept.: 21
Judge: Hon. Winifred Y. Smith

Reservation No.: R-2277974
Reservation No.: R-2277975

TAC Filed: June 9, 2021

PROOF OF SERVICE

I, Sandy Holstrom, declare:

I am a citizen of the United States and employed in San Francisco, California. I am over the age of eighteen years and not a party to the within-entitled action. My business address is DLA Piper LLP (US), 555 Mission Street, Suite 2400, San Francisco, CA 94105. On July 21, 2021, I served a copy of the within document(s):

- **DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S NOTICE OF DEMURRER AND DEMURRER TO PLAINTIFF'S THIRD AMENDED COMPLAINT; MEMORANDUM OF POINTS AND AUTHORITIES;**
- **DECLARATION OF SEAN NEWLAND IN SUPPORT OF DEFENDANTS' DEMURRER TO PLAINTIFF'S THIRD AMENDED COMPLAINT;**
- **REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S DEMURRER TO PLAINTIFF'S THIRD AMENDED COMPLAINT; and**
- **[PROPOSED] ORDER SUSTAINING DEMURRER TO THIRD AMENDED COMPLAINT**

☐ by placing the document(s) listed above in a sealed envelope with postage thereon fully prepaid, the United States mail at San Francisco, California addressed as set forth below.

☒ by transmitting via e-mail or electronic transmission the document(s) listed above to the person(s) at the e-mail address(es) set forth below.

Mark Todzo
Joseph Mann
Lexington Law Group
503 Divisadero Street
San Francisco, CA 94117
mtodzo@lexlawgroup.com
jmann@lexlawgroup.com

Attorneys for Plaintiff
Center for Environmental Health

I declare under penalty of perjury under the laws of the State of California that the above is true and correct.

Executed on July 21, 2021 at Dublin, California.

Sandy Holstrom

Exhibit 51

SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY; TARGET CORPORATION; APOTEX CORP.; GRANULES PHARMACEUTICALS, INC.; GRANULES USA, INC.; 7-ELEVEN, INC.; SANOFI-AVENTIS U.S. LLC; CHATTEM INC.; DR. REDDY'S LABORATORIES LOUISIANA, LLC; DR. REDDY'S LABORATORIES, INC. and DOES 1 to 20, inclusive,

Defendants.

Case No. RG 20054985

Assigned for All Purposes to Hon. Winifred Y. Smith - Dept 21

[PROPOSED] JUDGMENT OF DISMISSAL AFTER THE SUSTAINING OF DEMURRERS TO SECOND AMENDED COMPLAINT WITHOUT LEAVE TO AMEND

Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

On May 7, 2021, the Court entered an Order sustaining without leave to amend the demurrers of the following Defendants to the Second Amended Complaint brought by Plaintiff Center for Environmental Health:

1. Perrigo Company;
2. Granules USA, Inc.;
3. Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories Louisiana, LLC;
4. Apotex Corp.;
5. 7-Eleven, Inc.; and
6. Target Corporation

Therefore, having entered the Order,

IT IS HEREBY ORDERED, ADJUDGED AND DECREED that the above action is dismissed with prejudice as to the above Defendants, JUDGMENT be entered in favor of the above Defendants and against the Plaintiff, that Plaintiff take nothing against them, and that Defendants shall recover costs according to proof.

DATED: August 11, 2021

Winifred Y. Smith
Judge of The Superior Court
County of Alameda

Exhibit 52

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Danielle Vallone (SBN 302497)
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Attorneys for Defendant
PERRIGO COMPANY

SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY; TARGET CORPORATION; APOTEX CORP.; GRANULES PHARMACEUTICALS, INC.; GRANULES USA, INC.; 7-ELEVEN, INC.; SANOFI-AVENTIS U.S. LLC; CHATTEM INC.; DR. REDDY'S LABORATORIES LOUISIANA, LLC; DR. REDDY'S LABORATORIES, INC. and DOES 1 to 20, inclusive,

Defendants.

Case No. RG 20054985

Assigned for All Purposes to
Hon. Winifred Y. Smith - Dept 21

NOTICE OF ENTRY OF JUDGMENT

Complaint Filed: February 19, 2020
SAC Filed: January 4, 2021
Trial Date: None Set

TO ALL PARTIES AND THEIR ATTORNEYS OF RECORD:

PLEASE TAKE NOTICE that on August 11, 2021, the Court entered Judgment in favor of certain defendants after sustaining without leave to amend their respective Demurrers to Plaintiff's Second Amended Complaint.

The Judgment is attached hereto as "**Exhibit A".**

Dated: August 13, 2021

STEPTOE & JOHNSON LLP

By: _____

Dennis Raglin
Danielle Vallone
Attorneys for Defendant
PERRIGO COMPANY

EXHIBIT A

SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY; TARGET CORPORATION; APOTEX CORP.; GRANULES PHARMACEUTICALS, INC.; GRANULES USA, INC.; 7-ELEVEN, INC.; SANOFI-AVENTIS U.S. LLC; CHATTEM INC.; DR. REDDY'S LABORATORIES LOUISIANA, LLC; DR. REDDY'S LABORATORIES, INC. and DOES 1 to 20, inclusive,

Defendants.

Case No. RG 20054985

Assigned for All Purposes to Hon. Winifred Y. Smith - Dept 21

[PROPOSED] JUDGMENT OF DISMISSAL AFTER THE SUSTAINING OF DEMURRERS TO SECOND AMENDED COMPLAINT WITHOUT LEAVE TO AMEND

Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

On May 7, 2021, the Court entered an Order sustaining without leave to amend the demurrers of the following Defendants to the Second Amended Complaint brought by Plaintiff Center for Environmental Health:

1. Perrigo Company;
2. Granules USA, Inc.;
3. Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories Louisiana, LLC;
4. Apotex Corp.;
5. 7-Eleven, Inc.; and
6. Target Corporation

Therefore, having entered the Order,

IT IS HEREBY ORDERED, ADJUDGED AND DECREED that the above action is dismissed with prejudice as to the above Defendants, JUDGMENT be entered in favor of the above Defendants and against the Plaintiff, that Plaintiff take nothing against them, and that Defendants shall recover costs according to proof.

DATED: August 11, 2021

Winifred Y. Smith
Judge of The Superior Court
County of Alameda

PROOF OF SERVICE

F.R.C.P. 5 / C.C.P. 1013a(3)/ Rules of Court, Rule 2060

I am a resident of, or employed in the County of Los Angeles, State of California. I am over the age of 18 and not a party to this action. My business address is: Steptoe & Johnson LLP, 633 West Fifth Street, Suite 1900, Los Angeles, California 90071.

On **August 13, 2021,** I served the following listed document(s), by method indicated below, on the parties in this action: **NOTICE OF ENTRY OF JUDGMENT**

SERVICE LIST ATTACHED

☐ **BY U.S. MAIL**
By placing □ the original / □ a true copy thereof enclosed in a sealed envelope(s), with postage fully prepaid, addressed as per the attached service list, for collection and mailing at Steptoe & Johnson, LLP 633 West Fifth Street, Suite 1900 in Los Angeles, California 90071, following ordinary business practices. I am readily familiar with the firm's practice for collection and processing of document for mailing. Under that practice, the document is deposited with the United States Postal Service on the same day in the ordinary course of business. Under that practice, the document is deposited with the United States Postal Service on the same day as it is collected and processed for mailing in the ordinary course of business.

☐ **BY OVERNIGHT DELIVERY**
By delivering the document(s) listed above in a sealed envelope(s) or package(s) designated by the express service carrier, with delivery fees paid or provided for, addressed as per the attached service list, to a facility regularly maintained by the express service carrier or to an authorized courier or driver authorized by the express service carrier or to an authorized courier or deliver authorized by the express service carrier to receive documents. **Note:** Federal Court requirement: service by overnight delivery was made ☐ pursuant to agreement of the parties, confirmed in writing, or ☐ as an additional method of service as a courtesy to the parties or ☐ pursuant to Court Order.

☐ **BY PERSONAL SERVICE**
□ By personally delivering the document(s) listed above to the offices at the addressee(s) as shown on the attached service list.
□ By placing the document(s) listed above in a sealed envelope(s) and instructing a registered process server to personally delivery the envelope(s) to the offices at the address(es) set forth on the attached service list. The signed proof of service by the registered process server is attached.

☐ **BY ELECTRONIC SERVICE**
(via electronic filing service provider)
By electronically transmitting the document(s) listed above to File & ServeXpress, an electronic filing service provider, at www.fileandservexpress.com . To my knowledge, the transmission was reported as complete and without error. *See* Cal. R. Ct. R. 2.253, 2.255, 2.260.

☒ **BY EMAIL**
(to individual persons)
By electronically transmitting the document(s) listed above to the email address(es) of the person(s) set forth on the attached service list. To my knowledge, the transmission was reported as complete and without error. Service my email was made ☐ pursuant to agreement of the parties, confirmed in writing, or ☐ as an additional method of service as a courtesy to the parties or ☐ pursuant to Court Order. *See* Cal. Rules of Court, rule 2.260.

☐ **BY FACSIMILE**
By transmitting the document(s) listed above from Steptoe & Johnson in Los Angeles, California to the facsimile machine telephone number(s) set forth on the attached service list. Service by facsimile transmission was made ☐ pursuant to agreement of the parties, confirmed in writing, or ☐ as an additional method of service as a courtesy to the parties or ☐ pursuant to Court Order.

I declare under penalty of perjury under the laws of the *State of California* and the *United States of America* that the above is true and correct. Executed on **August 13, 2021,** at Los Angeles, California.

/s/ Carmen Markarian
Carmen Markarian

SERVICE LIST

Center for Environmental Health v. Perrigo Corp., et al.
Case No.: RG20054985

Matter No.: 26550-0005

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COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

Case No. RG 20-054985

ASSIGNED FOR ALL PURPOSES TO:
Hon. Evelio Grillo, Department 21

PLAINTIFF'S OPPOSITION TO DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S DEMURRER TO THIRD AMENDED COMPLAINT

Date: September 15, 2021
Time: 10:00 a.m.
Reservation Nos.: R-2277974, R-2277975

TAC Filed: June 9, 2021
Trial Date: None Set

[Filed concurrently with Declaration of Mark N. Todzo; Plaintiff's Request for Judicial Notice]

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I. INTRODUCTION

The Court's earlier demurrer order granted Plaintiff Center for Environmental Health ("CEH") leave to amend "to allege that the [n-nitrosodimethylamine ("NDMA")] exposure presented a 'clinically significant hazard' for which there is 'reasonable evidence of a causal association' with the drug" and that "as a result [Defendants Sanofi-Aventis U.S. LLC and Chattem, Inc. (hereinafter, "Sanofi")] could use the [Changes-Being-Effected ("CBE")] process to unilaterally strengthen the warning on the labeling without waiting for [U.S. Food and Drug Administration ("FDA")] approval." Order at 11:17-21. CEH's Third Amended Complaint ("TAC") does just that, adding the precise allegations that the Court believed were lacking.

Nevertheless, Sanofi's new demurrer attacks CEH's TAC for failing to support these allegations with what Sanofi contends are sufficient evidentiary facts. However, the Court's demurrer order explicitly ruled that "Plaintiff is not required to allege evidentiary facts to support this allegation." Order at 11:21. Sanofi's demurrer ignores this, as well as the applicable standard for federal "impossibility" preemption. The United States Supreme Court has dictated that a defendant raising an impossibility preemption defense in a failure-to-warn case involving federally-regulated drugs must produce "clear evidence" that the FDA would have rejected the warning required under state law. *See Wyeth v. Levine* (2009) 555 U.S. 555, 571-73. Such evidence entails demonstrating that the FDA was fully informed of the specific hazard, yet rejected attempts to add the state warning. *See Merck Sharp & Dohme Corp. v. Albrecht* (2019) 139 S. Ct. 1668, 1672. Sanofi fails to provide any evidence whatsoever on this point.

While not required under California pleading standards or the Court's prior order, the TAC further alleges that the FDA agrees with CEH that the NDMA levels in Sanofi's over-the-counter ("OTC") antacid products made with ranitidine as the active ingredient (the "Products") present an unacceptable cancer risk. Indeed, based on the very cancer hazard at issue in this case, the FDA will not allow the Products to be sold at all. Given the FDA's position regarding the cancer risk from the Products, Sanofi cannot possibly prove that the FDA would have rejected a Proposition 65 warning for the Products had it ever bothered to inform the FDA of the hazard in the first place.

Sanofi also rehashes its argument from the earlier demurrer that FDA label formatting

regulations categorically preclude the provision of Proposition 65 warnings on Products labels and by all other means of off-label communication (such as advertising). This position fails to acknowledge that Congress – the ultimate source of any preclusive intent – has expressly carved out Proposition 65 as the ***only*** state law that is exempted from the federal uniformity requirements on OTC drugs. Consequently, Sanofi may readily put Proposition 65 warnings on its labels and/or advertisements, as have other OTC drug manufacturers. Indeed, OTC drug advertisements are not even subject to regulation by the FDA.

At heart, Sanofi is challenging whether CEH will be able to defeat an impossibility defense on a motion for summary judgment or at trial, after full factual discovery. Whether or not this is so (and CEH surely doubts it), this is not appropriate in the demurrer context, where all of CEH's factual allegations are taken as true. Accordingly, Sanofi's demurrer should be overruled.

II. APPLICABLE LEGAL STANDARDS

A. Implied Impossibility Preemption by Federal Law.

In assessing claims of implied preemption, the Court's task is guided by a "presumption against preemption" of state law – one that is especially strong where "federal law touches a field that has been traditionally occupied by the States." *Solus Indus. Innovs., LLC v. Sup. Ct.* (2018) 4 Cal.5th 316, 332; *see also Chemical Specialties Mfrs. Ass'n, Inc. v. Allenby* (9th Cir. 1992) 958 F.2d 941, 943 (applying such presumption to Proposition 65 in rejecting preemption). An even further presumption against preemption applies when a state law is carved out from coverage by the express terms of the federal statute purporting to exclude state regulation. *See Farm Raised Salmon Cases* (2008) 42 Cal.4th 1077, 1091-92. In 1997, Congress amended the Federal Food Drug and Cosmetic Act's ("FDCA") provision on "National Uniformity for Nonprescription Drugs" – which generally disallows states from "establish[ing] or continu[ing] in effect any requirement … that is different from or in addition to, or that is otherwise not identical with, a requirement under this Act" – to expressly exclude "a State requirement adopted by a State public initiative or referendum enacted prior to September 1, 1997." 21 U.S.C. §379r(a) & (d)(2). "Proposition 65 is the ***only*** state enactment that falls within the savings clause." *Dowhal v. SmithKline Beecham Consumer Healthcare* (2004) 32 Cal.4th 910, 919 (emphasis added).

In order to find impossibility preemption, ***all*** manners of compliance with state law effectively must be forbidden by federal law. *See Florida Lime & Avocado Growers, Inc. v. Paul* (1963) 373 U.S. 132, 142-43 ("compliance with both" must be "a physical impossibility"). "To find that Proposition 65 is preempted [by a federal law], we must determine that ***all*** possible consumer product warnings that would satisfy Proposition 65 conflict with provisions of [that law]." *Committee of Dental Amalgam Mfrs. & Distribs. v. Stratton* (9th Cir. 1996) 92 F.3d 807, 810 (emphasis in original). Accordingly, it is impermissible for a court to simply determine that one method of Proposition 65 warning is preempted and then extrapolate this preclusive effect to all warning methods, as did the Court in its initial demurrer ruling.

In the context of impossibility preemption of a failure-to-warn claim related to brand-name drugs, the U.S. Supreme Court has held that the burden is on the drug manufacturer to show by "clear evidence" that the FDA would not have approved a change to the drug's label despite the CBE process. *Levine*, 555 U.S. at 571-73 ("[i]mpossibility pre-emption is a demanding defense"). "'[C]lear evidence' is evidence that shows the court that the drug manufacturer fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the drug manufacturer that the FDA would not approve a change to the drug's label to include that warning." *Risperdal & Invega Cases* (2020) 49 Cal.App.5th 942, 955-56 (citing *Albrecht*, 139 S. Ct. at 1672). Here, Sanofi has presented no such evidence.

B. Drug Label Changes Under the FDA's CBE Regulation.

OTC drugs are sold in the U.S. pursuant to an initial FDA authorization, with certain further changes to such a drug requiring FDA approval and others not. *See generally* 21 U.S.C. §355(a), (j); 21 C.F.R. §314.70(b)-(d). Specifically included as "moderate" changes that can be made as "Changes-Being-Effected" without FDA approval are "changes in the labeling to reflect newly acquired information" relating to "add[ing] or strengthen[ing] a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c)." 21 C.F.R. §314.70(c)(6)(iii)(A). Section 201.57(c), in turn, states that "the labeling must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug." *Id.*

§201.57(c)(6)(i) These provisions impose an affirmative, ongoing duty on the drug maker, for "the manufacturer bears responsibility for the content of its label at all times." *Levine*, 555 U.S at 570-71. Notably, a "causal association" means a potential link between the drug and the hazard – "a causal relationship need not have been definitely established." 21 C.F.R. §201.57(c)(6)(i) (includes "potential safety hazards"); *see also* 44 Fed. Reg. 37,434, 37,447 (June 26, 1979) (federal drug law "requires labeling to include warnings about both potential and verified hazards"). A "clinically significant" hazard is simply a "therapeutically significant" one, *i.e.*, one that affects decisions whether or not to take the drug. *See* 71 Fed. Reg. 3922, 3946 (Jan. 24, 2006); *Warner-Lambert Co. v. Heckler* (3d Cir. 1986) 787 F.2d 147, 154.

C. California Pleading and Demurrer Standards.

Under California law, a complaint need only contain "[a] statement of the facts constituting the cause of action, in ordinary and concise language." C.C.P. §425.10(a)(1). A plaintiff need not allege "evidentiary facts" bearing up the elements of this cause of action. *Doe v. City of Los Angeles* (2007) 42 Cal.4th 531, 549-50; *see also* Order at 11:21-23 (same).[1] Furthermore, a plaintiff is not required to anticipate and "plead around" a defendant's affirmative defenses. *See Stowe v. Fritzie Hotels, Inc.* (1955) 44 Cal.2d 416, 422.[2]

At the demurrer stage, the allegations in CEH's pleadings must be accepted as true. *See Del E. Webb Corp. v. Structural Materials Co.* (1981) 123 Cal.App.3d 593, 604; *Stevens v. Sup. Ct.* (1986) 180 Cal.App.3d 605, 609-10 ("Whether the plaintiff will be able to prove the pleaded facts is irrelevant to ruling upon the demurrer."). "[A] court reviewing a demurrer must also accept as true those facts that may be implied or inferred from those expressly alleged," while

[1] Sanofi incorrectly claims that "conclusory allegations" are "insufficient to state a claim" under California law. Demurrer at 18:12-13. The case it cites – *Rossberg v. Bank of Am., N.A.* (2013) 219 Cal.App.4th 1481 – involved a ***fraud*** claim; the elements of such claims must be alleged "with particularity." *Id.* at 1498. CEH's TAC does not allege fraud, and the issue of impossibility is an affirmative defense, not an element of CEH's Proposition 65 claim.

[2] California law recognizes a limited exception where complaint allegations "***clearly and affirmatively***" disclose some defense or bar to recovery, but "it is not enough that the complaint shows merely that the action ***may*** be barred." *Czajkowski v. Haskell & White, LLP* (2012) 208 Cal.App.4th 166, 174-75 (emphases added) (evaluating statute of limitations defense). Here, there are no TAC allegations "clearly and affirmatively" establishing an impossibility defense. The mere mention of the FDA's involvement in OTC drug regulation cannot satisfy this standard, especially given the express savings clause for Proposition 65 in the FDCA.

"draw[ing] inferences favorable to the plaintiff, not the defendant." *Perez v. Golden Empire Transit Dist.* (2012) 209 Cal.App.4th 1228, 1239 (citation omitted) (pleading allegations are "liberally construed"). In these regards, California's pleading standards are far less stringent than those demanded in federal court, where a "facial plausibility" standard applies. *E.g., Ashcroft v. Iqbal* (2009) 556 U.S. 662, 678; *see also Faulkner v. ADT Sec. Servs., Inc.* (9th Cir. 2013) 706 F.3d 1017, 1021 (applying different federal standards to removed complaint initially filed in California court). Thus, even after *Iqbal*, California courts continue to hold that "the facts alleged in the pleading are deemed to be true, however improbable they may be." *Hacker v. Homeward Residential, Inc.* (2018) 26 Cal.App.5th 270, 280.

Here, it is undisputed that the TAC (like its earlier iterations) properly pleads all of the elements of CEH's Proposition 65 cause of action. TAC ¶¶1-3, 5-6, 18, 37, 39-42, 46-50. As set forth below, the TAC also goes above and beyond the requirements of California law by alleging facts establishing the plausibility of its allegations that the Products suffered from a labeling deficiency that Sanofi could have corrected using the CBE process.

III. ARGUMENT

A. CEH Has Satisfied State Law Pleading Requirements in Alleging that Sanofi Could Have Provided a Warning Under the FDA's CBE Regulation.

The law regarding impossibility preemption in the context of federally regulated drugs is clear: the manufacturer bears the heavy burden of presenting "clear evidence" that the FDA would have rejected the specific warning that the plaintiff alleged was required. *Levine*, 555 U.S. at 571-73; *In re Avandia Mktg., Sales & Prods. Liab. Litig.* (3d Cir. 2019) 945 F.3d 749, 758-60; *Mason v. SmithKline Beecham Corp.* (7th Cir. 2010) 596 F.3d 387, 391, 395; *In re MDL 2700 Genentech Herceptin Trastuzumab Mktg. & Sales Practice Litig.* (10th Cir. 2020) 960 F.3d 1210, 1228, 1240. Here, Sanofi has presented ***no*** evidence, let alone clear evidence. Instead, Sanofi's opening brief reads as if the onus is on CEH to plead a host of facts demonstrating that the FDA would have accepted a proposed labeling change to add a Proposition 65 warning to the Products. Again, this is not the law in California courts.

The Court's demurrer order ruled that CEH's earlier pleading failed to "allege that [Sanofi]

could use the CBE process to present a Proposition 65 warning." Order at 10:23-24. The Court then granted CEH leave to amend to allege that NDMA presents a "clinically significant hazard" that is causally associated with ranitidine such that Sanofi could have added a Proposition 65 warning using the CBE regulation. *Id.* at 11:16-18. The TAC cures this perceived defect:

> Defendants could have added a clear and reasonable Proposition 65 warning to the label of their Products, or to other materials accompanying their Products, regarding the carcinogenic hazards of NDMA under the FDA's regulation without seeking agency approval. The cancer risk from consuming ranitidine or Products containing NDMA presents a "clinically significant hazard" for which "there is reasonable evidence of a causal association" with these drugs.

TAC ¶28. Thus, even if CEH were required to plead around Sanofi's impossibility defense under California law, it has directly satisfied the Court's mandate by way of its recent amendment.[3]

While clearly not required by California pleading standards, the TAC also includes numerous allegations demonstrating that the risk regarding NDMA is both "clinically significant" and "causally associated" with the Products. As to these factors, the TAC alleges:

- NDMA (and specifically NDMA in the Products at issue) causes cancer (TAC ¶¶18, 20, 22);
- Sanofi's Products contain NDMA at levels that the FDA has found to exceed its own cancer risk thresholds (*id.* ¶¶22, 24);
- The FDA disallowed all U.S. sales of ranitidine ***because of*** this cancer risk – this must be "clinically significant" (in the sense of "therapeutic") since the FDA believes ***no one*** should take the drug until NDMA levels are reduced (*id.* ¶¶24-26, 28); and
- Congress has effectively determined by statute that any risk requiring a Proposition 65 warning (like the one presented by NDMA in Products) is "clinically significant" (*id.* ¶27).

[3] Although the Court's demurrer order purported to recognize that CEH need not plead around Sanofi's preemption defense (Order at 11:23-12:1 (citing *Stowe*, 44 Cal.2d at 422)), it nonetheless found that CEH – ***not*** Sanofi – had the burden to "plead a labeling deficiency that [Defendants] could have corrected using the CBE regulation." (Order at 10:20-22 (citing *Gibbons v. Bristol-Myers Squibb Co.* (2d Cir. 2019) 919 F.3d 699, 708)). The *Gibbons* case, however, was decided under the federal *Iqbal* pleading standard – thus, that court was unwilling to accept the plaintiff's allegations on the existence of "newly acquired information" allowing a CBE label change as "conclusory," "vague," and "not plausibl[e]." 919 F.3d at 708. Since California law flatly disallows this sort of evaluation at the pleading stage, *Gibbons* and cases like it (including all of the federal pleading cases on which Sanofi relies) are inapplicable. *See* Demurrer at 16:28-18:5.

These detailed allegations – which go far beyond the requirement in C.C.P. §425.10(a)(1) to provide "[a] statement of the facts constituting the cause of action, in ordinary and concise language" – amply bear up CEH's averment that Sanofi could have added a Proposition 65 warning through the CBE process without seeking prior FDA approval.

B. Sanofi Has Provided No Evidence Whatsoever, Much Less "Clear Evidence," that the FDA Would Have Rejected Such a Warning.

Sanofi's opening brief is replete with citations to federal cases explaining the meaning of "reasonable evidence" of the link between a drug and a hazard, and the policy dangers of providing a warning based on "speculative or hypothetical risks" that could discourage consumer use of an otherwise beneficial drug. Demurrer at 16:28-18:5. What is conspicuously missing is any factual showing on the one thing that both the U.S. Supreme Court and California appellate courts hold is required to meet the "clear evidence" standard: that Sanofi fully informed the FDA of the cancer risk resented by NDMA in is Products and that the agency told Sanofi that a Proposition 65 warning would not be allowed. *See Albrecht,* 139 S. Ct. at 1672; *Risperdal,* 49 Cal.App.5th at 955-56. This omission is fatal to Sanofi's demurrer.

The federal case law cited by Sanofi does not assist it. Initially, ***all*** of these cases involve federal pleading standards under *Iqbal* requiring "facial plausibility"; here, CEH may simply plead (as it has done) that the CBE changes would have been allowed. *See Del E. Webb,* 123 Cal.App.3d at 604; *Hacker,* 26 Cal.App.5th at 280. Furthermore, as Sanofi's cases establish, "clear evidence" that the FDA would have rejected a labeling change is typically provided in one of two ways: (1) by the FDA's consideration and rejection of the same warning during the drug approval process, *e.g., Silverstein v. Boehringer Ingelheim Pharms., Inc.* (S.D. Fla. Oct. 7, 2020) 2020 U.S. Dist. LEXIS 188176, at *95, *105, *109; or (2) by the FDA's consideration and rejection of the same or a similar warning in response to a citizen petition seeking such a change, *e.g., In re Incretin-Based Therapies Prod. Liab. Litig.* (S.D. Cal. Mar. 9, 2021) 2021 U.S. Dist. LEXIS 44596, at *217-*218. Here, Sanofi has provided no evidence of this sort, and the facts alleged in the TAC demonstrate the contrary.

As to the first point, rather than disclosing information regarding the presence of NDMA in

ranitidine and the cancer risks this entailed during the initial drug approval process for the Products, Sanofi withheld it from the FDA. TAC ¶¶15-16, 23, 39. Accordingly, the agency was unable to consider it and potential warnings regarding this hazard, let alone reject such a warning. Plainly, the submission of evidence regarding NDMA in the Products to the FDA by an independent third-party is one example of "newly acquired information" that had not earlier been considered by the FDA. *Id.* ¶¶22-23. Thus, Sanofi's position here is much weaker than the defendant in *Levine*, where the hazard at issue was at least disclosed to FDA at the time of approval. 555 U.S. at 572-73. Nevertheless, the Court there rejected impossibility preemption.

As to the second point, the FDA has never stated (in response to a citizen petition or in any other context) that it would not permit Sanofi or others from adding a Proposition 65 warning regarding NDMA to ranitidine products under the CBE regulation. TAC ¶¶28, 31. In fact, the FDA did receive a citizen petition from an accredited laboratory that found high levels of NDMA in ranitidine, including Sanofi's Products. *Id.* ¶¶22-23. However, rather than rejecting a request to include a cancer warning for the Products, that petition led to the FDA's request for a market withdrawal. *Cf. Koho v. Forest Labs., Inc.* (W.D. Wash. 2014) 17 F.Supp.3d 1109, 1117 (CBE change would have been allowed despite earlier ***rejection*** of citizen petitions seeking warning).

While it is not CEH's burden to allege or prove that the FDA would have permitted warnings, the record here amply establishes that the FDA agrees that the NDMA levels found in Sanofi's Products are entirely unacceptable due to the cancer risk they present. *E.g.*, TAC ¶¶24-25. Requiring the market withdrawal of a product due to such a risk is far more severe than simply allowing a warning for this risk. Against this backdrop, it is bizarre for Sanofi to claim that the FDA would have required "statistically significant" studies on the cancer risks presented by NDMA (a substance that has only one function: causing cancer in lab animals) in Products before it would allow a warning under the CBE provision. Demurrer at 17:3-6, 18:21-25. It is telling that the FDA did not require such studies prior to halting all sales of the Products.

Likewise, it is odd for Sanofi to fret about "discourage[ing] appropriate use of a beneficial drug" by overwarning when the FDA has already determined that Sanofi's Products should not be ingested by consumers so long as they continue to contain high levels of NDMA. Demurrer at

17:21-23. This contrast starkly with the situation in *Dowhal*, which is the ***only*** published opinion to ever find any application of Proposition 65 to be preempted by federal drug law. There, the FDA had found (in response to a citizen petition) that a reproductive warning for nicotine – a Proposition 65-listed reproductive toxicant – on smoking-cessation patches would conflict with the federal policy of discouraging smoking. *See* 32 Cal.4th at 919-22. That case presented a rare "lesser of two evils" situation: where exposure to toxicants would occur either via smoking or by a nicotine patch designed to assist in smoking cessation, the FDA determined that the latter was preferable to the former. *See id.* at 922; *compare* TAC ¶20 (safer OTC alternatives to ranitidine exist). As the California Supreme Court observed, "in most cases FDA warnings and Proposition 65 warnings would serve the same purpose – informing the consumer of the risks involved in use of the product – and differences in wording would not call for federal preemption." 32 Cal.4th at 934. Here, the FDA has made no determination that the risk of heartburn outweighs the cancer risks associated with the Products. Instead, it has determined the exact opposite.

The judicially noticed materials supplied by Sanofi also do not support its position. Sanofi's demurrer presents a classic "strawman" argument: it claims that CEH's CBE allegations are based on the September 2019 citizen petition to the FDA and "selective references" to FDA press releases between September 2019 and April 2020 on NDMA and ranitidine. Demurrer at 16:24-27. Actually, CEH's CBE allegations are based on (1) the fact that Sanofi knew at all relevant times that its Products contained high levels of NDMA, and (2) the FDA would have deemed these levels to be unacceptable at any time (including now) and has never rejected a cancer warning. It is Sanofi that cherry-picks agency statements from September 2019 that "[t]he FDA is not calling for individuals to stop taking ranitidine," *i.e.*, ***before*** the agency had determined the true scope of the problem (*id.* at 19:2), and that the FDA "didn't observe unacceptable levels of NDMA in many of the samples … tested" (*id.* at 19:19-21). This is disingenuous, since Sanofi knows perfectly well that the FDA ***did*** find unacceptable levels of NDMA exceeding the agency's cancer risk thresholds in ***Sanofi's*** Products in November 2019, and thereafter ***did*** call for individuals to stop taking ranitidine based on this risk in April 2020. TAC ¶¶24-25; *see also* Declaration of Sean Newland ("Newland Decl."), Exh. B, at 2-3; *id.*, Exh. C, at 1-2.

Similarly, the more recent 2021 FDA report cited by Sanofi does not show "clear evidence" that the agency would have rejected a labeling change. Demurrer at 20:2-12.[4] Sanofi creatively quotes this document for the proposition that prior testing "had detected falsely high levels of NDMA in ranitidine drug products" (*id.* at 20:8-10), but fails to disclose the further statement in that report that, after the FDA had done its own testing, "these lower amounts of NDMA were still above the FDA-acceptable level, corresponding to a daily intake limit of 96 [nanograms ("ng")] NMDA per day, in many of the ranitidine lots tested." Newland Decl., Exh. E, at 1; *see also id.*, Exh. B, at 2-3 (FDA testing shows that NDMA levels in some of Sanofi's own Products exceed 96 ng NMDA per day).[5] Furthermore, these "lower" NDMA levels understate the actual levels to which consumers were exposed, since (as the FDA found in requesting market withdrawal) "the amounts of NDMA in ranitidine samples could increase over time." *Id.*, Exh. E, at 1; *see also id.*, Exh. C, at 2; TAC ¶¶16-17. The FDA's further finding that there is no significant additional formation of NDMA in the human body ***after ingestion*** – while surely good news from a public health perspective – does not remotely suggest that the FDA believes the Products to be safe now. *See, e.g.*, Newland Decl., Exh. E, at 3 ("FDA may consider allowing ranitidine products back on the market ***if*** they are proven to be stable, with ***low, acceptable amounts of NDMA*** that ***do not increase over time*** during storage.") (emphases added). The proof is in the pudding: the Products may not be sold even today because of the cancer risk that the FDA believes they pose. Thus, Sanofi has not met its burden of showing "clear evidence" that a Proposition 65 warning regarding the NDMA cancer risk would have been rejected.

C. A Proposition 65 Warning for Sanofi's Products Would Not Violate Any FDA Regulations on OTC Drugs.

Sanofi claims that, as a general matter, Proposition 65 warnings conflict with FDA regulations because such warnings "require disclosure of the mere presence of a potentially carcinogenic substance without regard to drug risks and benefits, or whether that substance causes

[4] Sanofi faults CEH for not citing this report in the TAC (Demurrer at 9:7-10), but overlooks that the TAC was filed on June 4, 2021, *i.e.*, 28 days ***before*** the FDA issued its report on July 2, 2021.

[5] The FDA's 96 ng/day level is based on a 1-in-100,000 likelihood of developing cancer based on exposure to NDMA over a 70-year period. *See* Newland Decl., Exh. E, at 2. This is the ***same*** as the risk threshold requiring a Proposition 65 cancer warning. TAC ¶13.

harm." Demurrer at 21:11-12 (citing 21 C.F.R. §201.66). Yet, Congress has determined the opposite. When it passed the express savings clause exempting Proposition 65 from OTC national uniformity requirements, Congress determined that Proposition 65 warnings do not need to comply with regulatory provisions demanding consistency in drug labeling, such as 21 C.F.R. §201.66. Sanofi is likely to argue that implied impossibility preemption may arise even despite the express terms of 21 U.S.C. §379r(d)(2). *See, e.g.*, *Dowhal*, 32 Cal.4th at 923-26. But if Sanofi is right that 21 C.F.R. §201.66 categorically disallows any Proposition 65 warning on a label, then there could ***never*** be such a warning on an OTC drug label. And since Sanofi further claims that "federal law broadly defines 'labeling' [to include advertising and other means of off-label communications] and requires consistency with FDA approved labeling" (Demurrer at 16:9-11), there could ***never*** be any other type of Proposition 65 warning regarding an OTC drug either. This would render 21 U.S.C. §379r(d)(2) a nullity, while allowing an agency regulation forbidding certain conduct to trump a federal statute condoning that conduct. Suffice it to say, this is not how implied preemption – or rulemaking generally – works. *See Albrecht*, 139 S. Ct. at 1679 ("[A]n agency literally has no power to act, let alone pre-empt the validly enacted legislation of a sovereign State, unless and until Congress confers power upon it.").

Even if 21 C.F.R. §201.66 governs warnings on OTC drug labels despite the express statutory exemption for Proposition 65, a cancer warning for NDMA would not run afoul of this regulation. In the first place, 21 C.F.R. §201.66 only governs the content of the familiar "Drug Facts" section of OTC drug labels; nothing in the regulation precludes additional information elsewhere on the label or in associated labeling materials. Indeed, Defendants take advantage of this by including "additional statements that are not contemplated by the FDA's regulations – such as 'tips' for reducing heartburn symptoms or statements about drug safety – on the drug's label, packaging, or inserted pamphlets, without objection from the FDA." TAC ¶30. If Sanofi were right, these statements would have been disallowed as contrary to 21 C.F.R. §201.66. Sanofi further claims that a Proposition 65 warning "is incompatible with the specific, therapeutic, clinically focused information about the entire drug, not constituents, FDA permits on OTC labels." Demurrer at 21:12-14. Of course, cancer ***is*** a "clinical" risk that the FDA believes to

impact decisions about whether to take ranitidine, and a Proposition 65 warning generally states that the entire drug can exposure the user to a chemical known to cause cancer. For this reason, "[m]any OTC drugs regulated by the FDA contain Proposition 65 warnings on their labels." TAC ¶29. In fact, this Court earlier approved a Consent Judgment in another CEH Proposition 65 enforcement action requiring a leading manufacturer of antiseptic skin cleansers (an FDA-regulated OTC drug product) to provide cancer warnings for cocamide DEA (a known carcinogen) right on the product's label. *See* Declaration of Mark N. Todzo, Exh. 1 ¶3.1. Again, if Sanofi were right in its interpretation of 21 C.F.R. §201.66, this should not be possible.

As Sanofi also notes, 21 C.F.R. §201.66 contains certain restrictions on the formatting of OTC drug warnings, which Sanofi claims to be inconsistent with Proposition 65's "safe harbor" warnings. Demurrer at 21:17-21. But Sanofi ignores that safe harbor warnings are not mandatory, *i.e.*, an entity is free to provide other warnings so long as they satisfy Proposition 65. *See Dowhal*, 32 Cal.4th at 918 (safe harbor warnings are "optional").[6] Moreover, the Proposition 65 regulation requiring a "prominent" or "conspicuous" display does not mean that such warnings must dilute or obscure other warnings (Demurrer at 21:21-22:2) – it just ensures that the Proposition 65 warning will actually be seen and apprehended by the product's user. Nor does it mean that a Proposition 65 warning needs to be contained within the "Drug Facts" box on a label. And, one can warn through non-label means that use completely different formatting without running afoul of 21 C.F.R. §201.66. For these various reasons, 21 C.F.R. §201.66 presents no impediment to providing Proposition 65 warnings regarding NDMA in the Products.

Moreover, neither 21 C.F.R. §201.66 nor any other FDA regulation preclude the provision of warnings by advertising. *See* Health & Safety Code §25249.11(f) (Proposition 65 warnings may be communicated by "general methods" such as advertising). Unlike prescription drugs,

[6] To the contrary, Sanofi cites *National Ass'n of Wheat Growers v. Becerra* (E.D. Cal. 2020) 468 F.Supp.3d 1247, 1261. Demurrer at 15:12-15. As an initial matter, a federal trial court cannot overrule the California Supreme Court on the proper interpretation of California law. Secondly, the holding in *Wheat Growers* was limited to its facts: there, the California Attorney General could identify no warning that would comply with Proposition 65 as to glyphosate only because there was significant scientific doubt as to whether glyphosate, in fact, causes cancer. *See id.* at 1261-63. Such doubt is wholly absent from the present dispute as to NDMA.

OTC drug advertising is not subject to FDA regulation at all. *See Mylan Pharms., Inc. v. Procter & Gamble Co.* (S.D.N.Y. 2006) 443 F.Supp.2d 453, 460; *Terry v. McNeil-PPC, Inc.* (E.D. Pa. Nov. 13, 2015) 2015 U.S. Dist. LEXIS 153970, at *8; *see also* Order at 13:16 (same). Contrary to Sanofi's assertion (Demurrer at 16:5-7), drug advertising does not become "labeling" under 21 U.S.C. §321(m) whenever it contains a warning.[7] Rather, the FDCA expressly distinguishes "advertisements" from "labeling," and nowhere states that any and all warning statements are "labeling." 21 U.S.C. §352(n); *see also* 21 U.S.C. §321(m) & (n) (defining "labeling" but also referring to "labeling or advertising" as separate concepts). Thus, "[a]dvertisers of OTC drugs are not limited to using FDA-approved labeling language when advertising an OTC drug for an FDA-approved purpose." *See Terry*, 2015 U.S. Dist. LEXIS 153970, at *8. Likewise, compelled statements in advertising do not transform such advertising into FDA-regulated "labeling." For instance, the FDCA's provision on misbranded drugs affirmatively compels prescription drug advertisements to include warnings (relating to "side effects" and "contraindications"), but specifies that this is ***not*** "labeling." 21 U.S.C. §352(n) ("This paragraph (n) shall not be applicable to any printed matter which the Secretary determines to be labeling as defined in [21 U.S.C. §321(m)]."). Thus, Sanofi could have provided a Proposition 65 warning regarding NDMA by way of Product advertising.[8]

In its earlier demurrer ruling, the Court found that "although the FDCA might not prevent the defendants from voluntarily putting Proposition 65 warnings in advertisements for the Products, the FDCA's regulation of warnings on labels and in labelling means that 'federal law governs warning in a manner that preempts state authority.'" Order at 23:12-15 (citing Health & Safety Code §25249.10(a)). The Court then extrapolated its determination that a ***label*** warning is preempted to encompass ***all*** forms of warning, based on its novel interpretation of Section 10(a).

[7] Sanofi quotes 21 U.S.C. §321(m) as defining the word "labeling" to expressly include the term "advertising." Demurrer at 16:6. Sanofi is wrong, as this provision does not mention advertising.

[8] Tellingly, in October 2019, Sanofi voluntarily issued a press release on the FDA's public website stating that the Products "may contain NDMA," which Sanofi described as "a probable human carcinogen," without prior FDA approval or subsequent FDA censure. TAC ¶32; *see also* Newland Decl., Exh. D, at 1-2. This is not to say that these representations satisfied Proposition 65 (which is doubtful, given the cagey language used by Sanofi so as to downplay the risks), but it does show that Sanofi can widely publicize this issue without hazarding FDA enforcement.

Order at 5:22-7:18. The Court's opinion is the first ever to suggest that Proposition 65 contains a "self-exception" that demands preemption even where compliance with Proposition 65 could be secured by methods other than warning (such as reformulating the product), or where only some methods of warning are federally preempted. To the contrary, every published case discussing Section 10(a) performs the usual constitutional analysis on preemption (requiring "physical impossibility"), without once indicating that Proposition 65 itself has in any way altered that analysis.[9] *See, e.g.*, *Stratton*, 92 F.3d at 810; *Physicians Comm. for Responsible Med. v. McDonald's Corp.* (2010) 187 Cal.App.4th 554, 565-66. The Court's conclusion is not required by the language of the statute (which is at best ambiguous), subverts the intent of the voters who enacted Proposition 65 by referendum, and runs contrary to the principle that Proposition 65 should be read "broadly" to achieve its "protective purpose." *People ex rel. Lungren v. Sup. Ct.* (1996) 14 Cal.4th 298, 314.

In any event, the TAC now includes allegations that were not before the Court earlier that would yield a different result. The first is that Sanofi earlier advertised its Products (thereby reaping substantial profits through the "incredible popularity" of Zantac) without disclosing the link between ranitidine and NDMA to the public or the FDA. TAC ¶¶21, 23. Since this advertising campaign was entirely voluntarily, Sanofi could have voluntarily included a Proposition 65 warning on NDMA without violating any federal law. The second is that Sanofi has made "safety" claims on Product labeling without disclosing the fact that the Products contain a known carcinogen. *Id.* ¶30. The Court's demurrer order noted that the "affirmative disclosure of information" can be "a remedy for previous consumer deception" (citing *Consumers Union of U.S., Inc. v. Alta- Dena Certified Dairy* (1992) 4 Cal.App.4th 963), but distinguished *Alta-Dena* by claiming that the court there used the term "warning" rather than "advertising" to refer to this

[9] This includes one of the principal cases on which the Court's demurrer order relied. *See American Meat Inst. v. Leeman* (2009) 180 Cal.App.4th 728, 735 n.2, 749-61 (even where Proposition 65 label warnings were concededly preempted, court analyzes whether shelf-tag warnings would also be preempted). If the Court's interpretation of Section 10(a) were correct, the *Leeman* court, as well as the appellate court in *Allenby* (958 F.2d at 945-47), would have stopped their inquiries after finding that warnings on product labels were precluded by federal law. *See also People ex rel. Lungren v. Cotter & Co.* (1997) 53 Cal.App.4th 1373, 1384-96 (same).

remedy. Order at 21:19-23 (citing 4 Cal.App.4th at 974-75 & n.6). This is not accurate: the *Alta-Dena* court squarely referred to the future corrective "warning" mandate as "advertising." *E.g.*, 4 Cal.App.4th at 971, 973. Accordingly, courts routinely hold that corrective advertising may be ordered to counteract false or misleading claims made as to FDA-regulated OTC drugs, even where the FDA has made certain findings supporting the earlier claims. *E.g.*, *Warner-Lambert Co. v. FTC* (D.C. Cir. 1977) 562 F.2d 749 (advertising required to rectify earlier marketing statements that Listerine prevents colds and sore throats). CEH is in a far better position here, where the FDA has never stated that it deems the present levels of NDMA in the Products to be safe. And, there is surely no good policy reason to allow Sanofi to affirmatively misrepresent the safety of its Products but not to demand that it take reasonable steps to correct these statements.

Lastly, Sanofi can also provide warnings through its own wholesale customers, such as retailers. Indeed, the TAC alleges that Sanofi already does this on other FDA-regulated OTC drug products it makes and sells. TAC ¶29. Sanofi protests that "[n]one of those allegations suggest ***Defendants*** put Proposition 65 warnings on any OTC product" (Demurrer at 20:17-18) (emphasis in original), but that is surely the inference here (especially since a third-party retailer would not know as readily as Sanofi that a certain drug contained a listed chemical). *See Perez*, 209 Cal.App.4th at 1239 (complaint to be construed in favor of plaintiff).[10] This is simply not a ***pleading*** defect, since CEH has otherwise adequately satisfied California law by properly alleging its Proposition 65 claim, and since Sanofi has made no adequate showing that a Proposition 65 warning would have been disallowed under the CBE process.

IV. CONCLUSION

Because Sanofi has failed to carry its burden of demonstrating federal impossibility preemption by "clear evidence," its demurrer should be overruled. However, should the Court nonetheless be inclined to grant the demurrer, the resultant dismissal should be without prejudice so that CEH may conduct discovery in furtherance of again amending its allegations.

[10] Sanofi also criticizes CEH for "offer[ing] no examples" of such warnings (Demurrer at 20:19), but overlooks that this is not CEH's job at the pleading stage since its allegations are deemed true.

DATED: August 20, 2021

LEXINGTON LAW GROUP

Mark N. Todzo
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Exhibit 54

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

Case No. RG 20-054985

ASSIGNED FOR ALL PURPOSES TO:
Hon. Evelio Grillo, Department 21

DECLARATION OF MARK N. TODZO IN SUPPORT OF PLAINTIFF'S OPPOSITION TO DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S DEMURRER TO THIRD AMENDED COMPLAINT

Date: September 15, 2021
Time: 10:00 a.m.
Reservation Nos.: R-2277974, R-2277975

TAC Filed: June 9, 2021
Trial Date: None Set

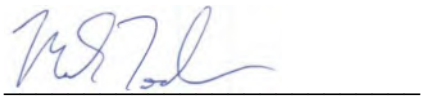
[Filed concurrently with Plaintiff's Opposition to Demurrer; Request for Judicial Notice]

I, Mark N. Todzo, declare as follows:

1. I am a partner with the Lexington Law Group ("LLG") and I represent Plaintiff Center for Environmental Health ("CEH") in this action. I have personal knowledge of the matters set forth below and, if called upon, I could and would competently testify thereto.

2. Attached hereto as Exhibit 1 is a true and correct copy of the Consent Judgment between CEH and Xttrium Laboratories, Inc. in the Proposition 65 enforcement action captioned as *Center for Environmental Health v. Xttrium Laboratories, Inc., et al.*, Alameda Sup. Ct. Case No. RG 19-011555 (entered July 25, 2019).

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct. Executed on August 20, 2021 in San Francisco, California.



Mark N. Todzo

Exhibit 1

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation, Plaintiff, v. XTTRIUM LABORATORIES, INC., *et al.*, Defendant.	Case No. RG19011555 **[PROPOSED] CONSENT JUDGMENT AS TO XTTRIUM LABORATORIES, INC.**

1. INTRODUCTION

1.1 The parties to this Consent Judgment are the Plaintiff Center for Environmental Health ("CEH") and Defendant Xttrium Laboratories, Inc. ("Xttrium") ("Settling Defendant"). CEH and Settling Defendant are referred to collectively as the "Parties."

1.2 Settling Defendant is a corporation that employs ten (10) or more persons and manufactures, distributes, and/or sells antiseptic skin cleansers that contain coconut oil diethanolamine condensate (cocamide diethanolamine) (hereinafter, "cocamide DEA") in the State of California or has done so in the past.

1.3 On May 25, 2018, CEH sent a 60-Day Notice of Violation under Proposition 65 (the Safe Drinking Water and Toxic Enforcement Act of 1986, California Health & Safety Code §§ 25249.5, *et seq.*) to Settling Defendant, the California Attorney General, the District Attorneys of every County in the State of California, and the City Attorneys for every City in the State of California with a population greater than 750,000 (the "Notice"). The Notice alleges violations of Proposition 65 with respect to cocamide DEA in antiseptic skin cleansers manufactured, distributed and/or sold by Settling Defendant and Cardinal Health, Inc., The Harvard Drug Group, LLC, CVS Pharmacy, Inc., McKesson Corporation and Rite Aid Corporation.

1.4 On March 19, 2019, CEH filed the action entitled *CEH v. Xttrium Laboratories, Inc.*, Case No. RG19011555 naming Settling Defendant as a defendant.

1.5 Xttrium manufactures each of the Covered Products. Xttrium has explored the possibility of reformulating its antiseptic skin cleansers to remove cocamide DEA as an ingredient. However, Xttrium asserts that doing so would require submitting the Covered Products to a lengthy and expensive approval process with the United States Food & Drug Administration. Moreover, based on Xttrium's research, such reformulation would ultimately result in a less effective product. Xttrium has been providing a Proposition 65 warning for the Covered Products for many years, although the warning was set forth on the interior of a peel-back label, which CEH contends is not clear and reasonable.

1.6 For purposes of this Consent Judgment only, the Parties stipulate that: (i) this Court has jurisdiction over the allegations of violations contained in the Complaint and personal jurisdiction over Settling Defendant as to the acts alleged in the Complaint; (ii) that venue is proper in the County of Alameda; and (iii) that this Court has jurisdiction to enter this Consent Judgment.

1.7 Nothing in this Consent Judgment is or shall be construed as an admission by the Parties of any fact, conclusion of law, issue of law or violation of law, nor shall compliance with the Consent Judgment constitute or be construed as an admission by the Parties of any fact, conclusion of law, issue of law, or violation of law, and all such allegations are specifically denied. Nothing in this Consent Judgment shall prejudice, waive or impair any right, remedy, argument or defense the Parties may have in any other legal proceeding. This Consent Judgment is the product of negotiation and compromise and is accepted by the Parties for purposes of settling, compromising and resolving issues disputed in this action.

2. DEFINITIONS

2.1 "Covered Products" means antiseptic skin cleansers containing cocamide DEA manufactured by Xttrium for retail sale.

2.2 "Effective Date" means the date on which this Consent Judgment is entered by the Court.

3. INJUNCTIVE RELIEF

3.1 **Clear and Reasonable Warnings for Covered Products.** For all Covered Products manufactured more than 180 days after the Effective Date, Settling Defendant shall provide a clear and reasonable warning on the outer packaging of each Covered Product that contains Cocamide DEA as an ingredient. The warning shall be prominently placed on the outer label with such conspicuousness as compared with other words, statements and designs on the label so as to render the warning likely to be read and understood by an ordinary individual under customary conditions of purchase and use.

3.2 **Warning Language**: The warning required by Section 3.1 shall be in one of the following two forms:

WARNING

This product can expose you to cocamide DEA, which is known to the State of California to cause cancer. For more information go to www.P65Warnings.ca.gov.

Or

WARNING

This product can expose you to coconut oil diethanolamine condensate, which is known to the State of California to cause cancer. For more information go to www.P65Warnings.ca.gov.

The symbol shall be no smaller than the height of the word "**WARNING**," and may appear above the language or to the left of it. If the label for the product is not printed using the color yellow, the warning symbol may be printed in black and white.

4. ENFORCEMENT

4.1 The Parties may, by motion or application for an order to show cause before the Superior Court of Alameda County, enforce the terms and conditions contained in this Consent Judgment. Prior to bringing any motion or application to enforce the requirements of Section 3 above, CEH shall provide Settling Defendant with a notice setting forth the factual basis for the alleged violation of Section 3. The Parties shall then meet and confer regarding the basis for CEH's anticipated motion or application in an attempt to resolve it informally. Should such attempts at informal resolution fail, CEH may file its enforcement motion or application. This Consent Judgment may only be enforced by the Parties.

5. PAYMENTS

5.1 **Payments by Settling Defendant.** Within five (5) days of the Effective Date, Settling Defendant shall pay the total sum of $65,000 as a settlement payment.

5.2 **Allocation of Payments.** The total Settlement Payment shall be paid in five (5) separate checks in the amounts specified below and delivered as set forth below. Any failure by

Settling Defendant to comply with the payment terms herein shall be subject to a stipulated late fee to be paid by Settling Defendant in the amount of $100 for each day the full payment is not received after the applicable payment due date set forth in Section 5.1. The late fees required under this Section shall be recoverable, together with reasonable attorneys' fees and costs, in an enforcement proceeding brought pursuant to Section 4 of this Consent Judgment. The Settlement Payment paid by Settling Defendant shall be allocated as set forth below between the following categories and made payable as follows:

5.2.1 Settling Defendant shall pay $8,860 as a civil penalty ("Civil Penalty") pursuant to Health & Safety Code §25249.7(b). The Civil Penalty payment shall be apportioned in accordance with Health & Safety Code §25249.12 (25% to CEH and 75% to the State of California's Office of Environmental Health Hazard Assessment ("OEHHA")). Accordingly, Settling Defendant shall pay the OEHHA portion of the Civil Penalty payment for $6,645 by check made payable to OEHHA and associated with taxpayer identification number 68-0284486. This payment shall be delivered as follows:

For United States Postal Service Delivery:

Attn: Mike Gyurics
Fiscal Operations Branch Chief
Office of Environmental Health Hazard Assessment
P.O. Box 4010, MS #19B
Sacramento, CA 95812-4010

For Non-United States Postal Service Delivery:

Attn: Mike Gyurics
Fiscal Operations Branch Chief
Office of Environmental Health Hazard Assessment
1001 I Street, MS #19B
Sacramento, CA 95814

Settling Defendant shall pay the CEH portion of the Civil Penalty payment for $2,215 by check made payable to the Center for Environmental Health and associated with taxpayer identification number 94-3251981. This payment shall be delivered to Lexington Law Group, 503 Divisadero Street, San Francisco, CA 94117.

5.2.2 Settling Defendant shall pay $6,640 as an Additional Settlement Payment

("ASP") to CEH pursuant to Health & Safety Code § 25249.7(b), and California Code of Regulations, Title 11, § 3204. CEH intends to place these funds in CEH's Toxics and Youth Fund and use them to support CEH programs and activities that seek to educate the public about cocamide DEA and other toxic chemicals in consumer products, work with industries to reduce exposure to cocamide DEA and other toxic chemicals, and thereby reduce the public health impacts and risks of exposure to cocamide DEA and other toxic chemicals in consumer products. CEH shall obtain and maintain adequate records to document that ASPs are spent on these activities, and CEH agrees to provide such documentation to the Attorney General within thirty days of any request from the Attorney General. The payment pursuant to this Section shall be made payable to the Center for Environmental Health and associated with taxpayer identification number 94-3251981. This payment shall be delivered to Lexington Law Group, 503 Divisadero Street, San Francisco, CA 94117.

5.2.3 Settling Defendant shall pay $49,500 as a reimbursement of a portion of CEH's reasonable attorneys' fees and costs. The attorneys' fees and cost reimbursement shall be made in two separate checks as follows: (a) $42,000 payable to the Lexington Law Group and associated with taxpayer identification number 94-3317175; and (b) $7,500 payable to the Center For Environmental Health and associated with taxpayer identification number 94-3251981. Both of these payments shall be delivered to Lexington Law Group, 503 Divisadero Street, San Francisco, CA 94117.

5.2.4 To summarize, Settling Defendant shall deliver checks made out to the payees and in the amounts set forth below:

Payee	**Type**	**Amount**	**Deliver To**
OEHHA	Penalty	$6,645	OEHHA per Section 5.2.1
Center For Environmental Health	Penalty	$2,215	LLG
Center For Environmental Health	ASP	$6,640	LLG
Lexington Law Group	Fee and Cost	$42,000	LLG
Center For Environmental Health	Fee and Cost	$7,500	LLG

6. MODIFICATION

6.1 **Written Consent.** This Consent Judgment may be modified from time to time only by: (1) express written agreement of the Parties; or (2) by an order of this Court upon motion and in accordance with law. Any modification to the Consent Judgment requires the approval of the Court and prior notice to the Attorney General's Office.

6.2 **Meet and Confer.** Any Party seeking to modify this Consent Judgment shall notify the other affected Party or Parties in writing, and the affected Parties shall thereafter attempt in good faith to meet and confer concerning the proposed modification. If the affected Parties are unable to resolve their dispute informally within sixty (60) days after the date of the written notification, or such other period as the affected Parties shall agree in writing, the Party that issued the written notification to seek the modification may bring a motion or proceeding to seek judicial relief as to the requested modification.

6.3 **Non-Exclusive Grounds for Modification.** Settling Defendant may move to modify this Consent Judgment to substitute any term that Plaintiff agrees to in a future consent judgment applicable to cocamide DEA in antiseptic skin cleanser products that are manufactured, sold, or distributed for sale in California by any competitor of Defendant, and Plaintiff agrees not to oppose any such motion except for good cause shown. Furthermore, if a court of competent jurisdiction or an agency of the federal government, including but not limited to the U.S. Food and Drug Administration, states through any communication with the force of law, final regulation, or other legally binding act, that federal law has preemptive effect on any of the requirements of this Consent Judgment, including but not limited to precluding Settling Defendant from providing the warning set forth in this Consent Judgment or restricting the manner in which such warnings are given, then Settling Defendant may move to modify this Consent Judgment to bring it into compliance with or avoid conflict with federal law, but the modification shall not be granted unless this Court concludes, in a final judgment or order, that such modification is necessary to bring this Consent Judgment into compliance with or avoid conflict with federal law. Likewise, if Proposition 65 or its implementing regulations are changed

from their terms as they exist on the Effective Date to establish that warnings for cocamide DEA in some or all of the Covered Products are not required, then Setting Defendant may move to modify this Consent Judgment to relieve Settling Defendant of its obligations with respect to such portion of the Covered Products as is appropriate.

7. CLAIMS COVERED AND RELEASED

7.1 Provided that Settling Defendant complies in full with its obligations under Section 5 of this Consent Judgment, this Consent Judgment is a full, final and binding resolution between CEH on behalf of itself and the public interest and Settling Defendant, and its parents, subsidiaries, affiliated entities that are under common ownership and their predecessors, successors and assigns, directors, shareholders, officers, employees, and attorneys ("Defendant Releasees"), and all entities to whom they directly or indirectly provide, distribute, or sell Covered Products, including but not limited to distributors, wholesalers, customers, retailers, franchisees, cooperative members, licensors and licensees, such as Cardinal Health, Inc., The Harvard Drug Group, LLC, CVS Pharmacy, Inc., McKesson Corporation and Rite Aid Corporation (individually or collectively "Downstream Releasees") of any violation or claimed violation of Proposition 65 that was or could have been asserted in the Complaint against Settling Defendant, Defendant Releasees, and Downstream Releasees, based on failure to warn about alleged exposure to cocamide DEA contained in Covered Products that were manufactured, sold, or distributed prior to the Effective Date.

7.2 Provided that Settling Defendant complies in full with its obligations under Section 5 of this Consent Judgment, CEH, for itself, its agents, successors, and assigns, releases, waives, and forever discharges any and all claims against Settling Defendant, Defendant Releasees, and Downstream Releasees arising from any violation of Proposition 65 that have been or could have been asserted by CEH individually or in the public interest regarding the failure to warn about exposure to cocamide DEA arising in connection with Covered Products manufactured, distributed, or sold by Settling Defendant prior to the Effective Date.

7.3 Provided that Settling Defendant complies in full with its obligations under Section 5 of this Consent Judgment, CEH, in its individual capacity only and not in its

representative capacity, also provides a release to Settling Defendant, Defendant Releasees, and Downstream Releasees which shall be effective as a full and final accord and satisfaction, as a bar to all actions, causes of action, obligations, costs, expenses, attorneys' fees, damages, losses, claims, liabilities, and demands of CEH of any nature, character, or kind, whether known or unknown, suspected or unsuspected, arising out of alleged or actual exposures to cocamide DEA in the Covered Products manufactured, distributed, or sold by Settling Defendant prior to the Effective Date.

7.4 Provided that Settling Defendant complies in full with its obligations under Section 5 of this Consent Judgment, compliance with the terms of this Consent Judgment by Settling Defendant and the Defendant Releasees shall constitute compliance with Proposition 65 by Settling Defendant, their Defendant Releasees and their Downstream Releasees with respect to any alleged failure to warn about cocamide DEA in Covered Products manufactured, sold, or distributed after the Effective Date.

7.5 Nothing in this Section 7 affects CEH's right to commence or prosecute an action under Proposition 65 against any person other than Settling Defendant, Defendant Releasees, or Downstream Releasees.

8. NOTICE

8.1 When CEH is entitled to receive any notice under this Consent Judgment, the notice shall be sent by first class and electronic mail to:

Mark Todzo
Lexington Law Group
503 Divisadero Street
San Francisco, CA 94117
mtodzo@lexlawgroup.com

8.2 When Settling Defendant is entitled to receive any notice under this Consent Judgment, the notice shall be sent by first class and electronic mail to:

Trenton H. Norris
Arnold & Porter
Three Embarcadero Center, 10th Floor
San Francisco, CA 94111
Trent.Norris@arnoldporter.com

8.3 Any Party may modify the person and address to whom the notice is to be sent by sending the other Party notice by first class and electronic mail.

9. COURT APPROVAL

9.1 This Consent Judgment shall become effective upon entry by the Court. The Parties acknowledge that, pursuant to California Health and Safety Code section 25249.7(f), a noticed motion is required for judicial approval of this Consent Judgment, which motion CEH shall draft and file and Settling Defendant shall support, appearing at the hearing if so requested. If any third party objection to the motion for approval is filed, CEH and Settling Defendant agree to work together to file a response and appear at any hearing. If such objection is overruled by the Court and then subsequently appealed by the third party, CEH and Settling Defendant agree to work together to file a response and appear at any hearing.

9.2 If the Court does not approve the Consent Judgment, the Parties agree to meet and confer as to whether to modify the language or appeal the ruling. If the Parties do not jointly agree on a course of action to take, then the case shall proceed in its normal course on the Court's trial calendar. If the Court's approval is ultimately overturned by an appellate court following an appeal by a third party, the Parties shall meet and confer as to whether to modify the terms of this Consent Judgment. If the parties do not jointly agree on a course of action to take then the case shall proceed in its normal course on the Court's trial calendar. In the event that this Consent Judgment is entered by the Court and subsequently overturned by any appellate court, then any monies that have been provided to CEH or its counsel under this Consent Judgment shall be refunded within 30 days of the appellate decision becoming final and the Parties shall reasonably cooperate to obtain a timely refund of monies paid to OEHHA under this Consent Judgment.

9.3 If this Consent Judgment is not entered by the Court within one year of the date it is fully executed by the Parties, it shall be of no force or effect and shall never be introduced into evidence or otherwise used in any proceeding for any purpose other than to allow the Court to determine if there was a material breach of Section 9.1.

10. ATTORNEYS' FEES

10.1 The prevailing Party on any motion, application for an order to show cause or other proceeding to enforce a violation of this Consent Judgment, shall be entitled to its reasonable attorneys' fees and costs incurred as a result of such motion or application.

10.2 Except as otherwise provided in this Consent Judgment, each Party shall bear its own attorneys' fees and costs.

11. OTHER TERMS

11.1 The terms of this Consent Judgment shall be governed by the laws of the State of California.

11.2 This Consent Judgment shall apply to and be binding upon CEH and Settling Defendant, and their respective divisions, subdivisions, and subsidiaries, and the successors or assigns of any of them.

11.3 This Consent Judgment contains the sole and entire agreement and understanding of the Parties with respect to the entire subject matter hereof, and any and all prior discussions, negotiations, commitments, or understandings related thereto, if any, are hereby merged herein and therein. There are no warranties, representations, or other agreements between the Parties except as expressly set forth herein. No representations, oral or otherwise, express or implied, other than those specifically referred to in this Consent Judgment have been made by any Party hereto. No other agreements not specifically contained or referenced herein, oral or otherwise, shall be deemed to exist or to bind any of the Parties hereto. No supplementation, modification, waiver, or termination of this Consent Judgment shall be binding unless executed in writing by the Party to be bound thereby. No waiver of any of the provisions of this Consent Judgment shall be deemed or shall constitute a waiver of any of the other provisions hereof whether or not similar, nor shall such waiver constitute a continuing waiver.

11.4 Nothing in this Consent Judgment shall release, or in any way affect any rights that Settling Defendant might have against any other party.

11.5 This Court shall retain jurisdiction of this matter to implement or modify the Consent Judgment.

11.6 The stipulations to this Consent Judgment may be executed in counterparts and by means of facsimile or portable document format (pdf), which taken together shall be deemed to constitute one document.

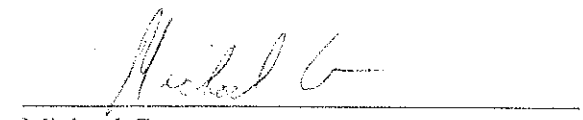
11.7 Each signatory to this Consent Judgment certifies that he or she is fully authorized by the Party he or she represents to stipulate to this Consent Judgment and to enter into and execute the Consent Judgment on behalf of the Party represented and legally to bind that Party.

11.8 CEH agrees to comply with the reporting form requirements referenced in Health and Safety Code section 25249.7(f).

11.9 The Parties, including their counsel, have participated in the preparation of this Consent Judgment and this Consent Judgment is the result of the joint efforts of the Parties. This Consent Judgment was subject to revision and modification by the Parties and has been accepted and approved as to its final form by all Parties and their counsel. Accordingly, any uncertainty or ambiguity existing in this Consent Judgment shall not be interpreted against any Party as a result of the manner of the preparation of this Consent Judgment. Each Party to this Consent Judgment agrees that any statute or rule of construction providing that ambiguities are to be resolved against the drafting Party should not be employed in the interpretation of this Consent Judgment and, in this regard, the Parties hereby waive California Civil Code § 1654.

IT IS SO STIPULATED:

CENTER FOR ENVIRONMENTAL HEALTH



Michael Green
Director

XTTRIUM LABORATORIES, INC.

Signature

Madeleine Creevy
Printed Name

Executive Vice President
Title

IT IS SO ORDERED:

Dated: July 25, 2019

Judge of the Superior Court
NOËL WISE

Exhibit 55

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

Case No. RG 20-054985

ASSIGNED FOR ALL PURPOSES TO:
Hon. Evelio Grillo, Department 21

REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF PLAINTIFF'S OPPOSITION TO DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S DEMURRER TO THIRD AMENDED COMPLAINT

Date: September 15, 2021
Time: 10:00 a.m.
Reservation Nos.: R-2277974, R-2277975

TAC Filed: June 9, 2021
Trial Date: None Set

[Filed concurrently with Plaintiff's Opposition to Demurrer; Declaration of Mark N. Todzo]

TO THE COURT, DEFENDANTS, AND THEIR ATTORNEYS OF RECORD:

Please take notice that, pursuant to California Evidence Code sections 452 and 453, Plaintiff Center for Environmental Health ("CEH") hereby requests that this Court take judicial notice of the following document, which is attached as Exhibit 1 to the accompanying Declaration of Mark. N. Todzo in support of CEH's Opposition to Defendants Sanofi-Aventis U.S. LLC and Chattem, Inc.'s (hereinafter, "Sanofi") Demurrer to CEH's Third Amended Complaint ("TAC") in the above-captioned action: the Consent Judgment between CEH and Xttrium Laboratories, Inc. in the Proposition 65 enforcement action captioned as *Center for Environmental Health v. Xttrium Laboratories, Inc., et al.*, Alameda Sup. Ct. Case No. RG 19-011555 (entered July 25, 2019).

MEMORANDUM OF POINTS AND AUTHORITIES

CEH requests that the Court take judicial notice of Exhibit 1, which is an order of a California court. Official court filings and Court orders are judicially noticeable under Evidence Code §452(d) as records of any court of this state. *See Williams v. Wraxall* (1995) 33 Cal.App.4th 120, 130 n.7. Exhibit 1 is further judicially noticeable under Evidence Code §452(c) as an "official act" of the judicial department of this state. The document is relevant since it supports CEH's allegation that "[m]any OTC drugs regulated by the FDA contain Proposition 65 warnings on their labels." TAC ¶29. It also refutes Sanofi's argument that such warnings are categorically forbidden by 21 C.F.R. §201.66, notwithstanding the express Congressional exemption of Proposition 65 from the Federal Food Drug and Cosmetic Act's provision on "National Uniformity for Nonprescription Drugs." *See* 21 U.S.C. §379r(a) & (d)(2). Accordingly, the Court should take judicial notice of Exhibit 1.

DATED: August 20, 2021

LEXINGTON LAW GROUP

Mark. N. Todzo
Attorneys for Plaintiff
CENTER FOR ENVIRONMENTAL HEALTH

Exhibit 56

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

Case No. RG 20-054985

ASSIGNED FOR ALL PURPOSES TO:
Hon. Evelio Grillo, Department 21

PROOF OF SERVICE RE PLAINTIFF'S OPPOSITION TO DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S DEMURRER TO THIRD AMENDED COMPLAINT

Date: September 15, 2021
Time: 10:00 a.m.
Reservation Nos.: R-2277974, R-2277975

TAC Filed: June 9, 2021
Trial Date: None Set

PROOF OF SERVICE

I, Owen Sutter, declare:

I am a citizen of the United States and employed in the County of San Francisco, State of California. I am over the age of eighteen (18) years and not a party to this action. My business address is 503 Divisadero Street, San Francisco, CA 94117 and my email address is osutter@lexlawgroup.com.

On August 20, 2021 I served the following document(s) on all interested parties in this action by placing a true copy thereof in the manner and at the addresses indicated below:

PLAINTIFF'S OPPOSITION TO DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S DEMURRER TO THIRD AMENDED COMPLAINT

DECLARATION OF MARK N. TODZO IN SUPPORT OF PLAINTIFF'S OPPOSITION TO DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S DEMURRER TO THIRD AMENDED COMPLAINT

REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF PLAINTIFF'S OPPOSITION TO DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S DEMURRER TO THIRD AMENDED COMPLAINT

☐ **BY MAIL**: I am readily familiar with the firm's practice for collecting and processing mail with the United States Postal Service ("USPS"). Under that practice, mail would be deposited with USPS that same day with postage thereon fully prepaid at San Francisco, California in the ordinary course of business. On this date, I placed sealed envelopes containing the above mentioned documents for collection and mailing following my firm's ordinary business practices.

☐ **BY FACSIMILE**: I caused all pages of the document(s) listed above to be transmitted via facsimile to the fax number(s) as indicated and said transmission was reported as complete and without error.

☒ **BY ELECTRONIC MAIL**: I transmitted a PDF version of the document(s) listed above via email to the email address(es) indicated on the attached service list [or noted above] before 5 p.m. on the date executed.

Please see attached service list

☐ **BY PERSONAL DELIVERY**: I placed all pages of the document(s) listed above in a sealed envelope addressed to the party(ies) listed above, and caused such envelope to be delivered by hand to the addressee(s) as indicated.

☐ **BY OVERNIGHT DELIVERY**: I deposited such document(s) in a box or other facility regularly maintained by FedEx, or delivered such document(s) to a courier or driver authorized by FedEx, with delivery fees paid or provided for, and addressed to the person(s) being served below.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed on August 20, 2021 at San Francisco, California.

Owen Sutter

SERVICE LIST
CEH v. Perrigo Company, et al.
RG 20-054985

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

CASE NO. RG20054985

ASSIGNED FOR ALL PURPOSES TO:
Hon. Evelio Grillo, Dept. 21

DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S REPLY IN SUPPORT OF DEMURRER TO THIRD AMENDED COMPLAINT

Date: September 15, 2021
Time: 10:00 a.m.
Dept.: 21
Judge: Hon. Evelio Grillo

Reservation Nos.: R-2277974
R-2277975

TAC Filed: June 9, 2021

I. INTRODUCTION

When the Court granted Defendants Sanofi-Aventis U.S. LLC and Chattem, Inc.'s (together, "Sanofi") demurrer to Plaintiff Center for Environmental Health's ("CEH") second amended complaint, it told CEH what was required to avoid federal preemption. CEH must allege "the NDMA exposure [from taking Zantac] presented a '***clinically significant hazard***' for which there is '***reasonable evidence of a causal association'*** with [Zantac] … and as a result [that Sanofi] could use the CBE process to unilaterally strengthen the warning on the labeling without waiting for FDA approval." Court Order Granting Demurrer ("Order") at 11 (emphasis added).

CEH did not heed that instruction. Instead, CEH's third amended complaint ("TAC") relies on conclusory statements, a reference to discredited third-party assertions, and cherry-picked citations to FDA statements on ranitidine—none of which plausibly constitutes new information showing "reasonable evidence of a causal association" before Zantac was voluntarily withdrawn from the market. CEH's Opposition does not rehabilitate any of the TAC's failings.

First, CEH misstates the law, contravening the Court's instruction in the Order and arguing the burden is on Sanofi to allege "clear evidence" that the FDA would have rejected a Changes Being Effected ("CBE") labeling change. (*See* Opp. at 11:17-26, 13:6-14, 16:1-20.) Not so. Sanofi's "clear evidence" obligation arises only *after* CEH has adequately alleged Sanofi could have used the CBE process. CEH fails this threshold burden, so its "clear evidence" argument is inapplicable.

Second, CEH argues its amended allegations indeed satisfy the Court's instruction (*see* Opp. at 11:27-13:4), but Sanofi's demurrer to the TAC ("Demurrer") has demonstrated their deficiencies: (1) CEH alleges some Zantac contains NDMA above FDA thresholds, but that is not an allegation of a "clinically significant hazard" as numerous courts have defined that term; (2) CEH offers no facts to adequately allege "reasonable evidence" and Sanofi's knowledge of that evidence before Zantac was withdrawn from the market, and "reasonable evidence" after is irrelevant because there was no label to change after the withdrawal; and (3) CEH does not allege a "causal association" between taking *Zantac* (as opposed to NDMA) and an increased risk of a person developing cancer.

Third, CEH fails to show that Sanofi could have simultaneously complied with Proposition 65 and federal OTC labeling regulations. CEH attempts to revive issues this Court resolved in the

Order (*e.g.*, that a warning committed via advertising isn't "labeling" for purposes of the preemption analysis), and then tries several other equally unavailing arguments. *See infra* § II(B). Contrary to the Opposition, federal law expressly governs warnings in and outside the "Drug Facts" panels and the Supremacy Clause does not require Sanofi to gamble on a warning outside Proposition 65's safe harbor warning regulations, which directly conflict with FDA regulations. (*See* Opp. at 17:19-21.)

For the reasons set forth in the Demurrer and in this Reply, CEH's TAC must be dismissed without leave to amend on preemption grounds.

II. ARGUMENT

A. Plaintiff Does Not Plead A "Clinically Significant Hazard" And "Reasonable Evidence Of A Causal Association" Between Taking Zantac And An Increased Risk Of Developing Cancer

CEH raises two arguments against the "clinically significant hazard" section of the demurrer. First, CEH tries to shift its threshold burden to Sanofi. It argues Sanofi did not offer "clear evidence" the FDA would have rejected a Prop 65 NDMA warning added to Zantac through the CBE process. (*See* Opp. at 11:17-26, 13:6-14, 16:1-20.) Second, CEH argues it adequately alleged the CBE process was available to Sanofi. (*See id.* at 11:27-13:4.) Each argument lacks merit.

1. *CEH's "Clear Evidence" Argument Ignores Its Burden (and Failure) to Adequately Allege Sanofi Could Have Accessed the CBE Process.*

This Court's Order required CEH to plead in its TAC a clinically significant hazard for which there is reasonable evidence of a causal association with Zantac. CEH's TAC does not comply with that instruction and instead seeks to shift the burden to Sanofi. CEH is wrong on the law and ignores the TAC's failure to plead what is required.

CEH argues manufacturers must present "'clear evidence' that the FDA would have rejected the specific warning … alleged[ly] … required" to establish preemption. (Opp. at 11:18-19.) That is incorrect. Under *Wyeth* and *Albrecht*,[1] and their progeny, an OTC manufacturer need only offer such "clear evidence" if it is first shown that it could use the CBE process at all. *Gibbons v. Bristol-*

[1] *Wyeth v. Levine*, 555 U.S. 555 (2009), *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668 (2019).

Myers Squibb Co., 919 F.3d 699 (2d Cir. 2019) ("Post-FDA approval preemption analysis proceeds in two stages. First the plaintiff must show that there existed 'newly acquired information' such that the defendants could unilaterally change the label pursuant to the CBE regulation without FDA approval."). Indeed, as *Albrecht* notes, a "manufacturer[] cannot propose a change that is not based on reasonable evidence." 139 S. Ct. at 1679 (citing 21 C.F.R. § 314.70(c)(6)(iii)(A)).

The phrase "clear evidence" appears once in *Wyeth* and only after the Court confirmed that after the risk of a hazard "became apparent, Wyeth had a duty to provide a warning [on the drug] …, and the CBE regulation permitted" warning before FDA approval. *Wyeth*, 555 U.S. at 571. The Court then stated:

> FDA retains authority to reject labeling changes made pursuant to the CBE regulation in its review of the manufacturer's supplemental application, just as it retains such authority in reviewing all supplemental applications. But absent clear evidence that the FDA would not have approved a change to [the] label, we will not conclude that it was impossible for Wyeth to comply with both federal and state requirements. *Id.*

Thus, CEH's heavy reliance on its "clear evidence" argument is misconceived. As the Court found in sustaining Sanofi's Demurrer to the SAC, it is CEH's threshold burden to allege the CBE process was available. (Order at 11:16-19.) That requires alleging newly acquired information of a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with Zantac. *Id*.; *Wyeth*, 555 U.S. at 568-69. CEH has not met its burden, and it is thus irrelevant whether there was "clear evidence" that the FDA would have rejected the Proposition 65 warning CEH seeks.

2. *The TAC Fails to Allege The Ultimate Facts Establishing That Sanofi Could Have Used The CBE Process To Add Warnings to Zantac Products.*

While leaning most heavily on its misconceived "clear evidence" arguments above, CEH also fails to demonstrate that the TAC's allegations accomplish what the Court instructed, *i.e.*, to show a clinically significant hazard for which there is reasonable evidence of a causal association.

CEH cannot meet its pleading burden by stating conclusions. (*See* Opp. at 10, n.1 (suggesting conclusions are sufficient.) Courts considering demurrers treat them "as admitting all material facts properly pleaded, but not contentions, deductions or conclusions of fact or law." *Evans v. City of Berkeley*, 38 Cal. 4th 1, 6 (2006). Accordingly, CEH's argument that ¶ 28 of the TAC satisfies the

Court's instruction to plead a "clinically significant hazard" for which "there is reasonable evidence of a causal association" by simply incanting those words is groundless. (Opp. at 12:1-9.) Rather, as explained above, this Court has articulated what is required here: CEH must plead facts that would establish there was a clinically significant hazard for which there is reasonable evidence of a causal association with Zantac. *See supra*, § I. The TAC does not adequately plead those elements.

Clinically Significant Hazard. CEH contends the TAC pleads a clinically significant hazard by alleging an indeterminant number of Zantac samples contained NDMA at levels above the FDA's "cancer risk thresholds." (*See* Opp. at 12:16-17 (citing TAC, ¶¶ 22, 24).) This approach fails. "A clinically significant hazard is … potentially fatal, serious even if infrequent, or can be prevented through appropriate use of the drug." *Silverstein v. Boehringer Ingelheim Pharms., Inc.*, 2020 WL 6110909, at *8 (S.D. Fla. Oct. 7, 2020).

Numerous courts have rejected merely reciting regulatory standards to establish hazards or harms and, to establish a clinically significant hazard under the CBE regulation, much more is required than just parroting the FDA and Proposition 65 thresholds. Regulatory "thresholds of proof" are insufficient to show causal "links" between "exposure" and "cancer." *Allen v. Pa. Eng'g Corp.*, 102 F.3d 194, 198 (5th Cir. 1996). "[R]egulatory levels generally overestimate potential toxicity levels for nearly all individuals," and thus "the theoretical risks from exposure at the guideline range level is likely to be substantially over-estimated for the large majority of individuals in the population." *McClain v. Metabolife Int'l, Inc*., 401 F.3d 1233, 1249 (11th Cir. 2005) (citation omitted). Regulations do not "establish the dose threshold above which [a] condition[] [is] likely [to] result from [an] exposure." *Williams v. Mosaic Fertilizer, LLC*, 889 F.3d 1239, 1246 (11th Cir. 2018). Courts have rejected that a regulatory threshold is a "danger point" and that "extra levels above [the threshold] are significantly harmful." *Gates v. Rohm & Haas Co.*, 265 F.R.D. 208, 226 (E.D. Pa. 2010), *aff'd*, 655 F.3d 255 (3d Cir. 2011). *Cf. Butler v. Denka Performance Elastomer*, 2020 WL 2747276, at *14 n.21 (E.D. La. May 27, 2020) (plaintiff failed to allege the "harmful level of exposure …, just that any level above the EPA threshold is unsafe").

As a matter of law, CEH's reliance on the FDA's finding that a small subset of the Zantac

samples tested contained NDMA at levels exceeding the FDA's cancer risk threshold does not establish there is a "clinically significant hazard."

***Reasonable Evidence of a Causal Association*.** After incorrectly arguing it can just incant the words of the CBE standard, CEH identifies specific allegations it argues demonstrate reasonable evidence of a causal association. (Opp. at 12:11-22 (citing TAC, ¶¶ 18, 20, 24-28).) The Demurrer describes why those allegations are insufficient (*id.* at 11:26-15:8), but several points warrant note.

First, CEH does not respond to the argument that manufacturers "must have knowledge of the alleged association." *Id.* at 17:15-19 (citing *O'Neal v. Smithkline Beecham Corp.*, 551 F. Supp. 2d 993, 1007 (E.D. Cal. 2008)). This is because the TAC does not plead Sanofi actually knew of an alleged association until September 2019 (*i.e.*, after the citizen petition and the FDA's response) and even that allegation is conclusory and does not suggest knowledge of a clinically significant hazard. TAC, ¶23 ("[D]espite their own knowledge of the contamination, Defendants never informed the FDA of this hazard."). Instead, CEH inappropriately borrows Proposition 65's completely separate "actual or constructive" knowledge standard, alleging (i) Sanofi "kn[e]w or should [have] know[n] that the Products contain NDMA and that individuals who use the Products will be exposed to NDMA," (ii) Sanofi "kn[e]w and intend[ed] that individuals will use the Products, thus exposing them to NDMA," and (iii) Sanofi "likely [has] always known that the Products contain NDMA." *See* TAC, ¶¶ 37-39. But nowhere is it alleged that Sanofi actually knew of a clinically significant hazard for which there is reasonable evidence of a causal association between taking Zantac and an increased risk of cancer. Such knowledge would be necessary for Sanofi to utilize the CBE process.

Second, and relatedly, CEH ignores that of the four events alleged to be reasonable evidence, only two (the September 9, 2019 citizen petition and September 13, 2019 FDA response) occurred *before* Zantac was voluntarily withdrawn from the market on October 18, 2019. (Demurrer at 19:4-5.) Any "evidence" after that date is irrelevant because there was no longer a label to change, and the two September 2019 events are plainly not "reasonable evidence of a causal association." (Demurrer at 8:28-9:13, 12:13-13:2, 13:16-15:8, 18:14-19:2.) Even if that post-withdrawal evidence were relevant, however, it does constitute "reasonable evidence," as the Demurrer explains. *Id.*

Finally, to establish access to the CBE process, CEH must plead a "causal association," but between what cause and effect? CEH focuses on an alleged association between NDMA and cancer. (*See* Opp. at 12:16-17 (*citing* TAC, ¶¶ 18 (Zantac has NDMA, a chemical Proposition 65 categorizes as a known carcinogen, *see id.*, ¶ 14), 20 (not providing a warning "is of particular concern in light of evidence that ingestion of NDMA causes cancer"), 22 (citizen petition "detected high levels of NDMA in ranitidine products")).) But the standard requires a causal association between *Zantac*, the drug—not a constituent chemical alleged to be in the drug—and the hazard. *See Wyeth*, 555 U.S. at 569 (association between Phenergan and gangrene); *Risperdal & Invega Cases*, 49 Cal. App. 5th 942, 957 (2020) (association between risperidone and gyncomastia) (latter cited at Opp. at 9:17-18, 13:13-14). Pleading a causal association between NDMA and cancer, with no account for how users interact with Zantac, fails the requisite standard.

This Court told CEH exactly what the TAC needed to allege in order to avoid preemption. CEH failed to heed the Court's instruction. Its attempt to shift the burden to Sanofi to allege "clear evidence" that the CBE was *not* available is unavailing. The TAC must be dismissed as preempted—and no further leave to amend should be granted to CEH because it has not demonstrated an ability to resolve these pleading failures through amendment.

B. Sanofi Need Not Choose Between an Inadequate Prop 65 Warning Or A Violation Of The Food, Drug, And Cosmetic Act

The Opposition also fails to refute Sanofi's argument that, as a matter of law, it could not comply with both Proposition 65 and federal law. The Opposition admits as much by rehashing arguments about whether OTC manufacturers can be required to circumvent the CBE and FDA approval requirements to provide Proposition 65 warnings. CEH devotes two Opposition pages to arguing that "Sanofi could have provided a Proposition 65 warning regarding NDMA by way of Product advertising" while conceding the Court rejected that position. (*See* Opp. 18:21-20:12.) CEH also tries to relitigate the Court's holding that because "[t]he FDCA approves 'warnings,' for OTC drugs, the Brand Name Manufacturers must use the FDA approved 'warnings,' it is impossible for the Brand Name Manufacturers to deviate from the approved warnings . . . so the H&S 25249.10(a) self-exception applies. Proposition 65 does not apply to exposures in the OTC drugs." (*See* Order at

14:1-5.) Those issues are decided.

What new arguments CEH does make (*e.g.*, that OTC manufacturers can unilaterally put unapproved and non-therapeutic warnings outside of the "Drug Facts") are readily refuted by reference to the facts and regulations. Sanofi could not have complied with federal *and* state law under the facts alleged here without inviting additional litigation and liability.

1. *CEH's Incorrectly Interprets Federal Law To Permit Unapproved Warnings Outside Of "Drug Facts."*

This Court has already held that the "FDCA's exclusion of Proposition 65 from the FDCA's express preemption clause does not exempt Proposition 65 from implied preemption," (Order at 7:1-2,) but CEH's Opposition ignores that determination. Contrary to the Opposition's argument, applying impossibility preemption here does not "nullify" 21 U.S.C. §379r(d)(2). (Opp. at 17:11-13.) Monograph OTCs, for example, are subject to less stringent requirements. *See* 21 C.F.R. § 330.1 (certain OTCs considered "generally recognized as safe and effective" and not misbranded if labeled in accordance with an "applicable monograph").

CEH also wrongly argues that federal labeling regulations are limited to the "Drug Facts" panel on OTC drugs, so a Proposition 65 warning, which state law conveniently does not expressly require in "Drug Facts," need not conflict with § 201.66. (*See* Opp. at 17:18-28.) To the contrary, § 201.66 requires, among other formatting requirements (*see, e.g.*, § 201.66(d)), placement of *all warnings* within the "Drug Facts" panel. § 201.66(c)(5)(viii) (indicating location of "[a]ny required warnings in an applicable OTC drug monograph, other OTC drug regulations, or approved drug application that do not fit within one of the [specified warning] categories"). The only categorical exception not requiring FDA approval is for products subject to other regulations or monographs, *see* § 201.66(a), which Zantac is not. *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 620 (2011).

Additionally, a drug marketed with a new, modified, or otherwise unapproved labeling must satisfy *both* § 201.66 and § 314.70, *i.e.*, even if federal law permits an additional warning as a "change being effected," the change must also conform to § 201.66. *See* 21 U.S.C. §§ 321, 355. Like § 201.66, with exceptions not relevant here, the CBE regulation does not provide carte blanche to add "additional statements" to OTC labeling. (Opp. at 17:22.) It only permits unilateral changes

to add or strengthen a *warning* for a hazard for which there is reasonable evidence of a casual association with the drug. 21 C.F.R. § 314.70(c)(6)(iii)(A). Neither § 314.70 nor § 201.66 creates an exception to the other, yet both are incompatible with a Proposition 65 warning for NDMA. *Id*.

To use the example the Opposition provides at 17:23, that "heartburn tips" appear on Zantac labels, therefore proves nothing except that the FDA must have approved them as part of the labeling for Zantac, which it did. *See* Declaration of Sperla In Support Of Demurrer to Second Amended Complaint, ¶¶ 4-7, Exhs. A-D (copies of approved Zantac labeling). Sanofi cannot remove or modify that content without FDA approval, nor could it add information to labeling under the CBE, regardless of whether compliant with § 201.66. "A Proposition 65 warning is a warning," Order at 13:21, but new heartburn tips are not. For the same reason, neither is Sanofi's press release announcing a voluntary withdrawal. (Opp. at 19 n.8, 20:14-16.) However, unlike a Proposition 65 warning for NDMA, heartburn information is compliant with § 201.66 and was approved by the FDA because it provides therapeutic information to Zantac users. *See* II.B.2, *infra*.

Additionally, CEH's reference to its own vague allegation of a past advertising campaign similarly conflates information outside of § 201.66's purview with product warnings within that purview (and which must be either FDA approved or permitted by the CBE regulation). As this Court explained, "[a] Proposition 65 warning on a 'label' (21 U.S.C. 321(k)) does not become less of a warning if it is on "labelling" (21 U.S.C. 321(m)) and does not cease to be a warning when it is in 'advertising.'" (Order at 13:21:23.) Sanofi has never been permitted to circumvent federal regulations either by avoiding the "Drug Facts" box or by communicating via different media, *e.g.*, radio advertising, or in different circumstances, *e.g.*, "through . . . wholesalers." *See Mensing*, 564 U.S. at 615 (holding "[a] Dear Doctor letter that contained substantial new warning information would not be consistent with the drug's approved labeling").

Finally, CEH cites cases interpreting laws that, unlike Proposition 65, have no self-exception like Health & Safety § 25249.10(a) and hold a disclosure can be *court-ordered* to correct misleading claims. (Opp. at 21:1-7.) This offers no support to suggest that Sanofi could have, inconsistent with its NDA, engaged in such conduct itself. *See* Order at 14:1-5 ("preemption . . . ends the analysis.").

2. *CEH's Conflates A Proposition 65 Warning for NDMA With A Therapeutic Product Warning Contemplated By Federal Regulations*

CEH concedes federal regulations only permit therapeutic, clinically focused information about entire drugs, not constituents, on OTC labels, but argues a Proposition 65 warning qualifies as such. (Opp. at 17:26-28 (quoting Demurrer at 21:12-14).) Not so. A Proposition 65 warning "for NDMA" is entirely distinct from a warning for Zantac. Missing from CEH's pleadings and from Proposition 65 requirements is any link between the presence of NDMA in Zantac and a risk of cancer associated with the use of Zantac. Proposition 65 addresses *only* the former. Federal law *requires* the latter. *See* 21 C.F.R. §§ 201.66, 314.70.

However communicated, in whatever medium (and regardless of what may or may not be in third-party consent judgments),[2] a Proposition 65 warning does not convey taking Zantac presents a "clinical risk" of anything, including a "clinical risk" of cancer, just an "exposure … to a chemical" determined by the State of California to cause cancer.[3] This satisfies neither § 201.66 nor § 314.70.

3. *The Constitution Does Not Require Sanofi To Gamble on A Non-Safe Harbor Warning To Save State Law From Preemption*

CEH has had three chances to identify the warning Sanofi could have given to comply with federal and state law. Despite continued assurances that such a warning has always been available to Sanofi, CEH has never described it. This is deliberate. CEH knows that, to avoid § 201.66(d)(7)'s incompatibility with Proposition 65's safe harbor warning, it must concoct a Proposition 65 warning that somehow meets that statute's "clear and reasonable" standard *without* complying with the statute's highly specific safe harbor provisions. 27 C.C.R. §§ 25601 *et seq.*

In similar contexts, Courts have been very clear—the safe harbor provisions are not optional in any practical sense and a plaintiff cannot argue a defendant should steer around them to avoid constitutional limits to Proposition 65. In assessing constitutional issues, a product manufacturer's

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[2] CEH's reference to alleged state consent judgements adopted by different courts under unknown circumstances (Opp. at 18:4-7) is unavailing. This Court cannot order Zantac to violate federal law because CEH alleges a court-approved settlement agreement somewhere in California at some time in the past 35 years did so.

[3] See discussion at I.A.2, *supra*.

only real option is to use the regulatorily approved safe harbor warning. *Nat'l Ass'n of Wheat Growers v. Becerra*, 468 F. Supp. 3d 1247, 1261 (E.D. Cal. 2020) (in First Amendment challenge, rejecting enforcer's "attempts to salvage the Proposition 65 warning by noting that the statute only requires 'clear and reasonable' warnings, not the particular language of the safe harbor warning").

Mensing requires a real possibility of compliance with state and federal law, not just "conjecture." *Mensing*, 564 U.S. at 621. In broadly alleging Sanofi could have offered "a cancer warning for NDMA," but ignoring that any warning short of the safe harbor would expose Sanofi to liability, CEH fails this standard. Sanofi must be able to comply with federal law *and* state law, not federal law and *maybe* state law, through a non-specified radio ad or something of the sort. *Mensing*, 564 U.S. at 621. The TAC does not, and cannot, allege such an option.

III. CONCLUSION

The Court told CEH what it needed to do to avoid federal preemption: plead facts showing a clinically significant hazard for which there is reasonable evidence of a causal association with Zantac. Instead, CEH stated conclusions and inadequate diversions. The Court also instructed that a "Proposition 65 warning is a 'warning' within the definition of the FDCA definition of 'warning,'" (Order at 13:24-25,) but CEH chose to ignore that and again erroneously asserted that Sanofi could do under state law what federal law prohibited. For these reasons and those above, Sanofi requests that its Demurrer be sustained without leave to amend.

Dated: September 3, 2021

DLA PIPER LLP (US)

By: _____

George J. Gigounas
Gregory G. Sperla
Sean A. Newland
Attorneys for Defendants
CHATTEM, INC. and SANOFI-AVENTIS U.S. LLC

Exhibit 58

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

CASE NO. RG20054985

ASSIGNED FOR ALL PURPOSES TO:
Hon. Evelio Grillo, Dept. 21

DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S RESPONSE AND OBJECTIONS TO PLAINTIFF'S REQUEST FOR JUDICIAL NOTICE SUBMITTED IN SUPPORT OF OPPOSITION TO DEFENDANTS' DEMURRER TO THIRD AMENDED COMPLAINT

Date: September 15, 2021
Time: 10:00 a.m.
Dept.: 21
Judge: Hon. Evelio Grillo

Reservation Nos.: R-2277974
R-2277975

TAC Filed: June 9, 2021
Trial Date: None Set

Defendants Chattem, Inc. and Sanofi-Aventis U.S. LLC (collectively "Sanofi") submit the following objections to the Request for Judicial Notice ("RJN") submitted by Plaintiff Center for Environmental Health ("CEH") in support of CEH's Opposition to Sanofi's Demurrer to the Third Amended Complaint. CEH's RJN seeks judicial notice of matters that are irrelevant or improper.

I. OBJECTIONS TO RJN EXHIBIT 1

MATERIAL OBJECTED TO	GROUNDS FOR OBJECTIONS	RULING ON OBJECTION
Consent Judgment between CEH and Xttrium Laboratories, Inc. in the Proposition 65 enforcement action captioned as *Center for Environmental Health v. Xttrium Laboratories, Inc., et al.*, Alameda Sup. Ct. Case No. RG 19-011555 (entered July 25, 2019).	Relevance	**Sustained: ____** **Overruled: ____**

II. ARGUMENT

The Xttrium Laboratories Consent Judgment ("Consent Judgment") attached as Exhibit 1 to the Declaration of Mark N. Todzo submitted with CEH's Opposition to Sanofi's Demurrer is wholly irrelevant to the issues in this action and Sanofi's Demurrer. This Court should not take notice of it.

CEH correctly notes that this Court may take notice of its own records or acts. *See* CEH RJN at 2 (citing Cal. Evid. Code § 452(c), (d); *Williams v. Wraxall*, 33 Cal. App. 4th 120, 130 n.7 (1995)). However, records for which judicial notice are sought are still susceptible to evidentiary objections, including on relevance grounds. *See Aquila, Inc. v. Superior Ct.*, 148 Cal. App. 4th 556, 569 (2007) ("Although a court may judicially notice a variety of matters [citation], only *relevant* materials may be noticed.") (emphasis in original) (citation and quotation marks omitted). The Consent Judgment is irrelevant to the critical issues in this case.

CEH does not argue the Consent Judgment is relevant to the first, independently dispositive issue in this case—whether CEH alleged a clinically significant hazard for which there is reasonable evidence of a causal association with Zantac. Instead, CEH argues the Consent Judgment is relevant to the second issue—whether requiring a Proposition 65 warning on Zantac would violate federal

regulations. Specifically, CEH contends: (1) it "supports CEH's allegation that '[m]any OTC drugs regulated by the FDA contain Proposition 65 warnings on their labels[;]" and (2) it "refutes Sanofi's argument that such warnings are categorically forbidden by 21 C.F.R. §201.66[.]" CEH RJN at 2.

The first argument is easily disposed of. The fact that one OTC manufacturer entered into a consent judgment with CEH "for purposes of settling, compromising and resolving issues disputed in th[e] [underlying legal] action" (*see* Consent Judgment, § 1.7) that included a warning provision is not, as a simple matter of semantics, evidence that "many" OTC manufacturers did anything.

The second argument fares no better. The Consent Judgment does not reference 21 C.F.R. § 201.66 or hold that its provisions comply with federal law. The Consent Judgment does not reference statutes, regulations, administrative rulings or statements, or other decisional law that would suggest Proposition 65 warnings are allowed on OTC drugs. The Consent Judgment does not represent that the FDA or any other federal regulatory body reviewed and approved the agreement, or was advised of it in any manner. In fact, the Consent Judgment itself suggests the exact opposite—*i.e.*, that the FDA was not consulted—and casts doubt on the propriety of the warning under federal law, stating:

> [I]f a court of competent jurisdiction or an agency of the federal government, including but not limited to the U.S. Food and Drug Administration, states through any communication with the force of law, final regulation, or other legally binding act, that federal law has preemptive effect on any of the requirements of this Consent Judgment, *including but not limited to precluding Settling Defendant from providing the warning set forth in this Consent Judgment or restricting the manner in which such warnings are given*, then Settling Defendant may move to modify this Consent Judgment to bring it into compliance with or avoid conflict with federal law[.]

Consent Judgment, § 6.3 (emphasis added).

Translation: CEH hoped but did not know in that case whether the warning (which, as Sanofi contended would be required in this case, followed Proposition 65's safe harbor warning regulations, *see* Demurrer at 15:10-15, n.7; Consent Judgment, § 3.2) complied with federal law, did not bother to confirm it would with the FDA or any other agency of the federal government, did not expressly bring that issue to the attention of the approving state court, but instead simply included the warning.

Given the foregoing, and given also that the Consent Judgment involves different parties and factual circumstances, including, but not limited to, a different product type, chemical, and route of exposure, the Consent Judgment is irrelevant to the instant case and notice should not be taken of it.

Dated: September 3, 2021

DLA PIPER LLP (US)

By: _____

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

CASE NO. RG20054985

ASSIGNED FOR ALL PURPOSES TO:
Hon. Evelio Grillo, Dept. 21

PROOF OF SERVICE

Date: September 15, 2021
Time: 10:00 a.m.
Dept.: 21
Judge: Hon. Evelio Grillo

Reservation No.: R-2277974
Reservation No.: R-2277975

TAC Filed: June 9, 2021
Trial Date: None Set

PROOF OF SERVICE

I am a citizen of the United States and employed in Sacramento, California. I am over the age of eighteen years and not a party to the within-entitled action. My business address is DLA Piper LLP (US), 400 Capitol Mall, Suite 2400, Sacramento, CA 95814. On September 3, 2021, I served a copy of the within document(s):

- **DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S REPLY IN SUPPORT OF DEMURRER TO THIRD AMENDED COMPLAINT**

- **DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S RESPONSE AND OBJECTIONS TO PLAINTIFF'S REQUEST FOR JUDICIAL NOTICE SUBMITTED IN SUPPORT OF OPPOSITION TO DEFENDANTS' DEMURRER TO THIRD AMENDED COMPLAINT**

☐ by placing the document(s) listed above in a sealed envelope with postage thereon fully prepaid, the United States mail at San Francisco, California addressed as set forth below.

☒ by transmitting via e-mail or electronic transmission the document(s) listed above to the person(s) at the e-mail address(es) set forth below.

Mark Todzo
Joseph Mann
Lexington Law Group
503 Divisadero Street
San Francisco, CA 94117
mtodzo@lexlawgroup.com
jmann@lexlawgroup.com

Attorneys for Plaintiff
Center for Environmental Health

I declare under penalty of perjury under the laws of the State of California that the above is true and correct. Executed on September 3, 2021, at Sacramento, California.

DEBBIE BLUM

EAST\184873630.1

Exhibit 60

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY, *et al.*,

Defendants.

Case No. RG 20-054985

NOTICE OF APPEAL

TO THE CLERK OF THE COURT, ALL PARTIES, AND THEIR ATTORNEYS OF RECORD:

NOTICE IS HEREBY GIVEN that Plaintiff Center for Environmental Health ("CEH") hereby appeals to the Court of Appeal of the State of California, First Appellate District, from the Judgment as to which Notice of Entry of Judgment was served upon all parties on August 13, 2021.

A true and correct copy of the Notice of Entry of Judgment is attached as Exhibit 1 to this Notice of Appeal. A true and correct copy of the underlying Judgment is attached as Exhibit A thereto.

DATED: October 4, 2021

LEXINGTON LAW GROUP

Mark N. Todzo
Joseph Mann
Attorneys for Plaintiff
Center for Environmental Health

Exhibit 1

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PERRIGO COMPANY

SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY; TARGET CORPORATION; APOTEX CORP.; GRANULES PHARMACEUTICALS, INC.; GRANULES USA, INC.; 7-ELEVEN, INC.; SANOFI-AVENTIS U.S. LLC; CHATTEM INC.; DR. REDDY'S LABORATORIES LOUISIANA, LLC; DR. REDDY'S LABORATORIES, INC. and DOES 1 to 20, inclusive,

Defendants.

Case No. RG 20054985

Assigned for All Purposes to
Hon. Winifred Y. Smith - Dept 21

NOTICE OF ENTRY OF JUDGMENT

Complaint Filed: February 19, 2020
SAC Filed: January 4, 2021
Trial Date: None Set

TO ALL PARTIES AND THEIR ATTORNEYS OF RECORD:

PLEASE TAKE NOTICE that on August 11, 2021, the Court entered Judgment in favor of certain defendants after sustaining without leave to amend their respective Demurrers to Plaintiff's Second Amended Complaint.

The Judgment is attached hereto as "**Exhibit A".**

Dated: August 13, 2021

STEPTOE & JOHNSON LLP

By: _____

Dennis Raglin
Danielle Vallone
Attorneys for Defendant
PERRIGO COMPANY

EXHIBIT A

SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

PERRIGO COMPANY; TARGET CORPORATION; APOTEX CORP.; GRANULES PHARMACEUTICALS, INC.; GRANULES USA, INC.; 7-ELEVEN, INC.; SANOFI-AVENTIS U.S. LLC; CHATTEM INC.; DR. REDDY'S LABORATORIES LOUISIANA, LLC; DR. REDDY'S LABORATORIES, INC. and DOES 1 to 20, inclusive,

Defendants.

Case No. RG 20054985

Assigned for All Purposes to Hon. Winifred Y. Smith - Dept 21

[PROPOSED] JUDGMENT OF DISMISSAL AFTER THE SUSTAINING OF DEMURRERS TO SECOND AMENDED COMPLAINT WITHOUT LEAVE TO AMEND

Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

On May 7, 2021, the Court entered an Order sustaining without leave to amend the demurrers of the following Defendants to the Second Amended Complaint brought by Plaintiff Center for Environmental Health:

1. Perrigo Company;
2. Granules USA, Inc.;
3. Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories Louisiana, LLC;
4. Apotex Corp.;
5. 7-Eleven, Inc.; and
6. Target Corporation

Therefore, having entered the Order,

IT IS HEREBY ORDERED, ADJUDGED AND DECREED that the above action is dismissed with prejudice as to the above Defendants, JUDGMENT be entered in favor of the above Defendants and against the Plaintiff, that Plaintiff take nothing against them, and that Defendants shall recover costs according to proof.

DATED: August 11, 2021

Winifred Y. Smith
Judge of The Superior Court
County of Alameda

PROOF OF SERVICE

I, Alexis Pearson, declare:

I am a citizen of the United States and employed in the County of San Francisco, State of California. I am over the age of eighteen (18) years and not a party to this action. My business address is 503 Divisadero Street, San Francisco, CA 94117 and my email address is apearson@lexlawgroup.com.

On October 4, 2021, I served the following document(s) on all interested parties in this action by placing a true copy thereof in the manner and at the addresses indicated below:

NOTICE OF APPEAL

☐ **BY MAIL**: I am readily familiar with the firm's practice for collecting and processing mail with the United States Postal Service ("USPS"). Under that practice, mail would be deposited with USPS that same day with postage thereon fully prepaid at San Francisco, California in the ordinary course of business. On this date, I placed sealed envelopes containing the above mentioned documents for collection and mailing following my firm's ordinary business practices.

☒ **BY ELECTRONIC MAIL**: I transmitted a PDF version of the document(s) listed above via email to the email address(es) indicated on the attached service list [or noted above] before 5 p.m. on the date executed.

David A. Salyer
Salyer Court Reporting Services, Inc.
800 W. 1st Street, Suite 1303
Los Angeles, CA, 90012
Davesal55@ccrola.com

Also please see attached service list

☐ **BY OVERNIGHT DELIVERY**: I deposited such document(s) in a box or other facility regularly maintained by FedEx, or delivered such document(s) to a courier or driver authorized by FedEx, with delivery fees paid or provided for, and addressed to the person(s) being served below.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed on October 4, 2021 at San Francisco, California.

Alexis Pearson

SERVICE LIST
CEH v. Perrigo Company, et al.
RG 20-054985

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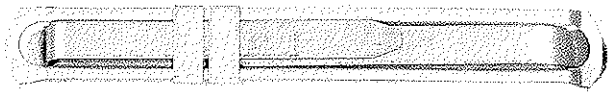
Gregory Sperla George Gigounas DLA Piper LLP 555 Mission Street, Suite 2400 San Francisco, CA 94105-2933 Greg.Sperla@us.dlapiper.com George.Gigounas@us.dlapiper.com	*Defendants* Sanofi-Aventus U.S. LLC Chattem, Inc.

Exhibit 61



22808014

ATTORNEY OR PARTY WITHOUT ATTORNEY	STATE BAR NUMBER: 168389	FOR COURT USE ONLY
NAME: Mark N. Todzo		ENDORSED FILED ALAMEDA COUNTY OCT 07 2021 CLERK OF THE SUPERIOR COURT By A. Jackson, Deputy
FIRM NAME: LEXINGTON LAW GROUP		
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ATTORNEY FOR (name): Plaintiff Center for Environmental Health		
SUPERIOR COURT OF CALIFORNIA, COUNTY OF ALAMEDA		
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CITY AND ZIP CODE: Oakland, CA 94612		
BRANCH NAME: Rene C. Davidson Courthouse		
PLAINTIFF/PETITIONER: Center for Environmental Health		
DEFENDANT/RESPONDENT: Perrigo Company, et al.		
OTHER PARENT/PARTY:		
APPELLANT'S NOTICE DESIGNATING RECORD ON APPEAL (UNLIMITED CIVIL CASE)		SUPERIOR COURT CASE NUMBER: RG 20-054985
RE: Appeal filed on *(date)*: October 4, 2021		COURT OF APPEAL CASE NUMBER *(if known)*:

Notice: Please read *Information on Appeal Procedures for Unlimited Civil Cases* (form APP-001-INFO) before completing this form. This form must be filed in the superior court, not in the Court of Appeal.

1. RECORD OF THE DOCUMENTS FILED IN THE SUPERIOR COURT

I choose to use the following method of providing the Court of Appeal with a record of the documents filed in the superior court *(check a, b, c, or d, and fill in any required information)*:

a. ☐ A clerk's transcript under rule 8.122. *(You must check (1) or (2) and fill out the clerk's transcript section (item 4) on pages 2 and 3 of this form.)*

(1) ☐ I will pay the superior court clerk for this transcript myself when I receive the clerk's estimate of the costs of this transcript. I understand that if I do not pay for this transcript, it will not be prepared and provided to the Court of Appeal.

(2) ☐ I request that the clerk's transcript be provided to me at no cost because I cannot afford to pay this cost. I have submitted the following document with this notice designating the record *(check (a) or (b))*:

(a) ☐ An order granting a waiver of court fees and costs under rules 3.50–3.58; or

(b) ☐ An application for a waiver of court fees and costs under rules 3.50–3.58. *(Use Request to Waive Court Fees (form FW-001) to prepare and file this application.)*

b. ☒ An appendix under rule 8.124.

c. ☐ The original superior court file under rule 8.128. (NOTE: *Local rules in the Court of Appeal, First, Third, and Fourth Appellate Districts, permit parties to stipulate (agree) to use the original superior court file instead of a clerk's transcript; you may select this option if your appeal is in one of these districts and all the parties have stipulated to use the original superior court file instead of a clerk's transcript in this case. Attach a copy of this stipulation.*)

d. ☐ An agreed statement under rule 8.134. *(You must complete item 2b(2) below and attach to your agreed statement copies of all the documents that are required to be included in the clerk's transcript. These documents are listed in rule 8.134(a).)*

2. RECORD OF ORAL PROCEEDINGS IN THE SUPERIOR COURT

I choose to proceed *(you must check a or b below)*:

a. ☐ WITHOUT a record of the oral proceedings (what was said at the hearing or trial) in the superior court. I understand that without a record of the oral proceedings in the superior court, the Court of Appeal will not be able to consider what was said during those proceedings in deciding whether an error was made in the superior court proceedings.

Form Approved for Optional Use
Judicial Council of California
APP-003 [Rev. January 1, 2019]

APPELLANT'S NOTICE DESIGNATING RECORD ON APPEAL
(Unlimited Civil Case)

Cal. Rules of Court, rules 3.50, 8.121–8.124, 8.128, 8.130, 8.134, 8.137
www.courts.ca.gov

CASE NAME: Center for Environmental Health v. Perrigo Company, et al.	SUPERIOR COURT CASE NUMBER: RG 20-054985

2. b. [x] WITH the following record of the oral proceedings in the superior court *(you must check (1), (2), or (3) below)*:

(1) [x] A reporter's transcript under rule 8.130. *(You must fill out the reporter's transcript section (item 5) on pages 3 and 4 of this form.)* I have *(check all that apply):*

(a) [ ] Deposited with the superior court clerk the approximate cost of preparing the transcript by including the deposit with this notice as provided in rule 8.130(b)(1).

(b) [ ] Attached a copy of a Transcript Reimbursement Fund application filed under rule 8.130(c)(1).

(c) [ ] Attached the reporter's written waiver of a deposit under rule 8.130(b)(3)(A) for *(check either (i) or (ii)):*

(i) [ ] all of the designated proceedings.

(ii) [ ] part of the designated proceedings.

(d) [x] Attached a certified transcript under rule 8.130(b)(3)(C).

(2) [ ] An agreed statement. *(Check and complete either (a) or (b) below.)*

(a) [ ] I have attached an agreed statement to this notice.

(b) [ ] All the parties have stipulated (agreed) in writing to try to agree on a statement. *(You must attach a copy of this stipulation to this notice.)* I understand that, within 40 days after I file the notice of appeal, I must file either the agreed statement or a notice indicating the parties were unable to agree on a statement and a new notice designating the record on appeal.

(3) [ ] A settled statement under rule 8.137. *(You must check (a), (b), or (c) below, and fill out the settled statement section (item 6) on page 4.)*

(a) [ ] The oral proceedings in the superior court were not reported by a court reporter.

(b) [ ] The oral proceedings in the superior court were reported by a court reporter, but I have an order waiving fees and costs.

(c) [ ] I am asking to use a settled statement for reasons other than those listed in (a) or (b). *(You must serve and file the motion required under rule 8.137(b) at the same time that you file this form. You may use form APP-025 to prepare the motion.)*

3. **RECORD OF AN ADMINISTRATIVE PROCEEDING TO BE TRANSMITTED TO THE COURT OF APPEAL**

[ ] I request that the clerk transmit to the Court of Appeal under rule 8.123 the record of the following administrative proceeding that was admitted into evidence, refused, or lodged in the superior court *(give the title and date or dates of the administrative proceeding):*

Title of Administrative Proceeding	Date or Dates

4. **NOTICE DESIGNATING CLERK'S TRANSCRIPT**

(You must complete this section if you checked item 1a above indicating that you choose to use a clerk's transcript as the record of the documents filed in the superior court.)

a. **Required documents.** The clerk will automatically include the following items in the clerk's transcript, but you must provide the date each document was filed, or if that is not available, the date the document was signed.

Document Title and Description	Date of Filing
(1) Notice of appeal	
(2) Notice designating record on appeal *(this document)*	
(3) Judgment or order appealed from	
(4) Notice of entry of judgment *(if any)*	
(5) Notice of intention to move for new trial or motion to vacate the judgment, for judgment notwithstanding the verdict, or for reconsideration of an appealed order *(if any)*	
(6) Ruling on one or more of the items listed in (5)	
(7) Register of actions or docket *(if any)*	

CASE NAME: Center for Environmental Health v. Perrigo Company, et al.	SUPERIOR COURT CASE NUMBER: RG 20-054985

4. **NOTICE DESIGNATING CLERK'S TRANSCRIPT**

b. **Additional documents.** *(If you want any documents from the superior court proceeding in addition to the items listed in 4a. above to be included in the clerk's transcript, you must identify those documents here.)*

☐ I request that the clerk include in the transcript the following documents that were filed in the superior court proceeding. *(You must identify each document you want included by its title and provide the date it was filed or, if that is not available, the date the document was signed.)*

	Document Title and Description	Date of Filing
(8)		
(9)		
(10)		
(11)		

☐ See additional pages. (*Check here if you need more space to list additional documents. List these documents on a separate page or pages labeled "Attachment 4b," and start with number (12).)*

c. **Exhibits to be included in clerk's transcript**

☐ I request that the clerk include in the transcript the following exhibits that were admitted in evidence, refused, or lodged in the superior court. *(For each exhibit, give the exhibit number, such as Plaintiff's #1 or Defendant's A, and a brief description of the exhibit. Indicate whether or not the court admitted the exhibit into evidence. If the superior court has returned a designated exhibit to a party, the party in possession of the exhibit must deliver it to the superior court clerk within 10 days after service of this notice designating the record. (Rule 8.122(a)(3).))*

	Exhibit Number	Description	Admitted (Yes/No)
(1)			
(2)			
(3)			
(4)			

☐ See additional pages. *(Check here if you need more space to list additional exhibits. List these exhibits on a separate page or pages labeled "Attachment 4c," and start with number (5).)*

5. **NOTICE DESIGNATING REPORTER'S TRANSCRIPT**

You must complete both a and b in this section if you checked item 2b(1) above indicating that you choose to use a reporter's transcript as the record of the oral proceedings in the superior court. Please remember that you must pay for the cost of preparing the reporter's transcript.

a. **Format of the reporter's transcript**

I request that the reporters provide *(check one):*

(1) ☒ My copy of the reporter's transcript in electronic format.

(2) ☐ My copy of the reporter's transcript in paper format.

(3) ☐ My copy of the reporter's transcript in electronic format and a second copy in paper format.

(Code Civ. Proc., § 271.)

CASE NAME: Center for Environmental Health v. Perrigo Company, et al.	SUPERIOR COURT CASE NUMBER: RG 20-054985

5. b. **Proceedings**

I request that the following proceedings in the superior court be included in the reporter's transcript. *(You must identify each proceeding you want included by its date, the department in which it took place, a description of the proceedings (for example, the examination of jurors, motions before trial, the taking of testimony, or the giving of jury instructions), the name of the court reporter who recorded the proceedings (if known), and whether a certified transcript of the designated proceeding was previously prepared.)*

	Date	Department	Full/Partial Day	Description	Reporter's Name	Prev. prepared?
(1)	5/5/2021	21	Partial	Demurrer Hearing	David A. Salyer (CSR No. 4410)	☒ Yes ☐ No
(2)						☐ Yes ☐ No
(3)						☐ Yes ☐ No
(4)						☐ Yes ☐ No

☐ See additional pages. *(Check here if you need more space to list additional proceedings. List these exhibits on a separate page or pages labeled "Attachment 5b," and start with number (5).)*

6. **NOTICE DESIGNATING PROCEEDINGS TO BE INCLUDED IN SETTLED STATEMENT**

(You must complete this section if you checked item 2b(3) above indicating you choose to use a settled statement.) I request that the following proceedings in the superior court be included in the settled statement. *(You must identify each proceeding you want included by its date, the department in which it took place, a description of the proceedings (for example, the examination of jurors, motions before trial, the taking of testimony, or the giving of jury instructions), the name of the court reporter who recorded the proceedings (if known), and whether a certified transcript of the designated proceeding was previously prepared.)*

	Date	Department	Full/Partial Day	Description	Reporter's Name	Prev. prepared?
(1)						☐ Yes ☐ No
(2)						☐ Yes ☐ No
(3)						☐ Yes ☐ No
(4)						☐ Yes ☐ No

☐ See additional pages. *(Check here if you need more space to list additional proceedings. List these proceedings on a separate page or pages labeled "Attachment 6," and start with number (5).)*

7. a. The proceedings designated in 5b or 6 ☐ include ☐ do not include all of the testimony in the superior court.

b. If the designated proceedings DO NOT include all of the testimony, state the points that you intend to raise on appeal. *(Rule 8.130(a)(2) and rule 8.137(d)(1) provide that your appeal will be limited to these points unless the Court of Appeal permits otherwise.)* Points are set forth: ☐ Below ☐ On a separate page labeled "Attachment 7."

Date: October 4, 2021

Mark N. Todzo
(TYPE OR PRINT NAME)

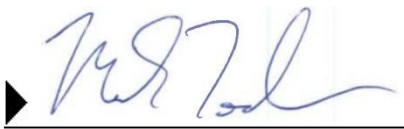
(SIGNATURE OF APPELLANT OR ATTORNEY)

Exhibit 1

SUPERIOR COURT OF THE STATE OF CALIFORNIA
FOR THE COUNTY OF ALAMEDA

DEPARTMENT 21 HON. WINIFRED Y. SMITH, JUDGE

CENTER FOR ENVIRONMENTAL HEALTH,)
)
Plaintiff,)
) SUPERIOR COURT
vs.) CASE NO. RG20054985
)
PERRIGO COMPANY, et al.)
)
Defendants.)
_____)

REPORTER'S TRANSCRIPT OF PROCEEDINGS
Wednesday, May 5, 2021

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(Appearances continued on next page.)

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INDEX FOR WEDNESDAY, MAY 5, 2021

CASE NUMBER: RG20054985

CASE NAME: CENTER V. PERRIGO

OAKLAND, CALIFORNIA WEDNESDAY, MAY 5, 2021

DEPARTMENT 21 WINIFRED Y. SMITH, JUDGE

REPORTER: DAVID A. SALYER, CSR 4410

TIME: 10:44 A.M.

-o0o-

THE COURT: Good morning, counsel. Thank you for waiting.

Calling Center for Environmental Health versus Perrigo Company, et al.

Let's see. I have quite a list of counsel.

I understand you have a court reporter I'm assuming who has taken all of the appearances.

But for plaintiff, Mark Todzo and Joseph Mann. Are you there?

MR. MANN: Yes, your Honor. This is Joe Mann. I'm here.

MR. TODZO: And Mark Todzo is here, as well, your Honor.

THE COURT: Okay. Thank you.

For defendants -- and I don't have all of the companies who you represent -- Derek Stikeleather -- okay, I do have it -- Sean Gugerty, Dennis Raglin for Perrigo, George Gigounas and Greg Sperla for Chattem, Paul Desrouchers and Megan Grossman for Granules, Jeff Margulies and Lauren Shoor for Target, Will Wagner and Vanessa Adriance for 7-Eleven, Brian Ledger for Dr. Reddy's Laboratories and Dr. Reddy's Louisiana

and Terry Henry for Apotex.

Did I capture everyone?

MS. CHANG: Your Honor, this is also Cheryl Chang on behalf of Apotex.

THE COURT: Okay. Thank you.

Anyone else? Excellent.

Center of Environmental Health has contested the tentative ruling. I will hear your argument now.

Who will be heard?

(Overspeaking.)

MR. LEDGER: I'm sorry to interrupt. This is Brian Ledger on behalf of Dr. Reddy's entities.

We did also have a motion or an application for pro hac vice admission of Megan Gramke on calendar today at the same time.

Would it be possible to have a ruling on that motion before we proceed with the hearing on the demurrers?

THE COURT: Hold on just one second.

So, counsel, we don't have any record of that. That means probably that it didn't get filed. We have a backup in our clerk's office which is quite lengthy.

I would suggest that I will allow parties to argue today on behalf of Dr. Reddy, and we'll see if we can find the pro hac vice application.

So I'm sorry about that, but things are not getting filed timely and scanned and imaged. If it's not in our register of actions, it doesn't exist.

We will have to do a little research and figure out

what happened to it.

Whoever is on and prepared to argue on behalf of Dr. Reddy's, which has a pending pro hac vice, I'll give you leave to argue today in court.

MR. LEDGER: Thank you very much, your Honor.

THE COURT: Okay. Anything before counsel begins?

I don't know who was starting to say that they were representing CEH in this argument or arguing on behalf of CEH today, but by all means go ahead.

MR. TODZO: Yes, your Honor. Mark Todzo. I will be arguing part of the hearing today, and then Joseph Mann, he'll be arguing part as well.

I will delineate that as we go, but especially the part of the hearing dealing with section 10(a) of Safety Code 25249, that's going to be Joe Mann, as will the CBE regulation portion of the argument.

The remainder I'll be arguing on behalf of CEH.

Like I said, I'll try to delineate and pass the baton along to Ms. Mann as appropriate.

So first off, your Honor, I just want to thank you for the lengthy tentative. In this particular instance, obviously I don't agree with the tentative, but I always appreciate this Court's tentatives because they make me think and they make me work. There is always something in there that was unexpected, and that was indeed the case here.

In terms of arguing against the tentative, though, today, I just want to start with what probably is not a maxim of jurisprudence yet, but maybe after today it will be, and

that is that which is possible is not impossible, okay?

So the Court's tentative ruling essentially determined that it's impossible for the defendants to comply both with Prop 65 and with the FDCA.

However, in the Court's tentative it also determined that there are a couple of steps that defendants could take that would allow them to comply with both, yet for various reasons decided that the defendants need not take those steps.

But the problem with the Court's tentative, and we'll get to this as we go, is that once you make a determination that something is possible, it can no longer be impossible.

So once the Court determined that when the defendants want to voluntarily provide information to consumers and that they are able to do so through advertising, then the Court can't turn around and say, yeah, but they can't provide a Prop 65 warning via that mechanism.

Once the Court has determined that they can plausibly and possibly comply with both, end of inquiry from an impossibility standpoint.

Again, like I said, we'll get to that in a minute.

Where I think the Court went wrong is that I believe that the Court was distracted by all the federal cases. There is a lot of federal case law on mainly prescription drugs. There is a lot of case law, preemption case law. The defendants cited a slew of those cases, and as a result I think the Court was distracted.

But this case is very different, and I think it's important to note the differences here.

So the first and main difference between this case and I believe about 99 percent of the cases that defendants cited is that this is an over-the-counter drug. It's not a prescription drug. So the reason why that matters is that there is an entirely different body of regulatory actions by FDA concerning prescription drugs as opposed to OTC.

Importantly here -- probably the most important here is that there are specific regulations having to do with prescription drug advertising, whereas there are no similar regulations for -- advertising.

Again, we'll touch on that again a little bit later.

Another real distinguishing factor that, again, matters here is that the particular hazard that we're talking about, which is the NDMA, the NDMA contamination of the products, it's a contaminant. It's an undisclosed contaminant.

When you look at all the prescription drug cases and, in fact, every case, every other case that was cited, with the one exception being the Zantac MDL, but we'll put that to the side for a minute, but every other case had to do with the active ingredient. And it's always the active ingredient.

There's some problem with an active ingredient in a prescription drug that was not disclosed properly. However, all of that information had already been provided to FDA. FDA had made a determination as to what the appropriate warnings were. So that's why courts generally then find preemption.

Here, however, we're talking about something that was never disclosed to FDA. It's an undisclosed contaminant. And it's not an ingredient in the products at all.

So that causes it to be different. Because, you know, for example, how could FDA -- when we're looking at impossibility, we have to say -- the Court has to be able to find that it would be illegal for defendants to comply with Prop 65.

So when we're talking about reducing or eliminating the NDMA content, which is, again, an undisclosed contaminant, what possible aspect of FDA law would the defendants be violating? There is nothing because it was undisclosed.

Anyway, again, we can touch on that a little bit more later.

So the other aspect here is that we -- typically in these kind of cases we don't really have -- there is not really a good indication of what FDA thinks about the particular hazard.

Here we know exactly what FDA thinks. The FDA thinks that the carcinogenic risk of the products is extremely strong, extremely, you know, important. That's why, you know, eventually, after first finding out -- the FDA didn't find out from the defendants. The defendants never bothered disclosing this contaminant, this hazard. Rather they found out through a third-party lab.

Once the FDA found out, the FDA was very concerned, took action, issued some statements about the hazards and ultimately required, you know -- requested that the defendants recall all the products, which has happened.

So in that process what we saw, then, is we saw that when defendants -- okay, so after the FDA issued its initial

statement about the hazard of NDMA, it hadn't told the defendants they needed to recall any of the products, yet the defendants began what they called voluntarily recalling the products.

What that meant, and what that meant in practice, is the defendants sent out public communications regarding the hazard of NDMA.

So when the defendants wanted to communicate with the public via press release, via internet, via their websites, when they wanted to communicate with the public directly about the hazard of NDMA in the products, they were able to do so, and they did so without prior FDA approval. And they also did so without any FDA repercussion.

So that really gets, you know, to what's possible cannot be impossible.

The other interesting part about the FDA's investigation is that once FDA started gathering up information on the NDMA contamination, what they determined is that the products varied from 0.02 parts per million NDMA contamination up to 2.37 parts per million concentration of NDMA.

So why does that matter?

Well, that matters because here you've got a whole body, a whole group of defendants, the generic manufacturers, who are telling the Court and telling us that they can't possibly do anything different with respect to the NDMA and the products without FDA's approval.

Yet that's obviously counter factual, because what we

have in terms of the facts here are the facts are that there is an incredibly large variation in the amounts between specific and individual defendants.

So, again, there's no other case that defendants cite that has this type of fact pattern.

So then the other thing that differs, that causes this case to be a little bit different, is the law itself.

So, you know, with respect to the preemption law, all cases -- we always have the same general preemption law, which is preemption is a function of congressional intent. We look to the manifest intent of Congress. We have presumptions in place. There is a presumption that you don't preempt state health and safety law unless it's the clear will of Congress.

You have certain implied things where you can imply the intent of Congress where maybe it's not expressed. So you have all those things all through here as well.

Again, what causes this to be a little bit different is that with respect to OTC drugs -- and now, again, this is one of the things that distinguishes this case from, you know, 99 percent of the cases cited by defendants, and in fact just about all the cases cited by the Court in its tentative, is that, you know, this is an OTC drug, and with the OTC drugs there is this very broad preemption provision.

And the broad preemption provision preempts all state requirements that are different from, in addition to or otherwise not identical from -- and this is key -- a requirement under the Act.

In essence, the states are free to regulate in the

interstices of the FDCA, but they cannot regulate whenever there is a specific reg in place.

Okay. At the time that this 379r -- this is 21 USC 379r(a) that I was just quoting from -- and at the time that that was enacted there was already a whole body of FDA regulatory, you know, actions that had been taken pursuant to the prior FDCA.

This was the FDCA Modernization Act.

Together in those regs there were already very, very detailed regulations addressing labeling for all drugs, prescription and OTC.

So when Congress enacted this, they realized that there was a gap, because you had labeling regulations for OTC and prescription drugs.

You had advertising regulations specific only to prescription drugs. And in essence there is this void with respect to other forms of public, you know, non-labeled forms of public communication with respect to OTC drugs.

So Congress wanted to close that loophole, so it enacted 379r(c)(2).

And what that did is that expanded the scope of requirements.

So that says:

> "A requirement that relates to the regulation of a drug shall be deemed to include any requirement relating to public information or any other form of public communication relating to a warning of any

kind of OTC drug."

So that's the congressional extension. That is Congress saying, okay, we're going to expand preemption to cover all forms of public communication.

However, in the very next subdivision of 379r -- this is 379r(d) -- they carve out Prop 65 from them.

So they say, "All forms of public communication with respect to warnings are preempted. However, this shall not apply ..." That's the exact language, "shall not apply." And it says, " ... to certain initiatives, statutes," of which there is only one, and that's Prop 65. And the Dowhal case goes through that in detail.

So that's important here because this is the only case. None of the other cases cited by defendants -- again with the exception of Dowhal -- touch on this. And Dowhal is important. So Dowhal is the one and only other case dealing with OTC drugs that also deals with FDCA preemption.

That case shows us exactly the high bar that is required in order to overcome all the various presumptions against preemption.

So in that case you have OTC drug manufacturers, manufacturers of nicotine replacement products who were sued for failing to warn about hazards associated with nicotine, nicotine again being the active ingredient.

So in that case there was no possibility of reducing or eliminating the nicotine exposure because the entire purpose of the drug was to expose people to nicotine.

So we can just put that -- that's a differentiation of

Dowhal from this case, where the undisclosed contaminant can be eliminated and it doesn't affect the drug at all.

So anyway, Dowhal, the plaintiff was suing for failure to warn. That fact pattern, Dowhal, the defendants in that case had actually requested specifically of FDA to put on certain Prop 65 warnings, and the FDA had rejected that.

The plaintiff said, well, that's not enough because there is plenty of other language that the defendants could have used.

That got past the initial hurdle of impossibility preemption, but then the FDA came in and FDA actually filed an amicus brief and said, no, no, no, putting any form of reproductive hazard warning is going to dissuade pregnant women from using the products, thereby causing them to smoke, and that's contrary to what we want. That's contrary to our objectives.

So the Court ended up ruling, well, based on precisely what FDA told them was their objective, that the Prop 65 claim was preempted on the basis of obstacle preemption.

So you have FDA explicitly saying what they meant and what they didn't mean.

So now that brings us here to the Court's ruling, where the Court is essentially saying that putting a warning in any form whatsoever, including public advertising -- and that's really what -- that's the heart of what I'm going to argue today, is on the public advertising piece, because I think it's important.

So here you have no express statement from FDA that

anytime you put a warning on a public ad that it becomes a label. You've got no such -- in fact, if anything, you have the opposite, where you have this void. You have a regulatory void.

You have the place where Congress felt it necessary to expand the scope of express preemption to cover all forms of public communication specifically because there was no regulation. There is no regulation.

So I think what the Court has done in trying to remedy that is say, well, we can look at the Kordel case. And the Kordel case takes this broad view of what constitutes a label, although Kordel never says anytime you have a warning that ad becomes a label. That's just not in the Kordel case.

What Kordel says is if something explains or accompanies the product, then it is labeling under the FDCA.

So here, you know, the idea that a Prop 65 warning necessarily is explanatory or comes with the product is different than reality here, which is, you know, if you have a public advertisement and it includes a Prop 65 warning, that could be something very, very different than explanatory. And there is nothing about saying this product contains a chemical that's known to cause cancer that, you know, in essence transmutes what would be an advertisement into something else.

Now, you know, it's easy for me to say that, but I think we should also look at what FDA has said.

FDA, with respect -- as I mentioned before, FDA does govern advertising of prescription drug products. And with respect to that, Congress explicitly gave FDA the right to

determine what is a label and what's an advertisement with respect to prescription drugs.

So when you look at 21 USC -- I believe it's 352 is the definition section. And they are side-by-side, 352(m) and (n).

352(m) is the definition of labeling.

352(n) is the definition of advertising.

And the two are defined in a way to exclude one another. So, in essence, advertisements are that which is not labeling. Then it goes on to say, however, FDA can determine exactly what is labeling.

So FDA went ahead and did that. FDA did that in 21 CFR 202.1(l). So that is the subsection where what constitutes an advertisement versus a label is explicitly defined.

Nowhere, nowhere does FDA say that once it has a warning, it becomes a label. Rather what FDA says is it's the method of administration of the particular, you know, ad that determines its context as either labeling or advertising.

So, for example, if something is placed in a -- so it says that advertisements subject to 502(c), which is the advertisement, not the label, include "advertisements in published journals, magazines, other periodicals and newspapers and advertisements broadcast through media such as radio, television and telephone communication systems."

So according to how FDA views what constitutes a label versus an advertisement, there is this whole slew of broadcast media where a Prop 65 warning could be broadcast that would not fall under the definition of labeling, okay?

And just to sort of hammer that point -- you know, most of the cases, when you look at all the cases that defendants cite, they don't really get down to this level of detail. Most of them dealt with doctor letters or, you know, other types of promotional materials that accompanied the product, because, again, remember, we're talking about prescription drug products.

So in those cases they all basically say, well, it accompanies the product, that advertisement, that promotional material. That is therefore covered by labeling.

But there's a case that actually gets down to this level of detail where it analyzes those differences, the differences in 202.1(l). That's the In Re Lipitor case, which is 185 F. Supp. 3d 761, and that's at 772.

So, you know, in sort of explaining the difference, then, between the two types of ads, those that are advertisements and those that are labels, it says, "In other words, advertising to the general public as opposed to materials for use by medical professionals is not considered labeling."

So here that's exactly what we're asking for. We want public communication, communication directly to the public where they explain hazards of NDMA in the product or provide a Prop 65 warning.

Then, again, in case there is any doubt that they can do so, the defendants themselves have provided us with conclusive evidence, conclusive evidence that when they want to provide public communication directly, directly to the

public about the hazards of NDMA, they can do so without FDA approval or, you know, without FDA repercussion.

So, you know, let me just find the cite there, because that's the recall notices, and they're attached to my declaration. I believe it's Exhibit 7 of my dec is one and Exhibit 4 of the Apotex's declaration -- or the Apotex's RJN is the other one.

The other sort of interesting and important point there, because it completely undermines and belies the argument that there is some duty of sameness that would apply to these public communications, if you look at the language of those two different ones -- in those two different ones, one of them is from Sanofi, the brand name manufacturer, the other is from Apotex, the generic manufacturer, and the two are different.

Not only that, but Apotex actually sent their public communication about the hazards of NDMA prior to that of Sanofi. So they weren't following the brand name manufacturer at all.

Okay. So that gets to the point that not all labeling -- I'm sorry, not all warnings constitute labeling.

So there was another piece of the Court's tentative where the Court essentially said -- and this is where I mentioned at the outset that I always appreciate when the Court comes up with something that the parties didn't really brief, and it's just something new and makes you think.

The Court said, well, you know what? The Prop 65 warning is also not advertising because advertising is

voluntary, whereas a compelled warning is involuntary.

And so, first of all, there is an obvious problem. The maxim, it violates the Todzo maxim of jurisprudence, where that which is possible is not impossible, because the Court is essentially acknowledging that it's possible.

In fact, the Court explicitly acknowledges that the generic manufacturers can communicate directly with the public. I believe -- anyway, I'll find that quote from the Court's tentative in a second.

Oh, yeah. So it's page 23 of the Court's tentative. You know, "A generic manufacturer must provide information about OTC drugs to consumers through FDA-approved labeling but can voluntarily provide additional information to consumers through advertising."

So the Court acknowledges that they can voluntarily provide information inclusive of a Prop 65 warning as long as it's voluntary. But as soon as they can do it voluntarily, then now it's no longer impossible, right? It's possible for them to do so.

Well, the other issue with this sort of advertising being voluntary, whereas labeling is mandatory, it's just contrary to California case law.

I apologize. I haven't had a ton of time to do research on this point, but it sort of jumped out at me that there was a case that that I used that discussed this issue. It's Consumers Union versus Alta-Dena Milk [sic], and it's 4 Cal. App. 4th 963.

And there's a part of it -- that case wasn't

specifically addressing compelled advertising, but it cites a bunch of cases that do, okay? And that's at pages 973 through 974. And it runs through just a whole list of case law of other cases where courts explicitly compelled statements in advertising.

So I just think it's important for the Court to understand that that distinction is not correct.

So then that's basically it unless the Court has specific questions as to the advertising.

I was just going to move on really quickly to the other form of where it's possible for the drug manufacturers to comply, which is on the reduction or elimination of the NDMA. But before we get there --

THE COURT: I don't have any questions, but I think we need to do a little time check because there is another case behind this case, but also I want to give defendants an opportunity to respond, and you're at about half an hour.

So if you can wrap it up in the next few minutes.

Hold on just one second.

(Proceedings held in unrelated matter.)

THE COURT: Mr. Todzo, if another attorney is going to argue, you'll have to wrap up pretty quickly if you have another attorney.

MR. TODZO: Well, your Honor, I appreciate that. And I apologize.

With respect to, you know -- all I'll say is that the Court itself identified that it is possible for the defendants to reduce or eliminate NDMA, at least under some

circumstances, without FDA approval.

And the Court specifically said that -- anyway, I can get the pin cite from the Court's tentative, but I think the Court probably knows its own tentative.

The Court, though, however, said that it need not go there; it need not even worry about all the possible means that defendants have for reducing or eliminating the exposure, thereby complying with Prop 65 because of section 10(a), which I referenced before, saying that essentially once defendants demonstrate that federal law governs warning in a way that preempts some state authority, that therefore all state authority is preempted.

I think there are problems with that, but I'm not the one to tell you about it. Joe Mann is going to step in now and he'll discuss the specific problems with the Court's ruling on section 10(a).

MR. MANN: Thank you, Mark.

Your Honor, I'm going to talk about Health and Safety Code section 25249.10(a). And for simplicity I'll just refer to that as section 10(a).

This provision certainly does not operate to preclude CEH's claims.

Mr. Todzo was discussing federal preemption, and this is a bit of a pivot because now we're talking about an interpretation of a state statute that is going to depend on what the voters who enacted Proposition 65 intended. There is the same result, though.

Certainly the Court's interpretation of 10(a) is not

compelled by the language of the statute, and in fact runs directly contrary to the intent of the voters who enacted it.

I think I know where the Court goes off track here, and I think I can explain it readily.

The Court starts out by correctly recognizing a party can comply with section 25249(6), which I'll call section 6, either by reducing or eliminating the exposures or by providing a warning.

So in the tentative ruling at page 4 the Court says, "The defendant can comply with Prop 65 and avoid liability by either providing a warning or ensuring its products have chemical exposure before the no significant risk level."

The Court then goes on to say that under section 7 it can order injunctions and civil penalties including ordering a warning.

That's certainly true. The Court can also order that there be no actionable exposure, and your Honor knows this from the CEH settlement approval context, where we were citing to you the attorney general settlement guidelines that tell you that reformulation in lieu of a warning not only allows compliance with Proposition 65 but can confer a substantial public benefit.

But here's where the Court goes off track. It suggests then that the formulation is only an issue as to remedies under section 7 and that section 6 is only about warnings.

So it's not deciding whether or not defendants can take any steps to reformulate their products to comply with Proposition 65 and to still focus on warnings. That's at

variance with what the Court said earlier.

There are two methods of compliance with section 6, no exposure, or if you're going to expose provide a warning.

Indeed, if you look at the injunctive terms in section 7(a), they refer both to section 6 and to section 5, which is a Prop 65 term regarding discharges into drinking water.

Section 5 doesn't involve warnings at all. That's not even a method of compliance. So it's clear that the injunction provisions are just tracking the liability provisions of the statute.

Likewise, in 7(b), which has a civil penalty provision, the factors include whether the violator took good faith steps or good faith measures to comply with this chapter.

That doesn't speak in terms of warnings. It speaks in terms of any method of compliance that Prop 65 allows.

Both these go to show that the scope of section 6 and section 7 are completely co-extensive. They are two sides of the same coin, your Honor. You cannot ignore reformulation in one and think it relevant to the other.

This matters because of how the Court is interpreting the term "state authority" in section 10(a). That section provides that, "Section 6 shall not apply to an exposure for which federal law governs warnings in a manner that preempts state authority."

The Court expresses its view on page 5 of the tentative, which says, "This provision means that if federal law on warning preempts state law on warning, then there is no liability for exposure under section 6, and thus the Court

cannot order any non-warning injunctive relief or award any penalty."

This is the heart of the Court's error. The Court is essentially inserting in place of the words "state authority" "state law on warning."

To put it another way, the Court is essentially saying the extent that federal law governs warning in a manner that preempts some state authority, the authority to require a warning, it preempts all state authority; i.e., the ability to require compliance with Proposition 65 through a warning.

So to reach this conclusion, the Court is effectively reading terms into the plain language of the statute. That's generally improper, but here it's even less proper because the Court is limiting the application of the statute.

The California Supreme Court's decision in Lungren says to read Prop 65 broadly to accomplish its protective purpose. The Court's reading is doing the exact opposite.

Now, notably no cases discussing section 10(a) adopt the Court's ruling. The Court will literally be the first Court anywhere to say this is what section 10(a) means.

If you look at the cases that do discuss section 10(a), they apply the usual constitutional analysis on conflict preemption. It's a physical impossibility of compliance with both federal and state law. It's conflicts the Todzo doctrine.

In fact, if you look at cases such as PCRM versus McDonald's, which is a California Appellate Court decision, that Court discussed section 10(a) but nonetheless held:

"Conflict preemption of state law by federal law does not automatically and necessarily result in a complete displacement of state law by federal law its in entirety. Rather, it does so insofar, but only insofar as there is a conflict."

In other words, despite section 10(a) you still look to whether all forms of compliance with the law -- when all forms of compliance have been precluded by federal law.

There is certainly nothing inexorable or necessary about the Court's interpretation of section 10(a), and several other interpretations are certainly apparent.

For instance, CEH believed it means that the only exposures that are exempted from the Prop 65 warning requirement are those for which federal law actually precludes the application of Proposition 65.

So, for instance, if defendants could have reduced NDMA to levels that don't require a Prop 65 warning by simply storing the ranitidine at the range that is already specified under the FDA-approved labels -- so here, your Honor, there is no conflict with federal law. The labels already say store at this temperature range. They have done that to comply with Proposition 65 potentially.

But your Honor is saying even if federal law might apply to some NDMA warnings -- sorry, in the case, they could have reduced the NDMA through proper storage, even if federal law applies to some warnings, like some label warnings, here

you can comply with Proposition 65 and comply with federal law just by taking a step other than that warning.

Other interpretations of section 10(a) are available, as well. For instance, adopting exactly the same reasoning the Court applies, you could read 10(a) to say that federal law preempts any state authority. It preempts all state authority.

This is essentially the pivot that the defendants took in the reply briefs. They said that if any type of warning is precluded by federal law, then Proposition 65 is precluded in its entirety.

We know from the other cases the Court cites, the Court does not agree with this view.

The point is once you go down the road that section 10(a) requires some -- or allows some federal authority to preempt all state law, there is no limiting principle as to how much authority has to be involved at the federal level.

So at worst for CEH, Proposition 65 -- I'm sorry -- section 10(a) is ambiguous as to its scope.

In that case you look to the purpose of the statute and the intent of the persons who enacted it.

Now, defendants do not dispute Prop 65 is a protected statute that should be read broadly and that California voters thought existing laws on toxics weren't tough enough and were looking for ways to enhance their state rights.

Why on earth would these voters want to extend the preclusive effect of federal law further than what the federal constitution requires so as to extinguish those state rights.

I think the Court's real concern here is it wants to give meaning to section 10(a). How could it be that it's just restating the law on federal preemption?

In fact, the Court says as much on page 5. It says the exception does more than state the obvious, which is that federal law preempts state law.

In the first place, to the voters who enacted Prop 65 this was hardly obvious. The Lungren appellate court decision tells you not to read a voter referendum in a hypertechnical manner that a lawyer might read it.

It certainly strains credibility to say that everyday voters thought they were modifying the standard on federal preemption at all, much less weakening protections under Proposition 65.

In fact, if you look at the ballot materials, not only do they not say this. They say the opposite.

The ballot materials that they were telling the voters what they were voting on says Proposition 65 will not in any way weaken any of California's existing protections to toxic law -- it would be quite a bait and switch, your Honor, to say that after telling the voters that, in fact, 10(a) is limiting their rights further than what the federal constitution requires.

And one function of this provision could be that they were -- the drafters of Prop 65 wanted to inform voters about federal preemption. In other words, even if you pass this law of voters, it may get struck down as being inconsistent with federal law.

Another possibility is that they were looking to preclude facial challenges that they knew were coming on preemption grounds, which indeed, that's the Cotter case and that's the Allenby case. And they wanted to preserve the operation of the law.

The Court seems to think there is something weird about the self-exception provision in 10(a) that is not part of other statutes. But in fact there are at least three provisions in the California Financial Code alone that essentially say if state law is precluded by federal law, it has no effect.

And these are sections -- California Financial Code 1014803 [sic] and 14001.5.

These show that even a facially superfluous provision that just reflects the existing law on federal preemption is not uncommon in California law. It's certainly not exclusive to Proposition 65.

One last observation on that point, your Honor. That's that the Court's interpretation also runs counter to the federal legislators who enacted the savings clause that Mr. Todzo referred to in 21 USC section 379r(d)(2).

Again, this is the only state provision that was exempted.

As stated in the opposition, the legislators at the federal level who enacted this provision believe that Proposition 65 accomplished at least two very important policy goals.

The first was that it reduced toxic contamination in a

number of consumer products sold in California, and the second was that it led FDA to adopt more stringent standards for some consumer products.

The Court's interpretation here, your Honor, subverts both of these goals.

The federal warnings alone can preempt anyone's right to demand reformulation under state law. There is going to be no toxics reduction.

And the FDA can't ably adopt more stringent toxic standards if it doesn't know what's feasible to be done in the way of reformulation, and that's something that litigation under Prop 65 can uncover.

Here, keep in mind, your Honor, you can't always rely on drug manufacturers to be completely straight on this. It took a third-party laboratory to uncover the NDMA contamination problem that they should have discovered themselves.

So the Court has adopted a reading that none of the California voters intended that is contrary to all case law on the issue and that runs contrary to the intent of the federal legislators in exempting Prop 65 and the express savings provision, and we believe that it cannot stand.

I can answer any questions that your Honor has at this point or go on to the changes being effectively enforced.

THE COURT: Okay. You have just a few minutes to do that, because I have to move on to allow defendants ample time to argue.

MR. MANN: I'll try to get through this quick, your

Honor.

This is the argument that CEH has to plead around the changes being effective regulations that say that brand name manufacturers can change their labels without seeking FDA approval. And this runs contrary, I believe, to California pleading standards.

Everyone here knows preemption is only coming up as an affirmative defense. And there's no requirement in California law, as a general matter, that we have to anticipate and plead around the defendants' affirmative defenses.

That was the Stowe case that was cited in the opposition. No one has even discussed or disputed that.

Moreover, California Civil Procedure Code section 425.10 requires only a concise statement of facts constituting the cause of action.

Defendants do not dispute that CEH has adequately pleaded its Prop 65 claims.

Now, on reply the brand name manufacturers cite to the Cryolife case. And this is the only case cited on this issue by the other side. That says that a demurrer may be proper when the complaint on its face clearly discloses some defense or bars for recovery.

The paradigm case there is statute of limitations, since the complaint can say it took place at a certain point. You didn't file until this point. Plaintiff, you have to explain to me what happened here.

There is nothing like this in the second amended complaint. We don't say anyway that the FDA has plenary

authority over OTC drug regulation. And it can't be enough that the mere mention of the FDA is enough to clearly raise a preemption defense especially because of the express savings provision in 379r.

Furthermore, putting the obligation on plaintiffs to plead around the preemption defense runs afoul of the norm that plaintiffs are not required to plead with specificity on matters dealing with defendants of equal or superior knowledge. And this is the Doe v. L.A. case.

The Court is treating this like there is some sort of heightened pleading standard here, like it's a fraud claim. It's not even an aspect of the plaintiff's prima facie case here, and even if it was, CEH would have no way of knowing the facts about this, if the case was an exemption.

How do I know what a clinically significant risk is of NDMA contamination. That would require expert testimony, not the sort of thing that's a pleading defect at the front of the case.

The only authority cited by the Court and defendants on this is the Gibbons case out of the Second Circuit, not a state case, not a California pleading case, not a Prop 65 case. That case suggests that plaintiffs must plead a labeling deficiency that plaintiffs could have corrected using the -- (inaudible) -- regulation.

Now, in the first place, that conflicts with Wyeth v. Levine, which says it's defendant's burden to show this by clear evidence that the FDA would not have approved the labeling change. And Gibbons did not hold that plaintiffs

have to plead clinically significant risk for which there is a reasonable evidence of causal association with the drug. And those are the terms used in 21 CFR 31470.

It just said you have to plead that newly -- new information revealed a risk that wasn't appreciated at the time of the NBA or ANBA approval.

Here it appears that no one alerted FDA to the presence of ranitidine at the FDA approval stage. So this is newly acquired information.

In fact, if you think that CEH has to plead that, section 36 of the complaint says specifically there is new testing by FDA as to NDMA ranitidine. And because of that testing, they urged them to recall their products.

We know from other judicially noticeable materials that the April 2020 FDA alert on market withdrawal, the FDA's specific concerns were unacceptable levels of NDMA which presented a cancer risk.

How is that not clinically significant?

Again, none of this was in front of the FDA before.

Defendants may have known earlier, but it was certainly new information to the FDA out of which the branding manufacturers could have relied in seeking authority to change their labels.

Your Honor, you can look at the recall provisions in 21 CFR 745.

FDA has to make a finding that public safety is going to be a fact of requiring a recall.

Defendants say the FDA didn't order a recall here.

But, first, we don't know what authority the FDA was operating under.

Second, it was an obvious precursor to requesting a recall.

If any of the drug manufacturers had said, no, we're going to keep the drug on the market, the FDA would have said, okay, now you have to recall it.

In any event, it's highly relevant the FDA thought no human should be putting ranitidine in their body until the NDMA problem was resolved. And it's far less extreme to change a label than to demand every manufacturer on the planet to stop selling ranitidine in the U.S. market.

So as with advertisements, defendants are sort of ignoring the facts on the ground here.

Lastly, even if the Court does require CEH to amend, I want to say that we should be allowed more time to take discovery on these issues.

We cited a case in the opposition Coleman v. Medtronic. That's a California Appellate Court case. That was even when a Court granted a demurrer as a, quote, "matter of law" in a preemption case involving drugs, further discovery is proper to allow a plaintiff to learn of information that's only available to the manufacturer or the FDA.

Here if the Court says that further allegations are required on the CBD provision, CEH is going to have to conduct discovery on the brand name manufacturers, and perhaps others, to determine facts regarding a clinically significant risk and reasonable evidence of the causal association of the drug.

Unfortunately, the Court's order specifies an amendment date of May 28th. That's three weeks away, your Honor. We think we're going to need more time in order to conduct discovery.

Your court issued a discovery guidance on March 8th saying essentially that the Court would permit further discovery if anyone said that the amendments were not sufficient.

Because of the timing of the demurrer, CEH has not yet served discovery on Sanofi, but we'd like the opportunity to do so and get their complete responses.

If they're going to be able to knock out our entire complaint on factual matters, we need factual development.

That's all I have, your Honor.

THE COURT: Thank you, Mr. Mann.

I'm not sure how to approach defendants' argument because there are so many of you on.

I don't know if you've organized yourselves around this, but I'll just take a stab at starting with Perrigo, since they are the first appearances that my clerk took.

If you have some other plan, that's fine as well.

MR. STIKELEATHER: Your intuition is right, your Honor. This is Derek Stikeleather for Perrigo.

We have, among ourselves, preferred that the generics go first followed by the other groups of defendants.

So I will begin and I intend to be brief.

The generic manufacturers have read the Court's tentative decision. We believe the Court has got it right.

We, because of the clarity of the law, particularly Mensing, the generic manufacturers are entitled to demurrer without leave to amend.

Unless the Court has questions, we will submit to the Court's tentative ruling.

THE COURT: Okay. Thank you. I mean, I'm you can all tell I've taken a deep dive into this. So I don't have questions. I'm just interested in hearing all your perspectives on the tentative ruling.

So thank you, counsel.

MR. STIKELEATHER: You're welcome, your Honor.

THE COURT: Next?

MR. GIGOUNAS: Your Honor, this is George Gigounas for Sanofi. I'm seeing that I'm muted. Can your Honor hear me?

THE COURT: Yes, I can hear you.

MR. GIGOUNAS: This is George Gigounas, your Honor, for Chattem and the Sanofi defendants.

We will be brief as well.

The arguments -- we feel the Court's tentative ruling was very well reasoned. We feel the arguments that plaintiff's counsel has put forward today are not persuasive.

A couple of points to make.

Plaintiff's counsel has spent a good amount of time attempting to argue around the plain language of section 10(a). And the fact is the plain language of section 10(a) addresses specifically section 6 of Proposition 65.

Section 6 of Proposition 65 deals specifically with a warning requirement. It does not prohibit activity. It does

not prohibit exposures. It requires a warning.

That is in stark contrast to section 5 of Proposition 65, which is the drinking water discharge prohibition.

So when the statute wants to prohibit activity, it does so in section 5. When the statute wants to require a warning, it does so in section 6.

That is very important, as the Court rightfully pointed out in its tentative. That is very important when the Court reads section 10(a), which specifically deals with section 6 and specifically states that section 6 "shall not apply to an exposure for which federal law governs a warning in a manner that preempts state authority."

Counsel has made a big deal about the fact that section 10(a) says state authority, not state law regarding warnings, but it's actually counsel that is reading in additional information into section 10(a), because 10(a) deals specifically with the preemption section 6, which is the warning requirement, no more no less.

It's important that Section 10 be read in context.

There was some discussion about the intent of the voters in Proposition 65. I will address that discussion simply by saying there is absolutely no authority in California or elsewhere that tells the Court that it must read a California statute contrary to its plain language and plain meaning just because it was passed by a referendum.

The intent of the voters in the referendum is clearly expressed in section 10(a). It's clearly expressed in section 6, which is a warning requirement. Therefore, the Court has

appropriately read that section in its tentative.

Regarding counsel's argument on alternative warning methods or the idea that the defendants could have issued radio or television advertisements and in some way magically transmuted a Proposition 65 warning into a mere advertisement or something that would not be governed by the EDD regulations under FDA.

The first thing to do, which the Court again rightfully does, is to step back and look at the common sense issue here.

Counsel is essentially saying that despite what counsel would certainly argue is meaningful information provided regarding the risks of the drug in a Prop 65 warning, somehow the FDA would be completely unconcerned about the communication of that information if it were only communicated through a radio advertisement or through a television advertisement.

That is clearly not the case.

And we don't actually need to debate that. The Supreme Court itself in Kordel made it quite clear that labeling under the FDCA is construed broadly. It does not need to be physically attached to the product itself. It specifically says that sound recordings constitute labeling, which is, you know, implicated by the plaintiff's argument here.

And it is simply impossible for the plaintiffs to get around the fact that a Proposition 65 warning conveys the type of information that the FDA would absolutely want to see in a CBE or would cover under the CBE or the other warning provisions regulating -- very specifically regulating OTC

drugs.

So there is sort of a lack of common sense in the arguments that are being made.

Counsel made the argument that the Court is somehow imposing a heightened pleading standard when it would require with respect to the brand manufacturers that the plaintiffs plead that the warning that they are requiring would fall under the CBE changes being affected by the provisions; in other words, that the plaintiffs are required to plead that there is a clinically significant hazard and reasonable evidence of a causal association.

Plaintiffs are assiduously avoiding making that pleading. And there are some obvious reasons that they are doing that.

But the fact is that the way the Court has read the CBE regulations is correct and that the plaintiff's pleadings as they stand in the second-amended complaint quite obviously present this affirmative defense of preemption.

It's far beyond the mere mention of the FDA, as counsel characterized their complaint.

The allegations of the complaint clearly establish that Zantac was an OTC drug, clearly establish that the FDA has authority over the way that that drug is distributed to the public and obviously the complaint clearly alleges that a Prop 65 warning is purportedly required.

Those are the salient facts that trigger this affirmative defense. There is no way for the plaintiffs to get around that.

The idea that the plaintiffs have pleaded that the FDA itself issued some communications that should therefore create some sort of implication of clinically significant hazard or some implication of reasonable evidence of a causal association is belied by the facts of the actual communications themselves. Those communications themselves absolutely avoid specifically making those statements.

And, again, those are not haphazardly issued communications from FDA or from any of the defendants.

So there is absolutely no implication that can properly be made that the FDA somehow established plaintiff's pleading for them when the FDA issued some communications regarding the ranitidine products.

The FDA did not order a recall. That is facially obvious from the FDA's statements. The plaintiff's implication otherwise is incorrect.

Why are the plaintiffs avoiding making this allegation? They're avoiding making this allegation because Prop 65 is simply a square peg in a round hole for this situation.

If they were to make the allegation that there was a clinically significant hazard and that there was a reasonable evidence of a causal association, they would essentially have to get in line with the other plaintiffs in the MDL and in the JCCP. They'd have to prove causal association. They would have to prove that there was reasonable evidence of a causal association.

They don't want to do that, so they don't plead that.

The idea that they should get discovery to somehow

support that type of pleading is also incorrect.

Plaintiffs cite Coleman versus Medtronic for this proposition. In Coleman versus Medtronic, which dealt with a medical device and dealt with the broad allegation that there was a manufacturing defect in that medical device and that there was some violation of the manufacturing specifications and of current manufacturing practices by the defendant, the defense in that case -- the preemption defense in that case said that the plaintiffs would have to specify what that specific manufacturing defect was.

The Court found -- hesitated to dismiss with prejudice a complaint in that situation because that type of information by its very nature was specifically held between the manufacturer and the FDA.

In this case that's absolutely not the case.

Obviously, the manufacturers here strongly deny that there is a causal -- or reasonable evidence of a causal association between the consumption of these products and cancers.

And all the plaintiff would be doing by seeking that discovery would be really getting to the merits of the cases in the MDL and in the JCCP. They would not be addressing a Proposition 65 case which is about whether or not a warning can be required.

The reason there is this disconnect is because, again, a Proposition 65 case just does not lie here, where the FDA governs through very specific OTC regulations the labeling as required and the circumstances under which that labeling can

be changed.

So, you know, we feel it's inappropriate here for the Court to order any discovery before the plaintiff is required to refile an amended complaint if it can.

THE COURT: Okay. Thank you, counsel.

Any additional arguments from defense counsel? Who's next?

No, yes?

All right, thank you. I'm going to give you five minutes to respond, Mr. Todzo and Mann, so you can divide your time however you want.

MR. TODZO: Thank you, your Honor. So this is Mark Todzo now for the purpose the court reporter.

Just, you know, two related points.

I think what we've determined is that FDA has never said that anytime a label has a warning or anytime that a warning is provided under any circumstances, that that written communication or any type of communication becomes a warning.

The FDA has never said that with respect to OTC drugs.

Congress has said it. The FDA never has. The Court would essentially be the first to say that.

So if we're talking about something that is, you know, somewhat ambiguous, which I think at best -- I think it's pretty clear that FDA doesn't govern public communications outside of, you know, 379r(c)(2). But to the extent there is any ambiguity, well, then, the presumption against preemption should apply.

So there should be no preemption of the Prop 65 claim.

And I'm going to say the same thing with respect to section 10(a).

So, you know, the tentative ruling for the Court essentially had to insert language into 10(a), had to insert with respect to warnings in order to arrive at its conclusion.

And defendants accuse us of reading language into -- which I don't think we do, but they accuse us of that.

Well, to the extent that there is ambiguity there, Ms. Mann already talked about how you need to read the statute in a way that accomplishes the purpose of it, but you also need to apply the presumption against preemption.

And in that case if it's a close call, if there is ambiguity, if you're not exactly sure what 10(a) says, in that case the case should proceed. There shouldn't be preemption under that guise.

Then that brings in all the possible, you know, actions that defendants can take.

I had mentioned that I didn't have the cite before, and it is the TR page 22, lines 6 through 9, where the Court explicitly found there were actions that defendants could take to reduce or eliminate the NDMA exposure, and thereby comply with Prop 65.

The Court very rightly, unlike defense counsel, has understood that section 6 compliance means you can either eliminate the exposure or provide a warning.

Obviously, if there is no exposure, there is nothing to warn about, and a defendant is necessarily in compliance with section 6.

I believe Ms. Mann had something briefly to say with respect to the pleading standards, so I'll let him speak to that.

THE COURT: Okay.

MR. MANN: Your Honor, thank you.

I guess I just want to say that on the notion that we're avoiding making some sort of argument as to the CBE in our pleading, under California law we don't have to. And under Gibbons, you only need to plead that there is new information, which the complaint already did.

In terms of the notion that the FDA withdrawal notice wasn't a recall, this just ignores the facts on the ground. Look what everybody hopped and did when FDA said this was the problem.

FDA believes that NDMA contamination presents a cancer risk that affects public health. And it just ignores the facts on the ground to believe that that is not good enough to have the FDA put a warning on the label.

I guess lastly, on the Coleman case, keep in mind that the plaintiffs there were pleading a manufacturing defect claim, so under California law they had to say what the defect was.

This is an affirmative defense. Under California law we don't have to say -- we don't have to plead around and anticipate their defenses. And to the extent we need to do it, yeah.

So I guess that's all I want to say on that, your Honor. Thank you so much for your time.

THE COURT: Thank you, everyone, for your time this morning.

I'll take this matter under submission, and I will issue a final ruling shortly.

I don't think we're here for case management.

Are we here for case management?

I don't think so.

MR. TODZO: We're not, your Honor. You had continued the case management conference to the end of June.

THE COURT: Okay. Thank you.

Well, I'm going to take it under submission. You'll hear from me soon. And I will see you at the end of June.

Thank you very much.

(Proceedings concluded at 11:50 a.m.)

SUPERIOR COURT OF THE STATE OF CALIFORNIA
FOR THE COUNTY OF ALAMEDA

DEPARTMENT 21 HON. WINIFRED Y. SMITH, JUDGE

CENTER FOR ENVIRONMENTAL HEALTH, Plaintiff,	)	
vs.	)	SUPERIOR COURT CASE NO. RG20054985
PERRIGO COMPANY, et al. Defendants.	)	

I, DAVID A. SALYER, Official Pro Tem Reporter of the Superior Court of the State of California, for the County of Los Angeles, do hereby certify that the foregoing pages, 1 through 41, inclusive, comprise a true and correct transcript of the proceedings taken in the above-entitled matter reported by me on May 5, 2021.

DATED: May 7, 2021.

DAVID A. SALYER, CSR, RMR, CRR
Official Pro Tem Court Reporter
CSR No. 4410

California Code of Civil Procedure

Article 5. Transcript or Recording

Section 2025.520

(a) If the deposition testimony is stenographically recorded, the deposition officer shall send written notice to the deponent and to all parties attending the deposition when the Original transcript of the testimony for each session of the deposition is available for reading, correcting, and signing, unless the deponent and the attending parties agree on the record that the reading, correcting, and signing of the transcript of the testimony will be waived or that the reading, correcting, and signing of a transcript of the testimony will take place after the entire deposition has been concluded or at some other specific time.

(b) For 30 days following each notice under subdivision (a), unless the attending parties and the deponent agree on the record or otherwise in writing to a longer or shorter time period, the deponent may change the form or the substance of the answer to a question, and may either approve the transcript of the deposition by signing it, or

refuse to approve the transcript by not signing it.

(c) Alternatively, within this same period, the deponent may change the form or the substance of the answer to any question and may approve or refuse to approve the transcript by means of a letter to the deposition officer signed by the deponent which is mailed by certified or registered mail with return receipt requested. A copy of that letter shall be sent by first-class mail to all parties attending the deposition.

(d) For good cause shown, the court may shorten the 30-day period for making changes, approving, or refusing to approve the transcript.

(e) The deposition officer shall indicate on the original of the transcript, if the deponent has not already done so at the office of the deposition officer, any action taken by the deponent and indicate on the original of the transcript, the deponent's approval of, or failure or refusal to approve, the transcript. The deposition officer shall also notify in writing the parties attending the deposition of any changes which the deponent timely made in person.

(f) If the deponent fails or refuses to approve the transcript within the allotted period, the

deposition shall be given the same effect as though it had been approved, subject to any changes timely made by the deponent.

(g) Notwithstanding subdivision (f), on a seasonable motion to suppress the deposition, accompanied by a meet and confer declaration under Section 2016.040, the court may determine that the reasons given for the failure or refusal to approve the transcript require rejection of the deposition in whole or in part.

(h) The court shall impose a monetary sanction under Chapter 7 (commencing with Section 2023.010) against any party, person, or attorney who unsuccessfully makes or opposes a motion to suppress a deposition under this section, unless the court finds that the one subject to the sanction acted with substantial justification or that other circumstances make the imposition of the sanction unjust.

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VERITEXT LEGAL SOLUTIONS
COMPANY CERTIFICATE AND DISCLOSURE STATEMENT

Veritext Legal Solutions represents that the foregoing transcript is a true, correct and complete transcript of the colloquies, questions and answers as submitted by the court reporter. Veritext Legal Solutions further represents that the attached exhibits, if any, are true, correct and complete documents as submitted by the court reporter and/or attorneys in relation to this deposition and that the documents were processed in accordance with our litigation support and production standards.

Veritext Legal Solutions is committed to maintaining the confidentiality of client and witness information, in accordance with the regulations promulgated under the Health Insurance Portability and Accountability Act (HIPAA), as amended with respect to protected health information and the Gramm-Leach-Bliley Act, as amended, with respect to Personally Identifiable Information (PII). Physical transcripts and exhibits are managed under strict facility and personnel access controls. Electronic files of documents are stored in encrypted form and are transmitted in an encrypted fashion to authenticated parties who are permitted to access the material. Our data is hosted in a Tier 4 SSAE 16 certified facility.

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PROOF OF SERVICE

I, Alexis Pearson, declare:

I am a citizen of the United States and employed in the County of San Francisco, State of California. I am over the age of eighteen (18) years and not a party to this action. My business address is 503 Divisadero Street, San Francisco, CA 94117 and my email address is apearson@lexlawgroup.com.

On October 4, 2021, I served the following document(s) on all interested parties in this action by placing a true copy thereof in the manner and at the addresses indicated below:

NOTICE OF DESIGNATION OF RECORD

☐ **BY MAIL**: I am readily familiar with the firm's practice for collecting and processing mail with the United States Postal Service ("USPS"). Under that practice, mail would be deposited with USPS that same day with postage thereon fully prepaid at San Francisco, California in the ordinary course of business. On this date, I placed sealed envelopes containing the above mentioned documents for collection and mailing following my firm's ordinary business practices.

☒ **BY ELECTRONIC MAIL**: I transmitted a PDF version of the document(s) listed above via email to the email address(es) indicated on the attached service list [or noted above] before 5 p.m. on the date executed.

David A. Salyer
Salyer Court Reporting Services, Inc.
800 W. 1st Street, Suite 1303
Los Angeles, CA, 90012
Davesal55@ccrola.com

Also please see attached service list

☐ **BY OVERNIGHT DELIVERY**: I deposited such document(s) in a box or other facility regularly maintained by FedEx, or delivered such document(s) to a courier or driver authorized by FedEx, with delivery fees paid or provided for, and addressed to the person(s) being served below.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed on October 4, 2021 at San Francisco, California.

Alexis Pearson

SERVICE LIST
CEH v. Perrigo Company, et al.
RG 20-054985

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Exhibit 62

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Superior Court of California, County of Alameda
Rene C. Davidson Alameda County Courthouse

Center for Environmental Health
Plaintiff(s)
VS.
Perrigo Company
Defendant(s)
(Abbreviated Title)

Case No. RG20054985

NOTIFICATION OF FILING NOTICE OF APPEAL

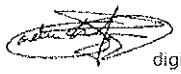
TO EACH PARTY OR TO THE ATTORNEY(S) OF RECORD FOR EACH PARTY:

Please take notice that a Notice of Appeal was filed in the above-entitled action.

APPEAL FILED: 10/07/2021

THIS NOTICE IS GIVEN PURSUANT TO CALIFORNIA RULE OF COURT 8.100(e).

Dated: 10/08/2021 Chad Finke Executive Officer / Clerk of the Superior Court

By  digital
Deputy Clerk

SHORT TITLE:	CASE NUMBER:
Center for Environmental Health VS Perrigo Company	RG20054985

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Superior Court of California, County of Alameda
Rene C. Davidson Alameda County Courthouse

Case Number: RG20054985
Notification of Filing Notice of Appeal of 10/08/2021

DECLARATION OF SERVICE BY MAIL

I certify that I am not a party to this cause and that a true and correct copy of the foregoing document was mailed first class, postage prepaid, in a sealed envelope, addressed as shown on the foregoing document or on the attached, and that the mailing of the foregoing and execution of this certificate occurred at 1225 Fallon Street, Oakland, California.

Executed on 10/08/2021.

Chad Finke Executive Officer / Clerk of the Superior Court

By _____ digital
Deputy Clerk

Exhibit 63

SUPERIOR COURT OF CALIFORNIA
COUNTY OF ALAMEDA

RG20054985 10/26/2021 Hearing on Demurrer - without Motion to Strike in Department 21

Tentative Ruling

The Demurrer to Complaint Filed by Sanofi-Aventis U.S. LLC, Chattem Inc. filed by Sanofi-Aventis U.S. LLC, Chattem Inc. on 07/21/2021 is Overruled.

The demurrer of Sanofi-Aventis and Chattem (collectively "Sanofi") (R#2277974 and R#2277975) is OVERRULED.

RELATED CASES

The court takes judicial notice of the existence of parallel mass tort proceedings concerning MDNA, ranitidine, and the Products. There is a Federal MDL in Florida that concerns claims for personal injuries. There is a California JCCP that concerns claims for personal injuries. (In re Ranitidine Cases, JCCP 5150.)

PROCEDURAL MATTERS

These are demurrers, so the court assumes "the truth of the properly pleaded factual allegations, facts that reasonably can be inferred from those expressly pleaded and matters of which judicial notice has been taken." (Redfearn v. Trader Joe's Co. (2018) 20 Cal.App.5th 989, 996.)

California law is that complaints must be in language that is "ordinary and concise" (CCP 425.10) and "allegations must be liberally construed, with a view to substantial justice between the parties" (CCP 452). In challenges to the pleadings, California courts use the CCP 430.10(e) standard as set out in Blank v. Kirwan (1985) 39 Cal.3d 311, 318.

Sanofi argues that the 3AC does not allege a claim that would not be barred by Sanofi's affirmative defense of preemption. Preemption is an affirmative defense. A plaintiff is not required to anticipate and "plead around" a defendant's anticipated affirmative defenses. (Stowe v. Fritzie Hotels, Inc. (1955) 44 Cal.2d 416, 422.)

Sanofi cites to federal case law for the standard of what a plaintiff must allege in a complaint. The federal case law is not relevant for that purpose. In Bell Atlantic Corp. v. Twombly (2007) 550 U.S. 544, 554-555, the United States Supreme Court set the standard for "what a plaintiff must plead in order to state a claim under § 1 of the Sherman Act." In Ashcroft v. Iqbal (2009) 556 U.S. 662, 678–679, the court extended the pleading requirements of Twombly to complaints generally. California law is different. Like federal law, "California requires a 'high degree of particularity' in the pleading of [antitrust] violations …, and therefore generalized allegations of antitrust violations are usually insufficient." (Marsh v. Anesthesia Services Medical Group, Inc. (2011) 200 Cal.App.4th 480, 493.) California has not, however, extended the heightened pleading standards from antitrust cases to complaints generally.

Sanofi cites to federal case law for the substantive law on preemption. The federal statues and

United States Supreme Court case law are relevant for that purpose. Regarding other federal courts, "While [California trial courts] are not bound by decisions of the lower federal courts, even on federal questions, they are persuasive and entitled to great weight. … where the decisions of the lower federal courts on a federal question are "both numerous and consistent," we should hesitate to reject their authority." (Etcheverry v. Tri-Ag Service, Inc. (2000) 22 Cal.4th 316, 320-321.) (Fair v. BNSF Railway Co. (2015) 238 Cal.App.4th 269, 287.)

The court DENIES Sanofi's requests for judicial notice of FDA press releases. (RJN Exhs A, B, and C.) The court GRANTS Sanofi's requests for judicial notice of its own press release on the withdrawal of Zantac on 10/23/19. (RJN Exh D.) The court is wary of permitting the use of judicial notice to turn a demurrer into a de facto motion for summary judgment. (Richtek USA, Inc. v. uPI Semiconductor Corporation (2015) 242 Cal.App.4th 651, 660.) The court is particularly wary where the basis of the demurrer is an affirmative defense rather than the failure of the plaintiff to state a claim.

The court GRANTS Plaintiff's request for judicial notice of a consent judgment between CEH and Xttrium Laboratories. (Exh 1.) The court can take judicial notice of documents in its own files. The consent judgment between plaintiff and a third party in a different case is, however, not relevant to the adequacy of the complaint in this case.

Plaintiff's opposition to this demurrer states in passing that that it disagrees with the Order's analysis of H&S 25249.10(a). (Oppo at 19-20.) This is not a motion for reconsideration. If plaintiff disagrees with the Order, then plaintiff may seek relief in the Court of Appeal.

THE THIRD AMENDED COMPLAINT (6/9/21)

Sanofi manufactured, imported, distributed, or sold the Products. (3AC, para 5, 6.) The Products are non-prescription, or "over the counter ("OTC") drugs. (3AC, para 1, 20.) The known carcinogen NDMA was in the Products when the consumers bought the products. (3AC, para 17.) Sanofi know or should have known there was NDMA in the Products. (3AC, para 23, 39.)

On 10/18/19, Sanofi initiated a voluntary recall of the Products based on the presence of NDMA. (Def RJN, ExhD.)

The 3AC assets a single cause of action against Sanofi under H&S 25249.6 alleging that it intentionally exposed individuals to NDMA without first giving clear and reasonable warnings. (3AC, para 45-50.)

IMPOSSIBILITY PREMPTION

The demurrer of Sanofi argues that the complaint is inadequate because it does not plead around Sanofi's expected affirmative defense that compliance with Proposition 65 is impossible given: (1) the ability of Sanofi to change labelling under the Changes Being Effected process and (2) the ability of Sanofi to add a Proposition 65 warning to the FDA approved warnings.

"A defendant cannot establish impossibility preemption "merely by demonstrating it is difficult or costly to comply. Rather, it must show using point of sale signs is a "physical impossibility." (People v. Cotter & Co (1997) 53 Cal.App.4th 1373, 1393-1394.)

THE CHANGES BEING MADE PROCESS

The Order of 5/7/21 at pp 9-12 states:

THE CHANGES BEING EFFECTED ("CBE") PROCESS

A Brand Name Defendant can change a label without FDA approval in certain limited circumstances. "Major changes" require FDA preapproval, while certain labeling changes separately defined as "moderate changes" do not. (21 CFR 314.70(c)(6)(iii).)

A Brand Name Defendants can unilaterally make moderate changes, but those are limited to "changes … to reflect newly acquired information … [t]o add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter." (21 CFR 314.70(c)(6)(iii).) The CBE process only permits changes "add[ing] or strengthen[ing] a contraindication, warning, precaution, or adverse reaction" for a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug. (21 CFR 201.57.)

Wyeth v., Levine (2009) 555 US 555, addresses the CBE process and preemption. Procedurally, Wyeth was decided after trial. In Wyeth, a consumer sued the brand-name drug manufacturer for failure to provide an adequate warning on the drug's labeling. (555 US at 559-560). The Supreme Court held that the consumer's labeling claims were not pre-empted because the Changes Being Effected ("CBE") process permitted the brand-name drug manufacturer to "unilaterally strengthen" the warning on the labeling, without waiting for FDA approval. (555 US at 568-569.) The Court stated that it could not conclude that it was impossible for the brand-name drug manufacturer to comply with both its federal-law and state-law duties "absent clear evidence that the FDA would not have approved" a labeling change. (555 US at 571) The brand-name drug manufacturer "offered no such evidence," and the fact that the FDA had previously approved the labeling did "not establish that it would have prohibited such a change." (555 US at 572-573.)

To state a claim for failure-to-warn that is not preempted by the FDCA, a plaintiff must plead "a labeling deficiency that [Defendants] could have corrected using the CBE regulation." (Gibbons v. Bristol-Myers Squibb Co. (2nd Cir. 2019) 919 F.3d 699, 708.)

Turning to this case, the 2AC does not allege that the Brand Name Manufacturers could use the CBE process to present a Proposition 65 warning.

The CBE process requires Brand Name Manufacturers to demonstrate that there a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the

drug. (21 C.F.R. 201.57.)

Proposition 65 applies unless a Brand Name Manufacturer can demonstrate that "the exposure poses no significant risk assuming lifetime exposure at the level in question for substances known to the state to cause cancer, and that the exposure will have no observable effect assuming exposure at one thousand (1,000) times the level in question for substances known to the state to cause reproductive toxicity. (H&S 25249.10(c).)

There is a gap where an exposure is above the level that arguably requires a Proposition 65 warning but below the level that permit a Brand Name Manufacturer to "unilaterally strengthen" the labelling by adding a CBE warning. If the NDMA exposure is in this gap, then federal law preempts Proposition 65. If the NDMA exposure is so high that it both requires a Proposition 65 warning and the manufacturer can use the CBE process, then there is no impossibility preemption because a defendant can comply with both state and federal law.

(End of block quotation.)

The court decides that the Third Amended Complaint adequately pleads a claim that Sanofi could make a label change under the CBE process. The Order at 11 states:

Plaintiff's may amend, if possible, to allege that the NDMA exposure presented a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug. (21 C.F.R. 201.57) and as a result the Brand Name Manufacturers could use the CBE process to unilaterally strengthen the warning on the labeling without waiting for FDA approval.

(End of block quotation.)

The 3AC alleges that the NDMA exposure presented a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug." (3AC at para 28.) This is sufficient.

Regarding the need for evidentiary facts, the Order at 11-12 states:

Plaintiff is not required to allege evidentiary facts to support this allegation. "[A] complaint ordinarily is sufficient if it alleges ultimate rather than evidentiary facts." (Doe v. City of Los Angeles (2007) 42 Cal.4th 531, 550.) Furthermore, preemption is an affirmative defense and a plaintiff is not required to anticipate and "plead around" a defendant's affirmative defenses. (Stowe v. Fritzie Hotels, Inc. (1955) 44 Cal.2d 416, 422.) That said, pleadings that define the issues clearly are important for framing discovery, summary judgment, and trial.

(End of block quotation.)

Sanofi argues that the 3AC does not contain adequate factual allegations to support the allegations. A complaint is not required to include that level of detail. A complaint must be a

statement of the facts constituting the cause of action, in ordinary and concise language." (CCP 425.10(a).) A complaint can be formulaic to some extent. The Judicial Council has approved form complaints. (Form PLD-C-100, Form PLD-PI-100.)

Sanofi argues implicitly that the 3AC must contain factual allegations that suggest that the claim will not be barred by Sanofi's affirmative defense of preemption. A plaintiff is not required to anticipate and "plead around" a defendant's affirmative defenses.

Assuming that plaintiffs generally had some obligation to anticipate and plead around affirmative defenses, plaintiffs in this case could not reasonably be expected to plead evidentiary facts. Sanofi's affirmative defense in this case is preemption under the FDCA. Under the CBE exemption, "a drug manufacturer can be held liable for a state law failure-to-warn claim if it could have revised its label using the CBE process but failed to do so. … state-law failure-to-warn claims concerning prescription drugs are preempted only where there is clear evidence that the FDA would have rejected the proposed label change." (Risperdal and Invega Cases (2020) 49 Cal.App.5th 942, 956.)

Plaintiff could not be expected to know information in defendants' control such as whether defendants had "newly acquired information" that might have permitted, or required, it to make a label change under the CBE procedure. (Compare Committee on Children's Television, Inc. v. General Foods Corp. (1983) 35 Cal.3d 197, 217 ["Less specificity is required [in fraud claims] when it appears from the nature of the allegations that the defendant must necessarily possess full information concerning the facts of the controversy"].)

THE ABILITY OF SANOFI TO ADD A PROPOSITION 65 WARNING TO AN OVER THE COUNTER DRUG LABEL

The parties agree that the Order of 5/7/21 did not address whether if Sanofi could have made a substantive label change under the CBE process whether it then would be impossible for any such label to comply with both the federal regulations regarding the format of warnings on OTC drugs and the format of the safe harbor warning under California's Proposition 65. (Opening at 9:15-16.)

The court decides that it might be possible for Sanofi to comply with both the federal law on OTC drug labels and California's Proposition 65.

Sanofi argues that 21 CFR 314.70 permits the CBE process only when a substantive change is necessary to "add or strengthen a contraindication, warning, precaution, or adverse reaction" (21 CFR 314.70(c)(6)) and that a Proposition 65 warning is just a warning of the possible presence of a hazardous chemical. This argument has no merit. The Order of 5/7/21 at p12 states; "If the NDMA exposure is so high that it both requires a Proposition 65 warning and the manufacturer can use the CBE process, then there is no impossibility preemption because a defendant can comply with both state and federal law."

Sanofi argues that 21 CFR 201.66 sets specific parameters for format of OTC drug labels and that it is impossible for it to comply with both the format requirements of 21 CFR 201.66 and the format requirement of the Proposition 65 safe harbor warning in 27 CCR 25601 et seq. This argument has no merit.

Sanofis's argument does not acknowledge the possibility that it could have added text about NDMA to its labelling that both complied with the format requirements of 21 CFR 201 and also provided the "clear and reasonable warning" required by Proposition 65. Sanofi instead argues implicitly that the only way to comply with the Proposition 65 warning requirement is to have a warning in the Proposition 65 safe harbor.

California law does not require use of the Proposition 65 safe harbor warning at 27 CCR 25601 et seq. Proposition 65 at H&S 25249.6 requires only a "clear and reasonable warning." The Proposition 65 safe harbor warnings define a safe harbor but they are not required. The Proposition 65 safe harbor warnings are "optional." (Dowhal v. SmithKline Beecham Consumer Healthcare (2004) 32 Cal.4th 910, 918.) The existence of a specific "safe harbor" for statutory compliance does not require the use of the safe harbor or prevent a person or entity from otherwise complying with a statute.

Sanofi's strongest argument is that 21 CFR 201.66(c) regulates the content of the "Drug Facts" and the permissible content does not permit a Proposition 65 warning. 21 CFR 201.66(c) states: "Content requirements. The outside container or wrapper of the retail package, or the immediate container label if there is no outside container or wrapper, shall contain the title, headings, subheadings, and information set forth in paragraphs (c)(1) through (c)(8) of this section, and may contain the information under the heading in paragraph (c)(9) of this section, in the order listed." The text of this suggests that if information is not identified at (c)(1) through (c)(9), then it cannot be in the "Drug Facts" section.

Sanofi's weaker argument is that 21 CFR 201.66(d) regulates the format of the "Drug Facts" and the permissible format does not permit a Proposition 65 warning. This has no merit because a Proposition 65 warning can be in any format that provides a "clear and reasonable warning." The FDA presumably decided that its 21 CFR 201.66(d) format for "Drug Facts" is "clear and reasonable."

Plaintiff's primary argument is that federal law permits Sanofi to make a Proposition 65 warning outside the "Drug Facts" or other FDA approved label or labelling This has support in general policy because Congress enacted an express preemption provision for OTC drugs (21 USC 379r(a) ["National uniformity for nonprescription drugs"]), but the preemption provision has an express exception for Proposition 65 (21 USC 379r(d)(2)). This strongly suggests that Congress did not intend to interfere with California's enforcement of Proposition 65 as it applies to OTC drugs.

A Proposition 65 warning must be made in the context of a permissible FDA approved label or labelling. Given the Congressional intent in 21 USC 379r(d)(2) to not interfere with interfere

with California's enforcement of Proposition 65 as it applies to OTC drugs, the court reads 21 CFR 201.66 to permit both a Proposition 65 warning in the context of "Drug Facts" or a Proposition 65 warning outside of "Drug Facts." Where Congressional intent in a statute conflict with a regulation and the two cannot be reconciled, then the Congressional intent in the statute prevails.

FURTHER PROCEEDINGS

Sanofi must file an answer on or before 11/19/21.

Exhibit 64

SUPERIOR COURT OF CALIFORNIA, COUNTY OF ALAMEDA

Rene C. Davidson Courthouse, Department 21

JUDICIAL OFFICER: HONORABLE EVELIO GRILLO

Courtroom Clerk: Sonya De Baca CSR: None

RG20054985 October 26, 2021
10:00 AM

Center for Environmental Health VS Perrigo Company

MINUTES

APPEARANCES:

Plaintiff Center for Environmental Health not appearing.
Defendant Perrigo Company not appearing.
Defendant Target Corporation not appearing.
Defendant Granules USA, Inc. not appearing.
Defendant Apotex Corp. not appearing.
Defendant 7-Eleven, Inc. not appearing.
Defendant Sanofi-Aventis U.S. LLC not appearing.
Defendant Chattem Inc. not appearing.
Defendant Reddy's Laboratories Louisiana, LLc not appearing.
Defendant Dr. Reddy's Laboratories, Inc. not appearing.
Defendant Granules Pharmaceuticals, Inc. not appearing.

Other Appearance Notes: Court Reporter:
Ryan Wheeler, CSR#13717
ryanwheeler91@yahoo.com

NATURE OF PROCEEDINGS: Hearing on Demurrer - without Motion to Strike; Case Management Conference

CMC continued 60 days, pending the court's ruling on the demurrer.

FURTHER CONFERENCE
A Case Management Conference is scheduled for 12/28/2021 at 10:00 AM in Department 21.

Updated Case Management Statements in compliance with Rule of Court 3.725, on Judicial Council Form CM-110, must be filed no later than 12/13/2021. If the foregoing date is a court holiday or a weekend, the time is extended to the next business day.

The Court takes the Hearing on Demurrer - without Motion to Strike under submission.

The Court orders counsel to obtain a copy of this order from the eCourt portal.

Chad Finke, Executive Officer / Clerk of the Court

By: S. Debaca, Deputy Clerk

Minutes of: 10/26/2021
Entered on: 10/26/2021

Exhibit 65

SUPERIOR COURT OF CALIFORNIA, COUNTY OF ALAMEDA
APPEALS UNIT
Rene C. Davidson Courthouse
1225 Fallon Street Rm G4, Oakland, CA 94612
(510)891-6001
Appealsunit@alameda.courts.ca.gov

Center for Environmental Health

Appellant(s)

Vs.

Perrigo Company, Target Corporation, Granules USA, Inc., Apotex Corp., 7-Eleven, Inc., Sanofi-Aventis U.S. LLC, Chattem Inc., Reddy's Laboratories Louisiana, LLc, Dr. Reddy's Laboratories, Inc., Granules Pharmaceuticals, Inc.

Respondent(s)

Case No.: RG20054985

Appellate No.:

C E R T I F I C A T E

I, Chad Finke, Executive Officer/Clerk of the Superior Court of the State of California, in and for the County of Alameda, which is a court of record of the State of California, having by law a seal, do hereby certify that in the above-entitled action:

Appellant proceeded 8.124 - The Recorder's Transcript dated: May 5, 2021 is attached to the Appellant's Designation.

IN WITNESS WHEREOF, I have hereby set my hand and affixed the seal of said Superior Court this 27th day of October, 2021.

Chad Finke, Executive Officer / Clerk of the Court

By: S. Martinez, Deputy Clerk

Exhibit 66

SUPERIOR COURT OF CALIFORNIA, COUNTY OF ALAMEDA

Rene C. Davidson Courthouse

Center for Environmental Health Plaintiff/Petitioner(s) vs. Perrigo Company et al Defendant/Respondent(s)	No. RG20054985 Date: 12/08/2021 Time: 11:43 AM Dept: 21 Judge: Evelio Grillo ORDER re: Ruling on Submitted Matter

The Court, having taken the matter under submission on 10/26/2021, now rules as follows: The demurrer of Sanofi-Aventis and Chattem (collectively "Sanofi") (R#2277974 and R#2277975) is OVERRULED.

RELATED CASES

The court takes judicial notice of the existence of parallel mass tort proceedings concerning MDNA, ranitidine, and the Products. There is a Federal MDL in Florida that concerns claims for personal injuries. There is a California JCCP that concerns claims for personal injuries. (In re Ranitidine Cases, JCCP 5150.)

PROCEDURAL MATTERS

These are demurrers, so the court assumes "the truth of the properly pleaded factual allegations, facts that reasonably can be inferred from those expressly pleaded and matters of which judicial notice has been taken." (Redfearn v. Trader Joe's Co. (2018) 20 Cal.App.5th 989, 996.)

California law is that complaints must be in language that is "ordinary and concise" (CCP 425.10) and "allegations must be liberally construed, with a view to substantial justice between the parties" (CCP 452). In challenges to the pleadings, California courts use the CCP 430.10(e) standard as set out in Blank v. Kirwan (1985) 39 Cal.3d 311, 318.

Sanofi argues that the 3AC does not allege a claim that would not be barred by Sanofi's affirmative defense of preemption. Preemption is an affirmative defense. A plaintiff is not required to anticipate and "plead around" a defendant's anticipated affirmative defenses. (Stowe v. Fritzie Hotels, Inc. (1955) 44 Cal.2d 416, 422.)

Sanofi cites to federal case law for the standard of what a plaintiff must allege in a complaint. The federal case law is not relevant for that purpose. In Bell Atlantic Corp. v. Twombly (2007) 550 U.S. 544, 554-555, the United States Supreme Court set the standard for "what a plaintiff must plead in order to state a claim under § 1 of the Sherman Act." In Ashcroft v. Iqbal (2009) 556 U.S. 662, 678–679, the court extended the pleading requirements of Twombly to complaints generally. California law is different. Like federal law, "California requires a 'high degree of

particularity' in the pleading of [antitrust] violations …, and therefore generalized allegations of antitrust violations are usually insufficient." (Marsh v. Anesthesia Services Medical Group, Inc. (2011) 200 Cal.App.4th 480, 493.) California has not, however, extended the heightened pleading standards from antitrust cases to complaints generally.

Sanofi cites to federal case law for the substantive law on preemption. The federal statues and United States Supreme Court case law are relevant for that purpose. Regarding other federal courts, "While [California trial courts] are not bound by decisions of the lower federal courts, even on federal questions, they are persuasive and entitled to great weight. … where the decisions of the lower federal courts on a federal question are "both numerous and consistent," we should hesitate to reject their authority." (Etcheverry v. Tri-Ag Service, Inc. (2000) 22 Cal.4th 316, 320-321.) (Fair v. BNSF Railway Co. (2015) 238 Cal.App.4th 269, 287.)

The court DENIES Sanofi's requests for judicial notice of FDA press releases. (RJN Exhs A, B, and C.) The court GRANTS Sanofi's requests for judicial notice of its own press release on the withdrawal of Zantac on 10/23/19. (RJN Exh D.) The court is wary of permitting the use of judicial notice to turn a demurrer into a de facto motion for summary judgment. (Richtek USA, Inc. v. uPI Semiconductor Corporation (2015) 242 Cal.App.4th 651, 660.) The court is particularly wary where the basis of the demurrer is an affirmative defense rather than the failure of the plaintiff to state a claim.

The court GRANTS Plaintiff's request for judicial notice of a consent judgment between CEH and Xttrium Laboratories. (Exh 1.) The court can take judicial notice of documents in its own files. The consent judgment between plaintiff and a third party in a different case is, however, not relevant to the adequacy of the complaint in this case.

Plaintiff's opposition to this demurrer states in passing that that it disagrees with the Order's analysis of H&S 25249.10(a). (Oppo at 19-20.) This is not a motion for reconsideration. If plaintiff disagrees with the Order, then plaintiff may seek relief in the Court of Appeal.

THE THIRD AMENDED COMPLAINT (6/9/21)

Sanofi manufactured, imported, distributed, or sold the Products. (3AC, para 5, 6.) The Products are non-prescription, or "over the counter ("OTC") drugs. (3AC, para 1, 20.) The known carcinogen NDMA was in the Products when the consumers bought the products. (3AC, para 17.) Sanofi know or should have known there was NDMA in the Products. (3AC, para 23, 39.)

On 10/18/19, Sanofi initiated a voluntary recall of the Products based on the presence of NDMA. (Def RJN, ExhD.)

The 3AC assets a single cause of action against Sanofi under H&S 25249.6 alleging that it intentionally exposed individuals to NDMA without first giving clear and reasonable warnings. (3AC, para 45-50.)

IMPOSSIBILITY PREMPTION

The demurrer of Sanofi argues that the complaint is inadequate because it does not plead around Sanofi's expected affirmative defense that compliance with Proposition 65 is impossible given: (1) the ability of Sanofi to change labelling under the Changes Being Effected process and (2) the ability of Sanofi to add a Proposition 65 warning to the FDA approved warnings.

"A defendant cannot establish impossibility preemption "merely by demonstrating it is difficult or costly to comply. Rather, it must show using point of sale signs is a "physical impossibility." (People v. Cotter & Co (1997) 53 Cal.App.4th 1373, 1393-1394.)

THE CHANGES BEING MADE PROCESS

The Order of 5/7/21 at pp 9-12 states:

THE CHANGES BEING EFFECTED ("CBE") PROCESS

A Brand Name Defendant can change a label without FDA approval in certain limited circumstances. "Major changes" require FDA preapproval, while certain labeling changes separately defined as "moderate changes" do not. (21 CFR 314.70(c)(6)(iii).)

A Brand Name Defendants can unilaterally make moderate changes, but those are limited to "changes … to reflect newly acquired information … [t]o add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter." (21 CFR 314.70(c)(6)(iii).) The CBE process only permits changes "add[ing] or strengthen[ing] a contraindication, warning, precaution, or adverse reaction" for a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug. (21 CFR 201.57.)

Wyeth v., Levine (2009) 555 US 555, addresses the CBE process and preemption. Procedurally, Wyeth was decided after trial. In Wyeth, a consumer sued the brand-name drug manufacturer for failure to provide an adequate warning on the drug's labeling. (555 US at 559-560). The Supreme Court held that the consumer's labeling claims were not pre-empted because the Changes Being Effected ("CBE") process permitted the brand-name drug manufacturer to "unilaterally strengthen" the warning on the labeling, without waiting for FDA approval. (555 US at 568-569.) The Court stated that it could not conclude that it was impossible for the brand-name drug manufacturer to comply with both its federal-law and state-law duties "absent clear evidence that the FDA would not have approved" a labeling change. (555 US at 571) The brand-name drug manufacturer "offered no such evidence," and the fact that the FDA had previously approved the labeling did "not establish that it would have prohibited such a change." (555 US at 572-573.)

To state a claim for failure-to-warn that is not preempted by the FDCA, a plaintiff must plead "a labeling deficiency that [Defendants] could have corrected using the CBE regulation." (Gibbons v. Bristol-Myers Squibb Co. (2nd Cir. 2019) 919 F.3d 699, 708.)

Turning to this case, the 2AC does not allege that the Brand Name Manufacturers could use the CBE process to present a Proposition 65 warning.

The CBE process requires Brand Name Manufacturers to demonstrate that there a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug. (21 C.F.R. 201.57.)

Proposition 65 applies unless a Brand Name Manufacturer can demonstrate that "the exposure poses no significant risk assuming lifetime exposure at the level in question for substances known to the state to cause cancer, and that the exposure will have no observable effect assuming exposure at one thousand (1,000) times the level in question for substances known to the state to cause reproductive toxicity. (H&S 25249.10(c).)

There is a gap where an exposure is above the level that arguably requires a Proposition 65 warning but below the level that permit a Brand Name Manufacturer to "unilaterally strengthen" the labelling by adding a CBE warning. If the NDMA exposure is in this gap, then federal law preempts Proposition 65. If the NDMA exposure is so high that it both requires a Proposition 65 warning and the manufacturer can use the CBE process, then there is no impossibility preemption because a defendant can comply with both state and federal law.

(End of block quotation.)

The court decides that the Third Amended Complaint adequately pleads a claim that Sanofi could make a label change under the CBE process. The Order at 11 states:

Plaintiff's may amend, if possible, to allege that the NDMA exposure presented a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug. (21 C.F.R. 201.57) and as a result the Brand Name Manufacturers could use the CBE process to unilaterally strengthen the warning on the labeling without waiting for FDA approval.

(End of block quotation.)

The 3AC alleges that the NDMA exposure presented a "clinically significant hazard" for which there is "reasonable evidence of a causal association" with the drug." (3AC at para 28.) This is sufficient.

Regarding the need for evidentiary facts, the Order at 11-12 states:

Plaintiff is not required to allege evidentiary facts to support this allegation. "[A] complaint ordinarily is sufficient if it alleges ultimate rather than evidentiary facts." (Doe v. City of Los Angeles (2007) 42 Cal.4th 531, 550.) Furthermore, preemption is an affirmative defense and a plaintiff is not required to anticipate and "plead around" a defendant's affirmative defenses. (Stowe v. Fritzie Hotels, Inc. (1955) 44 Cal.2d 416, 422.) That said, pleadings that define the issues clearly are important for framing discovery, summary judgment, and trial.

(End of block quotation.)

Sanofi argues that the 3AC does not contain adequate factual allegations to support the allegations. A complaint is not required to include that level of detail. A complaint must be a

statement of the facts constituting the cause of action, in ordinary and concise language." (CCP 425.10(a).) A complaint can be formulaic to some extent. The Judicial Council has approved form complaints. (Form PLD-C-100, Form PLD-PI-100.)

Sanofi argues implicitly that the 3AC must contain factual allegations that suggest that the claim will not be barred by Sanofi's affirmative defense of preemption. A plaintiff is not required to anticipate and "plead around" a defendant's affirmative defenses.

Assuming that plaintiffs generally had some obligation to anticipate and plead around affirmative defenses, plaintiffs in this case could not reasonably be expected to plead evidentiary facts. Sanofi's affirmative defense in this case is preemption under the FDCA. Under the CBE exemption, "a drug manufacturer can be held liable for a state law failure-to-warn claim if it could have revised its label using the CBE process but failed to do so. … state-law failure-to-warn claims concerning prescription drugs are preempted only where there is clear evidence that the FDA would have rejected the proposed label change." (Risperdal and Invega Cases (2020) 49 Cal.App.5th 942, 956.)

Plaintiff could not be expected to know information in defendants' control such as whether defendants had "newly acquired information" that might have permitted, or required, it to make a label change under the CBE procedure. (Compare Committee on Children's Television, Inc. v. General Foods Corp. (1983) 35 Cal.3d 197, 217 ["Less specificity is required [in fraud claims] when it appears from the nature of the allegations that the defendant must necessarily possess full information concerning the facts of the controversy"].)

THE ABILITY OF SANOFI TO ADD A PROPOSITION 65 WARNING TO AN OVER THE COUNTER DRUG LABEL

The parties agree that the Order of 5/7/21 did not address whether if Sanofi could have made a substantive label change under the CBE process whether it then would be impossible for any such label to comply with both the federal regulations regarding the format of warnings on OTC drugs and the format of the safe harbor warning under California's Proposition 65. (Opening at 9:15-16.)

The court decides that it might be possible for Sanofi to comply with both the federal law on OTC drug labels and California's Proposition 65.

Sanofi argues that 21 CFR 314.70 permits the CBE process only when a substantive change is necessary to "add or strengthen a contraindication, warning, precaution, or adverse reaction" (21 CFR 314.70(c)(6)) and that a Proposition 65 warning is just a warning of the possible presence of a hazardous chemical. This argument has no merit. The Order of 5/7/21 at p12 states; "If the NDMA exposure is so high that it both requires a Proposition 65 warning and the manufacturer can use the CBE process, then there is no impossibility preemption because a defendant can comply with both state and federal law."

Sanofi argues that 21 CFR 201.66 sets specific parameters for format of OTC drug labels and that it is impossible for it to comply with both the format requirements of 21 CFR 201.66 and the

format requirement of the Proposition 65 safe harbor warning in 27 CCR 25601 et seq. This argument has no merit.

Sanofis's argument does not acknowledge the possibility that it could have added text about NDMA to its labelling that both complied with the format requirements of 21 CFR 201 and also provided the "clear and reasonable warning" required by Proposition 65. Sanofi instead argues implicitly that the only way to comply with the Proposition 65 warning requirement is to have a warning in the Proposition 65 safe harbor.

California law does not require use of the Proposition 65 safe harbor warning at 27 CCR 25601 et seq. Proposition 65 at H&S 25249.6 requires only a "clear and reasonable warning." The Proposition 65 safe harbor warnings define a safe harbor but they are not required. The Proposition 65 safe harbor warnings are "optional." (Dowhal v. SmithKline Beecham Consumer Healthcare (2004) 32 Cal.4th 910, 918.) The existence of a specific "safe harbor" for statutory compliance does not require the use of the safe harbor or prevent a person or entity from otherwise complying with a statute.

Sanofi's strongest argument is that 21 CFR 201.66(c) regulates the content of the "Drug Facts" and the permissible content does not permit a Proposition 65 warning. 21 CFR 201.66(c) states: "Content requirements. The outside container or wrapper of the retail package, or the immediate container label if there is no outside container or wrapper, shall contain the title, headings, subheadings, and information set forth in paragraphs (c)(1) through (c)(8) of this section, and may contain the information under the heading in paragraph (c)(9) of this section, in the order listed." The text of this suggests that if information is not identified at (c)(1) through (c)(9), then it cannot be in the "Drug Facts" section.

Sanofi's weaker argument is that 21 CFR 201.66(d) regulates the format of the "Drug Facts" and the permissible format does not permit a Proposition 65 warning. This has no merit because a Proposition 65 warning can be in any format that provides a "clear and reasonable warning." The FDA presumably decided that its 21 CFR 201.66(d) format for "Drug Facts" is "clear and reasonable."

Plaintiff's primary argument is that federal law permits Sanofi to make a Proposition 65 warning outside the "Drug Facts" or other FDA approved label or labelling This has support in general policy because Congress enacted an express preemption provision for OTC drugs (21 USC 379r(a) ["National uniformity for nonprescription drugs"]), but the preemption provision has an express exception for Proposition 65 (21 USC 379r(d)(2)). This strongly suggests that Congress did not intend to interfere with California's enforcement of Proposition 65 as it applies to OTC drugs.

A Proposition 65 warning must be made in the context of a permissible FDA approved label or labelling. Given the Congressional intent in 21 USC 379r(d)(2) to not interfere with interfere with California's enforcement of Proposition 65 as it applies to OTC drugs, the court reads 21 CFR 201.66 to permit both a Proposition 65 warning in the context of "Drug Facts" or a Proposition 65 warning outside of "Drug Facts." Where Congressional intent in a statute conflict with a regulation and the two cannot be reconciled, then the Congressional intent in the statute

prevails.

FURTHER PROCEEDINGS

Sanofi must file an answer on or before 11/19/21.

The Court orders counsel to obtain a copy of this order from the eCourt portal.

Dated: 12/08/2021

Evelio Grillo / Judge