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 2 (EXHIBITS 19-34)(AA0384-AA659)

LEXINGTON LAW GROUP
Mark N. Todzo, State Bar No. 168389
Joseph Mann, State Bar No. 207968
503 Divisadero Street
San Francisco, CA 94117
Telephone: (415) 913-7800
Facsimile: (415) 759-4112

Attorneys for Appellant and Plaintiff
CENTER FOR ENVIRONMENTAL HEALTH

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GEORGE GIGOUNAS (Bar No. CA-209334)
george.gigounas@dlapiper.com
GREGORY SPERLA (Bar No. CA-278062)
greg.sperla@dlapiper.com
SEAN NEWLAND (Bar No. CA-300928)
sean.newland@dlapiper.com
DLA PIPER LLP (US)
555 Mission Street
Suite 2400
San Francisco, California 94105-2933
Tel: 415.836.2500
Fax: 415.836.2501

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

DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S NOTICE OF DEMURRER AND DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT; MEMORANDUM OF POINTS AND AUTHORITIES

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

TO ALL PARTIES AND TO THEIR ATTORNEYS OF RECORD HEREIN:

PLEASE TAKE NOTICE THAT on April 30, 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 Second 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 Greg Sperla, 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: February 25, 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 SECOND AMENDED COMPLAINT

Defendants Chattem, Inc. and Sanofi-Aventis U.S. LLC demur to Plaintiff Center for Environmental Health's Second 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: February 25, 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

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MEMORANDUM OF POINTS AND AUTHORITIES

I. INTRODUCTION

Requiring a Proposition 65 warning on the Food & Drug Administration ("FDA")-approved label of a federally regulated over-the-counter drug ("OTC") conflicts with mandatory, preemptive federal law governing drug labeling. As with all OTC drugs, Defendants may not change the Zantac label without prior FDA approval unless authorized via the narrow Changes Being Effected ("CBE") process. 21 C.F.R. § 314.70. But even then, a CBE-permitted warning would need to comply with the specific content and format requirements provided by federal regulations for OTC drugs. 21 C.F.R. § 201.66 ("An OTC drug product that is not in compliance with the format and content requirements in this section is subject to regulatory action."). The Proposition 65 warning sought by Plaintiff Center for Environmental Health conflicts with these mandatory federal requirements for OTC drugs and is therefore preempted by federal law.

By design, federal law does not grant drug manufacturers the discretion to alter drug labeling unilaterally—for good reason. *See Robinson v. McNeil Consumer Healthcare*, 615 F.3d 861, 873 (7th Cir. 2010) (failure to warn claim preempted where FDA decided requiring warning "would confuse rather than inform"). Federal law instead requires that OTC manufacturers provide *only* those warnings in OTC labeling approved by FDA as part of the New Drug Application ("NDA") process—in precisely the approved manner. 21 U.S.C. § 355. Accordingly, labeling-based claims like Proposition 65 can survive preemption only if the CBE permits an OTC manufacturer to modify its FDA-approved labeling on its own.

The Proposition 65 warning sought here does not satisfy the requirements for a label change under the CBE regulation and therefore its addition to the Zantac label would violate the prohibition in § 314.70(b)(2)(v)(A) against unauthorized changes. A Proposition 65 warning about the possible presence of a carcinogenic compound in Zantac is not a category of labeling information that may be modified through the narrow CBE process, nor does the Second Amended Complaint ("SAC") allege otherwise. 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. *See* 21 C.F.R. § 314.70,

§201.57. Yet, the SAC alleges neither a clinically significant hazard nor a casual association of such a hazard with Zantac, without which Defendants are prohibited from departing from FDA-approved labeling.

Moreover, Defendants could not include this warning without running afoul of the formatting regulations for OTC drugs. 21 C.F.R. § 201.66(d). OTC drug regulations only permit specific categories of warnings on OTC drug labels, not including Proposition 65-type warnings of N-Nitrosodimethylamine ("NDMA") exposure. *See id*. § 201.66(c)(5). Those regulations further specify content and formatting of OTC drug warnings down to the styles, fonts, colors, spacing, and graphics to be employed, virtually all of which are incompatible with the safe-harbor warning required of Proposition 65 regulations. *See* 27 C.C.R. §§ 25601, *et seq.* A Proposition 65 warning would force Defendants to violate the requirement that OTC labeling comply with those strictures. *See id*. § 201.66(g).

The Supremacy Clause of the United States Constitution preempts state laws in conflict with federal law, and California's Proposition 65 exempts chemical exposure warnings governed by federal law. Because Defendants cannot comply with both Proposition 65 and federal law, state and federal law bar this action, and this Court should sustain Defendants' demurrer with prejudice.

II. BACKGROUND

A. FDA's Exclusive Framework for Approval and Marketing of Drugs

Under the Federal Drug and Cosmetic Act ("FDCA"), before a manufacturer may introduce any new medication into the market—prescription or OTC—the FDA must evaluate it through a rigorous scientific review process and approve it as safe and effective for its intended use. 21 U.S.C. §§ 355(a), 393(b)(2)(B). Zantac started as a prescription drug and thus followed the NDA process. *See* 21 U.S.C. §§ 321(p), 352, 355(a); 21 C.F.R. §§ 330.1, 330.10. The FDA approved some dosages of Zantac for OTC use, but only after NDAs were submitted and after FDA conducted its scientific

review.[1] *See* Sperla Decl., ¶¶ 4-8, Exhs. A-E;[2] Request for Judicial Notice ("RJN").

A manufacturer seeking approval of a new medication through the NDA process must submit a detailed application with "substantial evidence" that affirmatively demonstrates the medication is safe and effective. *See* 21 U.S.C. §§ 355(a), (b)(1); 21 C.F.R. §§ 314.1–314.3, 314.50. If the FDA's independent review concludes the medication is safe and effective for the indication specified in the proposed label, it approves the NDA. *See* 21 U.S.C. § 355; 21 C.F.R. § 314.105(b). A manufacturer requesting approval for a new indication, dosage, or formulation must submit a Supplemental NDA, which again must undergo independent and rigorous FDA scientific review. *See* 21 C.F.R. § 314.70.

Where a manufacturer seeks approval for an OTC version of a prescription medication, the related NDA must include data showing FDA the medication is appropriate for self-administration. *See* 21 C.F.R. § 310.200(b); *see also* 21 U.S.C. §§ 353(b)(3), 355(c)–(d). This may include studies showing that the product's labeling can be read, understood, and followed by the consumer without a health care provider's guidance. *See* James T. O'Reilly and Katharine A. Van Tassel, *Prescription Drug to OTC Drug Switches*, Food and Drug Admin. § 13:37 (4th ed. 2020). The FDA reviews the new data with any information known about the medication from its history of prescription use. *Id.*

NDA approval is subject to the condition that the *exact* language approved by FDA in the marketing application process appears on the labeling or packaging. *See* 21 C.F.R. §§ 314.70(b), (c), 314.71. 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). "[T]he first clause 'clearly embraces advertising or descriptive matter that goes with the package in which the articles are transported.'" *Strayhorn v. Wyeth*

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[1] OTC drugs may be marketed in the United States in compliance with an OTC drug monograph, under the authority of an approved product-specific NDA, or an abbreviated new drug application. *See* 21 U.S.C. § 355(b)(1)-(2); § 355(j); 21 C.F.R. Part 300. Through the monograph process, the FDA reviews the active ingredients and labeling of certain groups of medications based upon therapeutic classes of drugs instead of evaluating individual medications. 21 C.F.R. §§ 330.1, 330.10. Zantac was approved pursuant to an NDA not a monograph.

[2] Exhibit A (FDA letter dated December 19, 1995 approving NDA for OTC Zantac 75mg); Exhibit B (FDA letter dated August 31, 2004 approving NDA for OTC Zantac 150mg); Exhibit C (copy of FDA drug information website page for Zantac 75mg listing the NDA number and FDA approval date, among other information); Exhibit D (copy of FDA drug information website page for Zantac 75mg listing the NDA number and FDA approval date, among other information); Exhibit E (copy of FDA's "Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations" listing both Zantac OTC formulations).

Pharmaceuticals, Inc., 737 F.3d 378, 394 (6th Cir. 2013) (quoting *Kordel v. United States*, 335 U.S. 345, 349-50 (1948)). "With respect to the second clause, '[o]ne article or thing is accompanied by another when it supplements or explains it…. No physical attachment one to the other is necessary.'" *Id.* (quoting *Kordel*, 335 U.S. at 349-50). Stated plainly, federal law *broadly* defines "labeling" to include "brochures, booklets, mailings, catalogues, films, sound recordings, and literature, among other things," and it requires "consisten[cy] with the drug's approved labeling." *Id*. (citing 21 C.F.R. §§ 202.1(l)(2), 201.100(d)(1), 202.1(e)(4)).

B. OTC Drug Labeling

FDA comprehensively dictates the form and substance of all drug labeling, including OTC drugs. Zantac, like all OTC drugs, is subject to specific requirements governing both its content and its formatting, including warnings, contraindications, and adverse reactions. *See* 21 C.F.R. § 201.66, § 314.105(b).

Most revisions to drug labels require prior FDA approval. *Id.* § 314.70(b) (describing "prior approval supplement[s]"). A brand manufacturer of an NDA-approved drug may change the labeling without FDA pre-approval only if those changes fit special criteria that are not met here. *See, e.g.*, *id.* § 314.70(c)(6)(iii)(A) ("Changes Being Effected" process). Advertising of an NDA-approved medication must stay consistent with the labeling. *See* 21 U.S.C. § 352(f)(1). Marketing a drug with a label that is not FDA-approved is unlawful. *See* 21 U.S.C. §§ 321(p), 331(a), (d), 332(a), 333(a), 334, 337, 355(a), (d). *See also* FDA, Guidance: Drug Safety Information – FDA's Communication to the Public, at 6-7 (Mar. 2012) ("FDA-approved prescribing information for health care professionals – and patient package inserts and Medication Guides for patients – is the primary source of established information about a drug's safety and efficacy; it summarizes the essential scientific information needed for the safe and effective use of the drug."); Sperla Decl., ¶ 9, Exh. F; RJN.[3]

The FDA also closely regulates changes to the ingredients or composition of drug products. Without its express prior approval, a manufacturer may not make any changes to the "qualitative or

[3] Available at www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm295217.pdf

quantitative formulation of the drug product, including active ingredients, or in the specifications provided in the approved application." 21 C.F.R. § 314.70(b)(2)(i). Active ingredient changes in an FDA-approved medication may not occur without an entirely new NDA process. *Id.* § 314.70(h).

C. Withdrawal of Zantac in 2019

Where it becomes known that an OTC drug contains a substance the FDA thinks may lead to significant illness or injury, and the problem rises to the level that the risks of use outweigh the benefits, the FDCA's consumer-protection mechanism as mandated in the statute is recall. *See* 21 C.F.R. § 7.45(a)(1)-(2) (the FDA "may request a firm to initiate a recall" where the product is in the market and may "present[] a risk of illness or injury"). On September 13, 2019, the FDA issued a statement that alerted the public it was investigating NDMA in ranitidine but advised that "[a]lthough NDMA may cause harm in large amounts, the levels the FDA [was] finding in ranitidine from preliminary tests barely exceed amounts you might expect to find in common foods." *See* Sperla Decl., ¶ 10, Exh. G (September 13, 2019 statement on NDMA in ranitidine); RJN. The FDA subsequently declined to issue a recall, *id.*, and Defendants issued a voluntary withdrawal of all Zantac products on October 18, 2019, 31 days before Plaintiff issued their Notice of Violation of Proposition 65.

The FDA issued several updates thereafter and then, on April 1, 2020, "announced it [was] requesting manufacturers withdraw all prescription and over-the-counter (OTC) ranitidine drugs from the market" as part of its ongoing NDMA investigation. *See* Sperla Decl., ¶ 11, Exh. H (April 1, 2020 announcement); RJN. The FDA request followed its determination "that the impurity in some ranitidine products increases over time and when stored at higher than room temperatures…." *Id*. The FDA did not "observe unacceptable levels of NDMA in many of the samples … tested," but opted to make the withdrawal request due to uncertainty about storage durations. *Id*.

D. Plaintiff's Allegations, Cause of Action, and Prayer for Relief

The SAC seeks to impose liability and force Proposition 65 labeling into FDA's comprehensive regulatory scheme for OTC drugs and active management of NDMA in ranitidine.

Plaintiff does not hide the fact that this action follows, and is based on, the FDA's regulatory actions on ranitidine products, including Zantac. Indeed, Plaintiff details that regulatory process

from its September 2019 beginning to the April 2020 withdrawal request; alleges the FDA investigation determined NDMA is formed by using "contaminated materials and ingredients," applying "inferior drug manufacturing process[es]," and improperly storing drugs after manufacture; and, on that basis, alleges "Defendants can reduce or eliminate NDMA from the Products by using cleaner ingredients and manufacturing processes and more careful storage techniques." *See* Compl., ¶¶ 24, 36.

Nodding briefly at the FDA's exclusive regulatory authority and skipping to the end of an ongoing FDA investigation, Plaintiff shifts to Proposition 65 by alleging Defendants exposed California Zantac consumers to NDMA without a Proposition 65 warning. *See* Compl., ¶¶ 1-2, 25, 34, 43. Since Zantac allegedly leads to NDMA exposure, Plaintiff alleges Defendants must give a "clear and reasonable warning" about its "carcinogenic hazards" under Proposition 65. Compl., ¶ 26; *see also id*., ¶ 37 (alleging "Defendants expose individuals to NDMA without prior clear and reasonable warnings" regarding its "carcinogenic hazards … even after the publicity and recalls"), ¶ 44 (Defendants failed "to provide clear and reasonable warnings regarding the carcinogenicity of NDMA to users of the Products"), ¶ 45 (Defendants exposed consumers to NDMA without a clear and reasonable warning). Plaintiff specifically demands an injunction on the sale of Zantac (which is already off the market) in California without a clear and reasonable warning (Health & Safety Code § 25249.7(a)), seeks civil penalties (*id.*, § 25249.7(b)) and attorneys' fees and costs of suit (Civ. Proc. Code § 1021.5). *See* Prayer, ¶¶ 1-4.

E. <u>Summary of Proposition 65</u>

California's Proposition 65—the Safe Drinking Water and Toxic Enforcement Act of 1986, codified at Health & Safety Code §§ 25249.5-25249.14—is a "right-to-know" statute that prohibits businesses from exposing California consumers to chemicals "known to the State to cause cancer" without a warning. *See* Health & Safety Code § 25249.6. Specifically, the statute requires that businesses give a "clear and reasonable warning" that "clearly communicate[s]" that the "chemical … is known … to cause cancer" *before* exposure occurs. *See id*., §§ 25249.6; 25249.10(b); 25601.

Under Proposition 65, if a product has even trace levels of a Prop-65 chemical, *not* providing a warning is often an impossibly risky business decision since it is "absurdly easy" for private

enforcers (private plaintiffs seeking to recover civil penalties) to bring Proposition 65 litigation. *Consumer Def. Grp. v. Rental Hous. Indus. Members*, 137 Cal. App. 4th 1185, 1215 (2006). Moreover, once a Proposition 65 action is filed, the burden shifts to the *defendant* to show "the exposure," if any, "poses no significant risk assuming lifetime exposure at the level in question." *See* Health & Safety Code § 25249.10(c). Proof that products fits into regulatory "safe harbor" level is an affirmative defense. *DiPirro v. Bondo Corp*., 153 Cal. App. 4th 150, 185 (2007); Cal. Health & Safety Code § 25249.10(c). Private enforcers "need not make any showing" on its applicability before filing suit. *Consumer Cause, Inc. v. SmileCare*, 91 Cal. App. 4th 454, 469 (2001).

Accordingly, even where a business' product inarguably qualifies for the exposure safe harbor, it is forced into a Hobson's choice: do not put a warning on its product, leaving itself open to the "lucrative" Proposition 65 private litigation business and the substantial cost of establishing a safe harbor defense (which requires detailed scientific analyses), or provide an unnecessary warning. James T. O'Reilly, *Stop the World, We Want Our Own Labels: Treaties, State Voter Initiative Laws, and Federal Pre-Emption*, 18 U. PA. J. INT'L ECON. L. 617, 635 (1997). *See also Consumer Cause, Inc.*, 91 Cal. App. 4th at 477-78 (Vogel, J., dissenting) (explaining that the Proposition 65 system forces even defendants who have not violated the law to "[s]ettle with the plaintiff, of course. Save the cost of the assessment [required to prove the level of use is safe]. Save the legal fees. Get rid of the case"). Most reasonably choose the latter.

Where a warning is offered under Proposition 65, the basic requirement is that the warning be "clear and reasonable." Plaintiff may argue that obligation can be met without offending federal law, but that position ignores the extremely narrow range of labeling revisions permitted without prior FDA approval—into which Proposition 65 warnings do not fit (*see supra,* § II(A-B))—and ignores a Proposition 65 reality. To avoid a private enforcement action, a manufacturer's only real option is to use a pre-approved "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 "Defendant['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").

Classifying Zantac as a consumer product, an NDMA safe harbor warning would read (in

font no smaller than that of the largest "product information" on the package):

> ⚠**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.

See 27 C.C.R. § 25603.

III. ARGUMENT

Under the U.S. Constitution's Supremacy Clause, federal law is "the Supreme Law of the Land." U.S. Const. art. VI, cl. 2. A state law that conflicts with federal law "is without effect." *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 516 (1992); *Cavalieri v. Avior Airlines C.A.*, 2019 WL 1099860, at *2 (S.D. Fla. Mar. 8, 2019) (where federal law preempts state law, a dismissal with prejudice is appropriate because any attempt to amend the pleading would be futile).

"Conflict" or "impossibility" preemption exists where "it is impossible for a private party to comply with both state and federal requirements." *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 618 (2011) (quotation marks and citation omitted). In the pharmaceutical context, the touchstone of impossibility preemption is whether parties can unilaterally satisfy state law duties without prior FDA authorization. "[W]hen a party cannot satisfy its state duties without … special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for pre-emption purposes." *Id.* at 623–24. *Gustavsen v. Alcon Laboratories,* 903 F.3d 1, 9-10 (lst Cir. 2018) (Where a party "cannot comply with state law without first obtaining the approval of a federal regulatory agency, then the application of that law to that private party is preempted.").

Because a Proposition 65 warning for NDMA exposure is neither the type of information FDA allows to be included on the label of OTC drugs, nor a warning Defendants may unilaterally add to an existing label without FDA approval, the relief Plaintiff seeks would make it impossible as a matter of law for Defendants "to comply with both state and federal requirements." *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1672 (2019).

That impossibility requires dismissal on preemption grounds irrespective of state law, but state law reinforces this result. Proposition 65 exempts from its warning requirement any exposures "for which federal law governs warning in a manner that preempts state authority," regardless of

how or why the exposure occurred. Health & Safety Code § 25249.10(a).

Plaintiff's claim thus cannot stand, and its SAC must be dismissed with prejudice.

A. Provision of a Proposition 65 Warning For Zantac Would Violate 21 C.F.R. § 201.66

As the FDA has explained, "[t]he primary purpose of prescription drug labeling is to provide practitioners with the essential information they need to prescribe the drug safely and effectively for the care of patients." Food & Drug Administration Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Product Labels, 65 FR 81082-01, 81082 (Proposed Rule, December 22, 2000). "Drug labeling serves as the standard under which FDA determines whether a product is safe and effective." 73 Fed. Reg. 2848-01, 2850.

Federal regulations governing the content and format of labeling for OTC drugs, including "the title, headings, subheadings, and information" that each OTC label "s*hall* contain" both pre- and post-approval by FDA, are codified in 21 C.F.R. § 201.66 (emphasis added). *See also* § 201.66(g) ("An OTC drug product that is not in compliance with the format and content requirements in this section is subject to regulatory action.").

Of the categories of information permissibly included on OTC drug labeling, only § 5 ("Warning" or "Warnings") relates to warnings or safety disclaimers such as those contemplated by Proposition 65, but it does not permit a statement, disclaimer, or warning bearing any resemblance to the Proposition 65 warning sought here. *See* 21 C.F.R. § 201.66. The OTC drug regulations provide for the presence of those warnings required "in an applicable OTC drug monograph, other OTC drug regulations, or approved drug application" (none of which relate to exposures to NDMA). *See* Sperla Decl., ¶¶ 12-15, Exhs. I-L (copies of most recent FDA-approved labeling and approval letters for Zantac 75 and 150); RJN. The only other warnings permitted by the OTC drug regulations under 21 C.F.R. § 201.66 are limited to specific categories: 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. The SAC seeks no such warnings; it seeks a bare disclosure of the mere presence of a potentially carcinogenic substance. That is incompatible

with the enumerated, therapeutic, and clinically focused categories of information relating to the *entire* drug product, not mere constituents, permitted by FDA on OTC drug labels.

The same approach is followed for prescription drug labeling, governed by 21 C.F.R. § 201.57. For prescription drugs, § 5 ("warnings and precautions") is limited to "clinically significant adverse reactions" and "other potential safety hazards." Section 5 does not permit or even contemplate disclosing the mere presence of potentially carcinogenic constituents by themselves. 21 C.F.R. § 201.57. Section 13 ("nonclinical toxicology") is limited to studies "that relate[] to a risk from the use *of the drug*," *e.g.* carcinogenesis, mutagenesis, impairment of fertility associated with ranitidine, none of which the SAC alleges. *Id*. (emphasis added). Like OTC drug labeling, prescription drug labeling does not require or permit warnings for risks associated only with drug components or contaminants such as NDMA, but that is the extent of the warning Proposition 65 requires. *See id*.

Where the FDA determines a warning about drug contents or ingredients on drug labels is necessary, the FDA can promulgate rules requiring them, and has done so. *See, e.g.*, Drug Labeling; Orally Ingested Over-the-Counter Drug Products Containing Calcium, Magnesium, and Potassium, 69 FR 13725-01 (codified at 21 C.F.R. §§ 201.70, 201.71, 201.72); Labeling for Oral and Rectal Over-the-Counter Aspirin and Aspirin-Containing Drug Products, 51 FR 8180-0121 (codified at 21 C.F.R. § 201.314). In direct contrast to Proposition 65 warnings, such warnings provide necessary, potentially life-saving therapeutic information to consumers, *e.g.* disclosures of calcium, magnesium, and potassium content to avoid "serious toxicity in people with impaired renal function." 69 Fed. Reg. at 13725.

Accordingly, although Proposition 65 concerns "warnings" in the vernacular sense of the word, the language it requires is categorically distinct from the "warnings" permitted on OTC drug labeling. Consistent with the FDA's primary goal of ensuring consumers are "able to make reasoned decisions about the drugs they take," none of the categories of permissible drug warnings bear any relation to the Proposition 65 NDMA exposure disclaimer allegedly required of Defendants under California law. In contrast to FDA's focus on balancing product safety with treatment and prevention of disease, Proposition 65 mandates disclosure *without regard* to whether the benefits of

a drug causing exposure outweigh the risks, or even whether the drug is actually harmful.[4]

Not only are federal regulations laser-precise about the content of warnings on OTC labels, they provide the specific formatting for warnings down to the letter casing (21 C.F.R. § 201.66(d)(1)), height or type (§ 201.66(d)(2)), and style, color, and spacing (§ 201.66(d)(3)). FDA also strictly prohibits other graphical images to interrupt these required provisions, which would include the triangular hazard symbol mandated for compliance with Proposition 65's safe harbor warning regulation, as described *supra* § II.E. § 201.66(d)(7) ("Graphical images (e.g., the UPC symbol) and information not described in paragraphs (c)(1) through (c)(9) of this section shall not appear in or in any way interrupt the required title, headings, subheadings, and information in paragraphs (c)(1) through (c)(9) of this section.").

Yet, a Proposition 65 warning is not deemed "clear and reasonable" unless it is "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). In practice, that means California requires that a Proposition 65 warning be prominently displayed and visible to consumers *before the* purchase, not buried among "other words, statements, designs or devices on the label."[5] Practically for Zantac, a Proposition 65 warning would need to conform to the safe-harbor warning regulations and be on the outer container of the packaging, notwithstanding the fact that the warning language is neither allowed nor approved by the FDCA or FDA regulators.

While Congress and FDA could have adopted a broad, indiscriminate warning regime of the type embodied in Proposition 65, they did not, choosing instead to focus on ensuring safe and

[4] Under Proposition 65, only carcinogen exposures presenting "No Significant Risk," defined as a 1 in 100,000 risk of cancer over a lifetime of regular use, are exempted from the state law warning requirement after defendants prove their case at trial. *See* Health & Safety Code § 25249.10(c), *supra* § II.E.

[5] *See, e.g.*, 27 C.C.R. §§ 25602(a)(1) (shelf warning must be at "point of display of the product"), 25602(a)(2) ("electronic device" warnings must "provide[] the warning to the purchaser prior to or during the purchase of the consumer product, without requiring the purchaser to seek out the warning"), 25602(b) (online warnings are "not prominently displayed if the purchaser must search for it in the general content of the website"); *see also Am. Meat Inst. v. Leeman*, 180 Cal. App. 4th 728, 760 (2009) (interpreting prior version of § 25601; warnings must be reasonably calculated to be available to consumers before exposure); *People ex rel. Brown v. Tri-Union Seafoods, LLC*, 171 Cal. App. 4th 1549, 1156 (2009) (same).

effective drugs are made available to consumers in the United States. Under § 201.66(g), which supersedes Proposition 65 under the Supremacy Clause, Defendants have no choice but to adhere to the FDA's approach and the regulations contained in § 201.66.

B. The CBE Regulation Preempts A Requirement To Provide A Proposition 65 Warning For Zantac

The CBE regulation additionally precludes the provision of a warning that is inconsistent with FDA regulations that define the type of permissible drug "warnings" to exclude a Proposition 65 warning, nor does it otherwise authorize warnings for OTC drugs contrary to § 201.66. *See* 21 C.F.R. § 314.70. Yet, 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]." *Gibbons v. Bristol-Myers Squibb Co.*, 919 F.3d 699, 708 (2nd Cir. 2019) (citing 21 CFR § 314.70(c)(6)(iii)) (internal quotations omitted). The SAC does not and cannot make that threshold showing here because, in addition to its inconsistency with § 201.66, a Proposition 65 warning does not qualify as a "contraindication, warning, precaution, or adverse reaction" associated with a "clinically significant hazard," which are the only categories of information that may be unilaterally altered using the CBE process. 21 C.F.R. § 314.70(b)(2)(v)(A) (requiring preapproval of any changes to labeling not authorized by 21 C.F.R. § 314.70(c)(6)(iii)).

Under federal regulations, drug labeling changes are stratified and classified by risk level. "Major changes" require FDA preapproval, while certain labeling changes separately defined as "moderate changes" do not. *See* 21 CFR § 314.70(c)(6)(iii).[6] Moderate changes that manufacturers may effect unilaterally are strictly 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). Section 201.57(c) provides that "[i]n accordance with §§ 314.70 and 601.12 [the CBE regulation for biologics] of this chapter, []

[6] Additionally included within the scope of "major changes" are "any change in the drug substance, drug product, production process, quality controls, equipment, or facilities that has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product." 21 CFR § 314.70(c)(6)(iii).

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."

A Proposition 65 warning on Zantac merely disclaiming possible exposure to NDMA cannot fall within the narrow scope of changes permitted by § 314.70(c)(6)(iii). In *Wyeth v. Levine*, 555 U.S. 555, 570-572 (2009), the U.S. Supreme Court held that the CBE regulation could defeat impossibility preemption in failure-to-warn cases if the manufacturer unilaterally could have modified the label to add plaintiffs' proposed warning. But unlike here, *Wyeth* dealt with addition of a "warning" or "precaution" purportedly authorized by the CBE regulation because the proposed warning contained clinically significant information that could have prevented the plaintiff's injury. *Wyeth*, 555 U.S. at 571 (holding that CBE regulation authorized defendant to unilaterally provide new drug warning "when the risk of gangrene from IV-push injection of Phenergan became apparent"). As explained *supra*, § III.A, the Proposition 65 warning the SAC would require does not constitute a contraindication, warning, precaution, or adverse reaction. 21 CFR § 201.57(c); *see also* FDA, Guidance for Industry, Changes to an Approved NDA or ANDA, at 26 (2004) (listing examples of permissible CBE changes as "1. Addition of an adverse event due to information reported to the applicant or Agency. 2. Addition of a precaution arising out of a postmarketing study. 3. Clarification of the administration statement to ensure proper administration of the drug product."); Sperla Decl., ¶ 16 Exh. M; RJN.[7]

Furthermore, the Proposition 65 warning Plaintiff seeks here would not warn of a "clinically significant hazard" and the SAC fails to allege any "evidence of a causal association" of any hazard presented by NDMA with Zantac, both of which the SAC must allege to defeat preemption. *See Gibbons*, 919 F.3d at 708. Consistent with Proposition 65's enforcement provisions, which permit a suit to enforce the law without regard to whether the product at issue is harmful or unsafe, the SAC offers nothing to suggest the presence of NDMA in Zantac is a hazard of any import, let alone one of clinical significance. *See* Health & Safety Code § 25249.7. Instead, Proposition 65 only requires, and the SAC only alleges, Defendants knowingly and intentionally exposed Zantac users

[7] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/changes-approved-nda-or-anda.

to NDMA, SAC at ¶¶ 34-37. Proposition 65 claims, reflecting no actual harm or threat of harm, unlike the injury the plaintiff sustained in *Wyeth*, would not even be sufficient to convey federal standing on Plaintiff. *See As You Sow v. Sherwin-Williams Co.*, 1993 WL 560086, at *2 (N.D. Cal. Dec. 21, 1993) (holding Proposition 65 does not confer injury on the plaintiff sufficient to satisfy federal standing requirements); *Brimer v. Amash Imports, Inc.*, 2012 WL 13080724, at *4 (N.D. Cal. Jan. 10, 2012) (same).

Additionally, the CBE regulation, read together with § 201.66(g)'s prohibition against labeling not in compliance with § 201.66, does not authorize OTC manufacturers to make changes to labeling that do not also conform to § 201.66. *See supra*, III.A. The FDA's requirements for condensed and consumer-friendly OTC labels were purposefully written so consumers—not doctors or pharmacists—could "better read and understand the information presented and apply this information to the safe and effective use of OTC drug products." Over-The-Counter Human Drugs; Labeling Requirements, 64 Fed. Reg. 13254-01 (March 17, 1999). To require OTC manufacturers to supplement OTC labeling with anything except necessary, clinically significant warnings permitted under § 201.66 (which a Proposition 65 warning by definition is not) works against that purpose. Thus, the only exception to the requirements of § 201.66 still requires OTC manufacturers to obtain an exemption from FDA, which is insufficient to defeat preemption. *See* § 201.66(e); s*ee also Gibbons*, 919 F.3d at 708; *cf. Wyeth*, 555 U.S. at 570-572. Neither § 201.66 nor 314.70(c)(6)(iii) gives discretion to OTC makers to unilaterally exempt themselves from the requirements contained in § 201.66, and both bar the warning sought here.

As discussed *supra*, § II.E, to comply with Plaintiff's version of Proposition 65's requirements, Defendants would need to do the impossible: unilaterally provide a warning on Zantac not contained in preapproved labeling and not 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 now comply, with the requirements of California law that the SAC seeks to enforce without running afoul of federal law. Under the

Supremacy Clause, such state law requirements are preempted and unenforceable as a matter of law. For these reasons, the SAC must be dismissed with prejudice.

Dated: February 25, 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

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 February 3, 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 SECOND AMENDED COMPLAINT; MEMORANDUM OF POINTS AND AUTHORITIES

☐ 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 February 3, 2021, at Sacramento, California.

Selena Paradee

SERVICE LIST

Mark Todzo Joseph Mann Lexington Law Group 503 Divisadero Street San Francisco, CA 94117 mtodzo@lexlawgroup.com jmann@lexlawgroup.com	*Plaintiff* Center for Environmental Health
Dennis Raglin Danielle Vallone Steptoe & Johnson LLP 633 West Fifth St., Suite 1900 Los Angeles, CA 90071 draglin@steptoe.com dvallone@steptoe.com	*Defendant* Perrigo Company
Jeffrey B. Margulies Lauren A. Shoor Andy Guo Norton Rose Fulbright US LLP 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Telephone: (213) 892-9200 Facsimile: (213) 892-9494 jeff.margulies@nortonrosefulbright.com lauren.shoor@nortonrosefulbright.com andy.guo@nortonrosefulbright.com	*Defendant* Target Corporation
Cheryl S. Chang Erika R. Schulz Blank Rome LLP 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Chang@BlankRome.com ESchulz@BlankRome.com	*Defendant* Apotex Corp.
Megan E. Grossman Lewis Brisbois Bisgaard & Smith LLP 550 E. Swedesford Road, Suite 270 Wayne, PA 19087 Megan.Grossman@lewisbrisbois.com	*Defendant* Granules USA, Inc.

Will Wagner
Greenberg Traurig LLP
1201 K Street, Suite 1100
Sacramento, CA 94111
wagnerw@gtlaw.com

Trenton H. Norris
Arnold & Porter Kaye Scholer LLP
Three Embarcadero Center, 10th Floor
San Francisco, CA 94111
trent.norris@arnoldporter.com

Defendant
7-Eleven, Inc.

EAST\179606299.2

Exhibit 20

GEORGE GIGOUNAS (Bar No. CA-209334)
george.gigounas@dlapiper.com
GREGORY SPERLA (Bar No. CA-278062)
greg.sperla@dlapiper.com
SEAN NEWLAND (Bar No. CA-300928)
sean.newland@dlapiper.com
DLA PIPER LLP (US)
555 Mission Street
Suite 2400
San Francisco, California 94105-2933
Tel: 415.836.2500
Fax: 415.836.2501

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

DECLARATION OF GREG G. SPERLA IN SUPPORT OF DEFENDANTS' 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

I, Greg Sperla, declare as follows:

1. I am an attorney at law duly authorized to practice before courts of the State of California, and associate of DLA Piper LLP (US), counsel for Defendants Chattem, Inc. and Sanofi-Aventis U.S. LLC ("Defendants").

2. I hereby submit this declaration in support of Defendants' Request for Judicial Notice in Support of Demurrer to Plaintiff Center for Environmental Health's ("Plaintiff" or "CEH") Second Amended Complaint. The matters stated in this declaration are based on my personal knowledge, and if called to testify I could and would testify competently thereto.

3. I met and conferred with counsel for Plaintiff by email and telephonically at least five days in advance of the deadline for Defendants' responsive pleading pursuant to California Code of Civil Procedure § 430.10 *et seq*. Counsel and I discussed the grounds for Defendants' demurrer and whether any agreement could be reached to resolve the objections to be raised in demurrer. Ultimately no agreement was reached.

4. A true and correct copy of the Food and Drug Administration's ("FDA") December 19, 1995 letter approving Zantac 75mg as an over-the-counter ("OTC") drug is attached hereto as Exhibit A.

5. A true and correct copy of the FDA's August 31, 2004 letter approving Zantac 150mg as an OTC drug is attached hereto as Exhibit B.

6. A true and correct copy of the FDA's drug information page for Zantac's 75mg OTC formulation listing, among other information provided on the website, the formulation's New Drug Application ("NDA") and FDA approval date is attached hereto as Exhibit C.

7. A true and correct copy of the FDA's drug information page for Zantac's 150mg OTC formulation listing, among other information provided on the website, the formulation's NDA and FDA approval date is attached hereto as Exhibit D.

8. A true and correct copy of the FDA's Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book") is attached hereto as Exhibit E. The Orange Book lists all FDA-approved drugs and the companies authorized to manufacture and sell each listed drug by way of an NDA in Defendants' case, or an abbreviated NDA for generic drugs.

9. A true and correct copy of the FDA guidance document titled "Guidance: Draft Safety Information – FDA's Communication to the Public" dated March 2012 is attached hereto as Exhibit F.

10. 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 G.

11. 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 H.

12. A true and correct copy of the September 18, 2019 letter from the FDA approving Defendants' supplemental new drug application ("sNDA") concerning labeling revisions for Zantac 150mg is attached hereto as Exhibit I.

13. A true and correct copy of the Zantac 150mg labeling approved by the FDA on September 18, 2019 is attached hereto as Exhibit J.

14. A true and correct copy of the September 18, 2019 letter from the FDA approving Defendants' sNDA concerning labeling revisions for Zantac 75mg is attached hereto as Exhibit K.

15. A true and correct copy of the Zantac 75mg labeling approved by the FDA on September 18, 2019 is attached hereto as Exhibit L.

16. A true and correct copy of the FDA guidance document titled "Guidance for Industry, Changes to An Approved NDA or ANDA" dated April 2004 is attached hereto as Exhibit M.

17. All attached exhibits are available and were obtained on the FDA's website.

18. Exhibits A-D and I-L were accessed on the FDA's Drug Databases, Drugs@FDA page (URL: https://www.accessdata.fda.gov/scripts/cder/daf/). Searching "Zantac" in that database allows the searching party to access regulatory information—including labels, approval letters, and other drug information—for Zantac's 75mg and 150mg OTC formulations.

19. Exhibit E was accessed on the FDA's "Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations" page (URL: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm). Searching "ranitidine" leads to a page listing various companies identified as applicants authorized to market ranitidine products, including Defendants.

20. FDA Guidance documents (Exhibits F and M) can be searched for and are available through this URL: https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

21. The FDA statements regarding ranitidine are available on an FDA page named "FDA Updates and Press Announcements on NDMA in Zantac (ranitidine)" (URL: https://www.fda.gov/regulatory-information/search-fda-guidance-documents).

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct. Executed this 25th day of February, 2021 in Sacramento, California.

GREG SPERLA

EXHIBIT A

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-520

DEC 19 1995

Glaxo Wellcome, Inc.
Attention: Andrew Gustafson, Ph.D.
Five Moore Drive
P.O. Box 13358
Research Triangle Park, NC 27709

Dear Dr. Gustafson:

Please refer to your September 30, 1994 new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ZANTAC 75 (ranitidine hydrochloride) Tablets, 75 mg.

We acknowledge receipt of your amendments dated August 3, 11, and 16; October 12 and 31; November 29 and December 7, 1995.

This new drug application provides a 75 mg dose up to twice daily for the treatment of episodic heartburn.

We have completed the review of this application including the submitted draft labeling and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the draft labeling in the submissions dated October 31, 1995 (for the package insert and blister card backings) and December 7, 1995 (for the carton labels) with the revisions listed below. Accordingly, the application is approved effective on the date of this letter. The revisions are as follows:

1. Delete the statement "Since 1988, the medicine in Zantac 75 has been the #1 prescribed acid reducer" from the package insert.

2. The statement "(Please read all of this information before taking Zantac 75. Save this leaflet for future reference.)" before the body of text in the package insert should be more prominent. Please increase the font size and separate it from the body of text.

3. Concerning the section entitled "Clinical studies prove Zantac 75 is effective", display the efficacy response rates for the pivotal studies ROC-300 and ROC-301 separately as medians of the all-episode proportion successfully treated of the intent to treat population (i.e., the efficacy graphs displayed in Version B of your October 31, 1995 submission).

4. The tradename logo in the package insert (including on the coupon) and on the blister card backings should more closely resemble that used on the carton.

These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as requested, in the product's final printed labeling (FPL) may render the product misbranded and an unapproved new drug.

Please submit seventeen copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy weight paper or similar material. For administrative purposes this submission should be designated "FINAL PRINTED LABELING" for approved NDA 20-520. Approval of this labeling by FDA is not required before it is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

Validation of the regulatory methods has not been completed At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Please submit one market package of the drug when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Michael Folkendt
Consumer Safety Officer
(301) 443-0487

Sincerely yours,

Robert Temple, M.D.
Office Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Original NDA 20-520
HFD-180/Div. files
HFD-180/CSO/M.Folkendt
HFD-2/M.Lumpkin
HFD-103/P.Botstein
HFD-101/L.Carter
DISTRICT OFFICE
HF-2/medwatch
HFD-80
HFD-40/DDMAC
HFD-613
HFD-009/J.Tracy

drafted: MF/December 12, 1995/20520512.2mf 12/14/95
r/d Initials: K.Robie-Suh 12/12/95
S.Fredd 12/14/95
final: 12/14/95

APPROVAL

EXHIBIT B

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-698

Pfizer Consumer Healthcare
Division of Warner-Lambert Company, LLC
Attention: John Jacobs, VP Global Regulatory Affairs
201 Tabor Rd
Morris Plains, NJ 07950

Dear Mr. Jacobs:

Please refer to your new drug application (NDA) dated October 31, 2003, received October 31, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zantac 150 (ranitidine hydrochloride) tablets.

We acknowledge receipt of your submissions dated November 25, 2003, February 23, March 26, April 14, 28, May 6, 13, June 30, and August 18 and 30, 2004.

This new drug application provides for the use of Zantac 150 (ranitidine hydrochloride) Tablets for:

1. Relieves heartburn associated with acid indigestion and sour stomach, and

2. Prevents heartburn associated with acid indigestion and sour stomach brought on by certain foods and beverages when taken 30 to 60 minutes before eating or drinking.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the revisions listed below.

1. The content of the blister carton, bottle carton, and the 1-count pouch labeling should be identical.

2. In the package insert, under the "Do not use" subheading, in the first bullet that begins, "if you have trouble or pain . . ." replace the misspelled word "bloddy" with the word "bloody" and add periods as shown, so that the bullet reads " if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor."

The final printed labeling (FPL) must be identical to, except for including the revisions listed, the enclosed labeling (package insert and bottle carton labeling submitted on August 30, 2004, and 1 tablet pouch labeling, blister backing immediate container and bottle immediate container labels submitted on May 6, 2004), and all carton labeling, must be in the "Drug Facts" format (21 CFR 201.66). These revisions are terms of the NDA approval. Marketing the product(s) before making the revisions,

exactly as stated, in the products' labeling and in the required format may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-698**." Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirements for this application.

In addition, we request that you submit two copies of the introductory promotional materials you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Please send one of the copies to the Division of Gastrointestinal and Coagulation Drug Products and the other copy, along with the labeling, to Division of Over-the-Counter Drug Products, HFD-560.

Please submit one market package of the drug product when it is available.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

Oversight of this application is being transferred to the Division of Over-the-Counter Drug Products.

If you have any questions, call Keith Olin, Regulatory Project Manager, R.Ph. at (301) 301-827-2293.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Acting Director
Division of Gastrointestinal & Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Charles J. Ganley
Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Charles Ganley
8/31/04 04:54:37 PM

Joyce Korvick
8/31/04 05:08:35 PM

EXHIBIT C

Drugs@FDA: FDA-Approved Drugs

Home (index.cfm) | Previous Page

New Drug Application (NDA): 020520
Company: SANOFI US

Products on NDA 020520

CSV | Excel | Print

Drug Name	Active Ingredients	Strength	Dosage Form/Route	Marketing Status	TE Code	R
ZANTAC 75	RANITIDINE HYDROCHLORIDE	EQ 75MG BASE	TABLET;ORAL	Over-the-counter	None	Ye

Showing 1 to 1 of 1 entries

Approval Date(s) and History, Letters, Labels, Reviews for NDA 020520

Original Approvals or Tentative Approvals

AA0367

CSV | Excel | Print

Action Date	Submission	Action Type	Submission Classification	Review Priority; Orphan Status	Letters, Reviews, Labels, Patient Package Insert
12/19/1995	ORIG-1	Approval	Type 3 - New Dosage Form	STANDARD	

Showing 1 to 1 of 1 entries

Supplements

CSV | Excel | Print

Action Date	Submission	Supplement Categories or Approval Type	Letters, Reviews, Labels, Patient Pac
09/18/2019	SUPPL-38	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda Letter (PDF) (https://www.accessdata.fd**
04/04/2019	SUPPL-37	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda Letter (PDF) (https://www.accessdata.fd**
07/27/2016	SUPPL-33	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda.gov/drugsa Letter (PDF) (https://www.accessdata.fda.gov/drugsa**
01/26/2016	SUPPL-32	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda Letter (PDF) (https://www.accessdata.fd**

Action Date	Submission	Supplement Categories or Approval Type	Letters, Reviews, Labels, Patient Pac
11/20/2015	SUPPL-30	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda** **Letter (PDF) (https://www.accessdata.fd**
09/24/2015	SUPPL-31	Manufacturing (CMC)	
01/30/2015	SUPPL-28	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda.gov/drugsa** **Letter (PDF) (https://www.accessdata.fd**
07/25/2013	SUPPL-26	Manufacturing (CMC)	
02/28/2005	SUPPL-15	Labeling	**Letter (PDF) (https://www.accessdata.fd** **Review (PDF) (https://www.accessdata.f**
12/03/2002	SUPPL-13	Manufacturing (CMC)	
05/30/2002	SUPPL-12	Manufacturing (CMC)	

Action Date	Submission	Supplement Categories or Approval Type	Letters, Reviews, Labels, Patient Pac
05/29/2001	SUPPL-10	Labeling	
11/08/2000	SUPPL-9	Manufacturing (CMC)	
06/07/2000	SUPPL-8	Manufacturing (CMC)	
02/28/2000	SUPPL-6	Manufacturing (CMC)	
06/08/1998	SUPPL-1	Efficacy-New Indication	**Review (PDF) (https://www.accessdata.f**
05/22/1998	SUPPL-3	Manufacturing (CMC)-Packaging	
04/01/1998	SUPPL-5	Manufacturing (CMC)-Packaging	

Action Date	Submission	Supplement Categories or Approval Type	Letters, Reviews, Labels, Patient Pac
12/08/1997	SUPPL-4	Manufacturing (CMC)	
03/26/1997	SUPPL-2	Manufacturing (CMC)-Packaging	

Showing 1 to 20 of 20 entries

Labels for NDA 020520

Other OTC Drugs with the Same Active Ingredient, Strength and Dosage Form/Route

EXHIBIT D

Drugs@FDA: FDA-Approved Drugs

Home (index.cfm) | Previous Page

New Drug Application (NDA): 021698
Company: SANOFI US

Products on NDA 021698

CSV | Excel | Print

Drug Name	Active Ingredients	Strength	Dosage Form/Route	Marketing Status	TE Code	R
ZANTAC 150	RANITIDINE HYDROCHLORIDE	EQ 150MG BASE	TABLET;ORAL	Over-the-counter	None	Ye
ZANTAC 150	RANITIDINE HYDROCHLORIDE	EQ 150MG BASE	TABLET;ORAL	Over-the-counter	None	Ye

Showing 1 to 2 of 2 entries

Approval Date(s) and History, Letters, Labels, Reviews for NDA 021698

Original Approvals or Tentative Approvals

CSV | Excel | Print

Action Date	Submission	Action Type	Submission Classification	Review Priority; Orphan Status	Letters, Revi
08/31/2004	ORIG-1	Approval	Type 3 - New Dosage Form	STANDARD	**Label (PDF) (h Letter (PDF) (h Review (https:**

Showing 1 to 1 of 1 entries

Supplements

CSV | Excel | Print

Action Date	Submission	Supplement Categories or Approval Type	Letters, Reviews, Labels, Patient Pac
09/18/2019	SUPPL-31	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda Letter (PDF) (https://www.accessdata.fd**
04/04/2019	SUPPL-29	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda Letter (PDF) (https://www.accessdata.fd**
08/26/2016	SUPPL-24	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda.gov/drugsa Letter (PDF) (https://www.accessdata.fd**
07/27/2016	SUPPL-23	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda.gov/drugsa Letter (PDF) (https://www.accessdata.fda.gov/drugsa**
03/21/2016	SUPPL-22	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda Letter (PDF) (https://www.accessdata.fd**

Action Date	Submission	Supplement Categories or Approval Type	Letters, Reviews, Labels, Patient Pac
12/11/2015	SUPPL-19	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda Letter (PDF) (https://www.accessdata.fd**
11/20/2015	SUPPL-20	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda Letter (PDF) (https://www.accessdata.fd**
03/12/2015	SUPPL-18	Labeling-Container/Carton Labels	**Label (PDF) (https://www.accessdata.fda Letter (PDF) (https://www.accessdata.fd**
12/07/2012	SUPPL-13	Manufacturing (CMC)	
03/13/2007	SUPPL-3	Labeling-Container/Carton Labels, Labeling-Package Insert	**Letter (PDF) (https://www.accessdata.fd**

Showing 1 to 10 of 10 entries

Labels for NDA 021698

Other OTC Drugs with the Same Active Ingredient, Strength and Dosage Form/Route

EXHIBIT E

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Mkt.Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A211058	CAPSULE	ORAL	EQ 150MG BASE	AB			AUROBINDO PHARMA LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075742	CAPSULE	ORAL	EQ 150MG BASE	AB			DR REDDYS LABORATORIES LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074655	CAPSULE	ORAL	EQ 150MG BASE	AB			SANDOZ INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A211058	CAPSULE	ORAL	EQ 300MG BASE	AB			AUROBINDO PHARMA LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075742	CAPSULE	ORAL	EQ 300MG BASE	AB			DR REDDYS LABORATORIES LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074655	CAPSULE	ORAL	EQ 300MG BASE	AB		RS	SANDOZ INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A079076	INJECTABLE	INJECTION	EQ 25MG BASE/ML	AP			MYLAN LABORATORIES LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074777	INJECTABLE	INJECTION	EQ 25MG BASE/ML	AP			WEST-WARD PHARMACEUTICALS INTERNATIONAL LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077458	INJECTABLE	INJECTION	EQ 25MG BASE/ML	AP			WEST-WARD PHARMACEUTICALS INTERNATIONAL LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A091534	INJECTABLE	INJECTION	EQ 25MG BASE/ML	AP			ZYDUS PHARMACEUTICALS USA INC
RX	RANITIDINE HYDROCHLORIDE	ZANTAC	N019090	INJECTABLE	INJECTION	EQ 25MG BASE/ML	AP	RLD	RS	TELIGENT OU
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A090623	SYRUP	ORAL	EQ 15MG BASE/ML	AA			AUROBINDO PHARMA LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078890	SYRUP	ORAL	EQ 15MG BASE/ML	AA			LANNETT CO INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A091288	SYRUP	ORAL	EQ 15MG BASE/ML	AA			LANNETT CO INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077405	SYRUP	ORAL	EQ 15MG BASE/ML	AA		RS	PHARMACEUTICAL ASSOCIATES INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074680	TABLET	ORAL	EQ 150MG BASE	AB			APOTEX INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A076705	TABLET	ORAL	EQ 150MG BASE	AB			DR REDDYS LABORATORIES INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078542	TABLET	ORAL	EQ 150MG BASE	AB			GLENMARK PHARMACEUTICALS INC USA
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075180	TABLET	ORAL	EQ 150MG BASE	AB			PAR PHARMACEUTICAL INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074467	TABLET	ORAL	EQ 150MG BASE	AB			SANDOZ INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A211289	TABLET	ORAL	EQ 150MG BASE	AB			VKT PHARMA PRIVATE LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074680	TABLET	ORAL	EQ 300MG BASE	AB			APOTEX INC

Mkt.Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A076705	TABLET	ORAL	EQ 300MG BASE	AB			DR REDDYS LABORATORIES INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078542	TABLET	ORAL	EQ 300MG BASE	AB			GLENMARK PHARMACEUTICALS INC USA
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075180	TABLET	ORAL	EQ 300MG BASE	AB			PAR PHARMACEUTICAL INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074467	TABLET	ORAL	EQ 300MG BASE	AB			SANDOZ INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A211289	TABLET	ORAL	EQ 300MG BASE	AB			VKT PHARMA PRIVATE LTD
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A207579	TABLET	ORAL	EQ 75MG BASE				AUROBINDO PHARMA LTD
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075294	TABLET	ORAL	EQ 75MG BASE				DR REDDYS LABORATORIES LTD
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A076195	TABLET	ORAL	EQ 75MG BASE				L PERRIGO CO
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210250	TABLET	ORAL	EQ 75MG BASE				UNIQUE PHARMACEUTICAL LABORATORIES A DIVISION OF J.B. CHEMICALS AND PHARMACEUTICALS LTD
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A207578	TABLET	ORAL	EQ 150MG BASE				AUROBINDO PHARMA LTD
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078192	TABLET	ORAL	EQ 150MG BASE				DR REDDYS LABORATORIES LTD
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A091429	TABLET	ORAL	EQ 150MG BASE				PERRIGO R AND D CO
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A091429	TABLET	ORAL	EQ 150MG BASE				PERRIGO R AND D CO
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210228	TABLET	ORAL	EQ 150MG BASE				UNIQUE PHARMACEUTICAL LABORATORIES A DIVISION OF J.B. CHEMICALS AND PHARMACEUTICALS LTD
OTC	RANITIDINE HYDROCHLORIDE	ZANTAC 150	N021698	TABLET	ORAL	EQ 150MG BASE		RLD	RS	SANOFI US
OTC	RANITIDINE HYDROCHLORIDE	ZANTAC 150	N021698	TABLET	ORAL	EQ 150MG BASE		RLD		SANOFI US
OTC	RANITIDINE HYDROCHLORIDE	ZANTAC 75	N020520	TABLET	ORAL	EQ 75MG BASE		RLD		SANOFI US
DISCN	RANITIDINE BISMUTH CITRATE	TRITEC	N020559	TABLET	ORAL	400MG				GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A209859	CAPSULE	ORAL	EQ 150MG BASE				AJANTA PHARMA LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A211893	CAPSULE	ORAL	EQ 150MG BASE				APPCO PHARMA LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075564	CAPSULE	ORAL	EQ 150MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210681	CAPSULE	ORAL	EQ 150MG BASE				NOVITIUM PHARMA LLC

Mkt.Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075557	CAPSULE	ORAL	EQ 150MG BASE				TEVA PHARMACEUTICALS USA INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A209859	CAPSULE	ORAL	EQ 300MG BASE				AJANTA PHARMA LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A211893	CAPSULE	ORAL	EQ 300MG BASE				APPCO PHARMA LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075564	CAPSULE	ORAL	EQ 300MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210681	CAPSULE	ORAL	EQ 300MG BASE				NOVITIUM PHARMA LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075557	CAPSULE	ORAL	EQ 300MG BASE				TEVA PHARMACEUTICALS USA INC
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 150	N020095	CAPSULE	ORAL	EQ 150MG BASE **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**		RLD		GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 300	N020095	CAPSULE	ORAL	EQ 300MG BASE **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**		RLD		GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 150	N020251	GRANULE, EFFERVESCENT	ORAL	EQ 150MG BASE/PACKET				GLAXO GROUP LTD ENGLAND DBA GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074764	INJECTABLE	INJECTION	EQ 25MG BASE/ML				BEDFORD LABORATORIES DIV BEN VENUE LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC IN PLASTIC CONTAINER	N019593	INJECTABLE	INJECTION	EQ 1MG BASE/ML				TELIGENT OU
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC IN PLASTIC CONTAINER	N019593	INJECTABLE	INJECTION	EQ 50MG BASE/100ML				TELIGENT OU
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A076124	SYRUP	ORAL	EQ 15MG BASE/ML				ACTAVIS MID ATLANTIC LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A091078	SYRUP	ORAL	EQ 15MG BASE/ML				AKORN OPERATING CO LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078312	SYRUP	ORAL	EQ 15MG BASE/ML				AMNEAL PHARMACEUTICALS
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A090054	SYRUP	ORAL	EQ 15MG BASE/ML				ANDA REPOSITORY LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077602	SYRUP	ORAL	EQ 15MG BASE/ML				APOTEX INC

Mkt.Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078684	SYRUP	ORAL	EQ 15MG BASE/ML				NOSTRUM LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A091091	SYRUP	ORAL	EQ 15MG BASE/ML				NOSTRUM LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078448	SYRUP	ORAL	EQ 15MG BASE/ML				RANBAXY INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077476	SYRUP	ORAL	EQ 15MG BASE/ML				TARO PHARMACEUTICALS USA INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A090102	SYRUP	ORAL	EQ 15MG BASE/ML				TORRENT PHARMA INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A079211	SYRUP	ORAL	EQ 15MG BASE/ML				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A079212	SYRUP	ORAL	EQ 15MG BASE/ML				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC	N019675	SYRUP	ORAL	EQ 15MG BASE/ML		RLD		GLAXO GROUP LTD ENGLAND DBA GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075212	TABLET	ORAL	EQ 75MG BASE				ANI PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075296	TABLET	ORAL	EQ 75MG BASE				ANI PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075167	TABLET	ORAL	EQ 75MG BASE				APOTEX INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075094	TABLET	ORAL	EQ 75MG BASE				CONTRACT PHARMACAL CORP
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075497	TABLET	ORAL	EQ 75MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075254	TABLET	ORAL	EQ 75MG BASE				RANBAXY PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075519	TABLET	ORAL	EQ 75MG BASE				SANDOZ INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A201745	TABLET	ORAL	EQ 75MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A209160	TABLET	ORAL	EQ 75MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075132	TABLET	ORAL	EQ 75MG BASE				SUN PHARMACEUTICAL INDUSTRIES LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A076760	TABLET	ORAL	EQ 75MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078884	TABLET	ORAL	EQ 75MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077824	TABLET	ORAL	EQ 150MG BASE				AMNEAL PHARMACEUTICALS NY LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074488	TABLET	ORAL	EQ 150MG BASE				ANI PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077426	TABLET	ORAL	EQ 150MG BASE				ANI PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A200172	TABLET	ORAL	EQ 150MG BASE				APOTEX INC

Mkt.Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074662	TABLET	ORAL	EQ 150MG BASE				BOEHRINGER INGELHEIM CORP
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210243	TABLET	ORAL	EQ 150MG BASE				GRANULES INDIA LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210243	TABLET	ORAL	EQ 150MG BASE				GRANULES INDIA LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075165	TABLET	ORAL	EQ 150MG BASE				HERITAGE PHARMA LABS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074023	TABLET	ORAL	EQ 150MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074552	TABLET	ORAL	EQ 150MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A203694	TABLET	ORAL	EQ 150MG BASE				NOSTRUM LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075000	TABLET	ORAL	EQ 150MG BASE				RANBAXY PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A200536	TABLET	ORAL	EQ 150MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A205512	TABLET	ORAL	EQ 150MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A209161	TABLET	ORAL	EQ 150MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210010	TABLET	ORAL	EQ 150MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075439	TABLET	ORAL	EQ 150MG BASE				SUN PHARMACEUTICAL INDUSTRIES LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074864	TABLET	ORAL	EQ 150MG BASE				WATSON LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075208	TABLET	ORAL	EQ 150MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078653	TABLET	ORAL	EQ 150MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078701	TABLET	ORAL	EQ 150MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077824	TABLET	ORAL	EQ 300MG BASE				AMNEAL PHARMACEUTICALS NY LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074488	TABLET	ORAL	EQ 300MG BASE				ANI PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077426	TABLET	ORAL	EQ 300MG BASE				ANI PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074662	TABLET	ORAL	EQ 300MG BASE				BOEHRINGER INGELHEIM CORP
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075165	TABLET	ORAL	EQ 300MG BASE				HERITAGE PHARMA LABS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074023	TABLET	ORAL	EQ 300MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074552	TABLET	ORAL	EQ 300MG BASE				MYLAN PHARMACEUTICALS INC

Mkt.Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A203694	TABLET	ORAL	EQ 300MG BASE				NOSTRUM LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075000	TABLET	ORAL	EQ 300MG BASE				RANBAXY PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A205512	TABLET	ORAL	EQ 300MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210010	TABLET	ORAL	EQ 300MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075439	TABLET	ORAL	EQ 300MG BASE				SUN PHARMACEUTICAL INDUSTRIES LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074864	TABLET	ORAL	EQ 300MG BASE				WATSON LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075208	TABLET	ORAL	EQ 300MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078701	TABLET	ORAL	EQ 300MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 150	N018703	TABLET	ORAL	EQ 150MG BASE **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**		RLD		GLAXO GROUP LTD ENGLAND DBA GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 300	N018703	TABLET	ORAL	EQ 300MG BASE **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**		RLD		GLAXO GROUP LTD ENGLAND DBA GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 150	N020251	TABLET, EFFERVESCENT	ORAL	EQ 150MG BASE				GLAXO GROUP LTD ENGLAND DBA GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 25	N020251	TABLET, EFFERVESCENT	ORAL	EQ 25MG BASE				GLAXO GROUP LTD ENGLAND DBA GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 75	N020745	TABLET, EFFERVESCENT	ORAL	EQ 75MG BASE **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**		RLD		SANOFI US

EXHIBIT F

Guidance
Drug Safety Information – FDA's Communication to the Public

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Edward Staffa 301-796-5301, or (CBER) Office of Communication, Outreach and Development at 301-827-1800 or 800-835-4709.

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)

March 2012
Drug Safety

Revision 1

Guidance

Drug Safety Information – FDA's Communication to the Public

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Office of Communications
Division of Drug Information, WO51, Room 2201
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone: 301-796-3400; Fax: 301-847-8714
druginfo@fda.hhs.gov
http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

and/or

Office of Communication, Outreach and Development, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Rockville, MD 20852-1448
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm
(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)

March 2012
Drug Safety

Revision 1

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Guidance[1]
Drug Safety Information – FDA's Communication to the Public

This draft guidance, when finalized, will represent 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. You can use an alternative approach if the 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.

INTRODUCTION

This guidance explains how FDA develops and disseminates information to the public about important drug safety issues, including emerging drug safety information.[2] Timely communication of important drug safety information provides health care professionals, patients, consumers, and other interested persons with access to the most current information concerning the potential risks and benefits of a marketed drug, helping them to make more informed treatment choices.

This guidance revises the March 2007 guidance, *Drug Safety Information – FDA's Communication to the Public*[3] by providing updated information about FDA's approach to communicating important drug safety information. The revised guidance describes the Center for Drug Evaluation and Research's (CDER's) single, standardized format for electronic drug safety communications about marketed drugs and provides information about the Center for Biologics Evaluation and Research's (CBER's) safety communication activities. In addition, the revised guidance describes FDA's posting of other safety assessments on its Web site in accordance with the requirements of the Food and Drug Administration Amendments Act of 2007 (FDAAA) and to further our transparency objectives. When finalized, this guidance will replace the 2007 guidance.

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[1] This guidance has been prepared by the Office of Communications in the Center for Drug Evaluation and Research (CDER) in consultation with CDER's Safety First Steering Committee at the Food and Drug Administration and in cooperation with the Center for Biologics Evaluation and Research (CBER).

[2] For purposes of this guidance, all references to *drugs* include both human drugs and biological drug products. This guidance does not apply to human cells, tissues, and cellular and tissue-based products regulated solely under section 361 of the Public Health Service Act.

[3] We update guidance documents periodically. To make sure you have the most recent version of a guidance, check the Guidances (Drugs) page at http://www.fda.gov/RegulatoryInformation/Guidances/default.htm. Although this guidance addresses drug safety communications in general, it is not meant to be a comprehensive description of our communications for the wide range of products regulated by FDA (e.g., vaccines). FDA's Web site contains more specific information for certain classes of products.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

BACKGROUND

All drugs have risks, and health care professionals and patients must balance the risks and benefits of a drug therapy when making decisions about whether to use the drug. The general risks and benefits of a drug therapy are described in the product's prescribing information. In addition, however, FDA provides information on drug risks and benefits to health care professionals and patients when that information has generated a specific concern, usually waiting until that information has been fully evaluated and has prompted a regulatory action, such as a revision to the drug's prescribing information. In recent years, FDA has begun making information on potential drug risks available to the public earlier — often while the Agency is still evaluating the data and determining whether any regulatory action is warranted. FDA believes that timely communication of important drug safety information will give health care professionals, patients, consumers, and other interested persons access to the most current information concerning the potential risks and benefits of a marketed drug, helping them to make more informed individual treatment choices.

The following questions and answers provide general guidance on how FDA communicates important safety information to the public.

QUESTIONS AND ANSWERS

1. What Is This Guidance About?

This guidance describes how FDA develops and disseminates information to the public about important drug safety issues, including emerging drug safety information. As discussed in more detail below, an *important drug safety issue* is one that has the potential to alter the benefit–risk analysis for a drug in such a way as to affect decisions about prescribing or taking the drug. Examples of important drug safety issues include, but are not limited to:

- Serious adverse drug reactions identified after drug approval

- Medication errors, which include, but are not limited to, confusion between drug names and confusion regarding drug labeling. These may lead to improper use of the drug, to prescribing or administering an improper dose, or to a patient's taking another medication with which the drug interacts.

We use the term *emerging drug safety information* to describe information FDA is monitoring or analyzing that may have the potential to alter the benefit–risk analysis for a drug in a way that would affect decisions about prescribing or taking the drug, but that has not yet been fully analyzed or confirmed. Such information may relate to new risks or new information about known risks.

FDA may disseminate important drug safety information by other methods and at other times than those described in this guidance. For example, FDA may decide to issue a Public Health Alert or a press release about a medical product or hold a media briefing to communicate important risk information.

2. How Does FDA Evaluate Drug Safety Information?

FDA monitors and reviews safety information about a drug throughout the product's lifecycle, interacting with sponsors during product development and clinical investigation of the drug, closely reviewing safety issues during consideration of a marketing application, and, if the drug is approved, monitoring safety reports after the drug is marketed. Every approved drug has labeling (e.g., prescribing information) that contains, among other things, information about the benefits and risks of using the drug.

After drug approval, FDA may learn of new, or more serious or more frequent, adverse drug reactions from, for example, postapproval voluntary or mandatory reporting of adverse drug reactions during use of the drug, postapproval clinical trials exploring new uses of the drug, other postapproval studies including epidemiologic studies or active surveillance evaluations. For example, additional adverse drug reactions, some of them serious, may be identified once a drug is used more widely and under more diverse conditions (e.g., concurrent use with other drugs), or when the drug is prescribed for off-label uses. In some cases, medication errors can occur because of name confusion or other factors that influence safe use of the medication.

As new information related to a drug becomes available, the Agency reviews the data and evaluates whether there is an emerging drug safety concern. When such a concern arises, relevant medical and scientific experts within FDA engage in a prompt review and analysis of available data. Often, however, there is a period of uncertainty while FDA evaluates the emerging safety information to determine whether there is an important drug safety issue related to a specific drug or drug class and whether regulatory action is appropriate and, if so, what type of action is necessary.[4]

[4] FDA recently issued a draft guidance to FDA staff for comment on *Classifying Significant Postmarket Drug Safety Issues.* This guidance describes the methodological framework by which FDA will classify significant postmarket drug safety issues as *priority*, *standard*, or *emergency*. This guidance is available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm. The draft, when finalized, will reflect the Agency's current thinking on this issue.

During this period, FDA also is actively engaged in scientific efforts to gather additional safety information. Drug sponsors[5] also gather and evaluate emerging safety information and provide the results of their analyses to FDA. As additional data relevant to an emerging drug safety issue become available (e.g., data from an ongoing study or trial, data from surveillance evaluations, or data from available clinical databases), these data are considered in the analysis and decision-making process. FDA may decide that, based on evaluation of additional data related to the drug, further regulatory action, such as requiring a revision to prescribing information or a Risk Evaluation and Mitigation Strategy (REMS), may be appropriate.

Interpreting postmarket safety data is complex, involving analysis of clinical data and detailed review of a wide range of potentially relevant information, including adverse drug experience spontaneous reports, pertinent controlled clinical trials and epidemiologic studies, active surveillance efforts, estimates of drug usage and adverse drug experience reporting rates, estimates of background rates of the adverse event, and other relevant information. Decisions about how to address a safety concern often are a matter of judgment about which reasonable and adequately informed persons with relevant expertise may disagree. We engage in robust and comprehensive discussions within the Agency regarding potential drug safety issues to ensure that all points of view are considered before making a decision on how to proceed.[6] We may consult the Drug Safety Oversight Board, established by FDA in February 2005, asking it to provide recommendations to the center director regarding the management and communication of an emerging drug safety issue.[7] We also may engage in external discussions by convening an Advisory Committee, or coordinating with other public health agencies, such as the Centers for Disease Control and Prevention, or the National Vaccine Program Office, regarding an emerging drug safety issue.

As the Agency evaluates a drug safety issue to determine whether regulatory action is warranted, we may decide to communicate further information to the public at appropriate points during the decision-making process. Consistent with our public health mandate, we may advise the public of an emerging drug safety concern as well as the next steps the Agency may take regarding an important drug safety issue, and there may be updates to this information.

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[5] The term *sponsor* is used broadly in this guidance to refer to the individual or entity that markets a drug or that takes responsibility for and initiates a clinical investigation of a drug. Usually, the sponsor is the owner of the application (*application holder*) for the drug. The *sponsor* also might be the manufacturer of the drug.

[6] See the Manual of Policies and Procedures (MAPP) 4151.1, *Scientific/Regulatory Dispute Resolution for Individuals Within a Management Chain*, Revision 1, effective September 16, 2010; MAPP 4151.2, *Resolution of Differing Professional Opinions: Review by Ad Hoc Panel and CDER Director*, Revision 1, effective September 16, 2010; and MAPP 4151.8, *Equal Voice: Discipline and Organizational Component Collaboration in Scientific and/or Regulatory Decisions*, effective September 16, 2010. These MAPPs can be accessed at http://www.fda.gov/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/default.htm. See also the CBER Standard Operating Procedure and Policy (SOPP) 8006: Resolution of Differences in Scientific Judgment in the Review Process, Version #2, effective January 15, 2009, available at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm109584.htm.

[7] The DSB was subsequently established by statute as part of the Food and Drug Administration Amendments Act of 2007 (FDAAA), creating section 505-1(j) of the Federal Food, Drug, and Cosmetic Act.

3. When Does FDA Communicate Emerging Drug Safety Information to the Public?

FDA currently disseminates emerging drug safety information after having completed an analysis of available data and, in some cases, before having reached a decision about whether regulatory action is warranted. FDA communications about emerging drug safety information can help achieve certain long-standing public health goals, including enhanced vigilance on the part of health care professionals who also may be prompted to increase their reporting of safety observations to FDA.

FDA recognizes the potential public health implications of providing emerging drug safety information, and we are particularly concerned about possible unintended consequences, such as inappropriate modification or discontinuation of useful treatment. We attempt to anticipate and address these possible consequences through our risk communications by (1) describing the nature of a safety concern and what is known about its relationship to a particular drug and (2) making recommendations for health care professionals and patients about how to monitor for and manage the concern.

With respect to potentially important information, the dual goals of having people informed as early as possible and having that information thoroughly substantiated inevitably creates tension. Despite this tension, we lean toward early communication of emerging drug safety information unless, in our judgment, the information available is not reliable enough to be useful and could mislead the public. We recognize this means that, in some cases, we will have to say that a safety concern "has not yet been substantiated." Our goal is to make emerging drug safety information available to the public in a balanced, impartial manner so that health care professionals and patients can consider the information when making decisions about medical treatment, despite uncertainties in the data. FDA is committed to providing accurate, clear, reliable, and useful drug safety information.

FDA considers many factors in the course of evaluating an emerging drug safety issue and deciding whether emerging drug safety information should be made available to the public. These factors may include, but are not limited to, the following:

- Seriousness of the event (e.g., severity and reversibility) relative to the benefits of treatment
- Magnitude of the risk (e.g., likelihood of occurrence)
- Strength of the evidence of a causal relationship between the use of a drug and the adverse event[8]
- Extent of patient exposure (e.g., how broadly the drug is used)
- Disproportionate impact on particular populations (e.g., children or the elderly)

[8] See, for example, guidance for industry on *Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment* at pages 6 to 7 and 17 to 18, available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

- Potential for preventing or mitigating the risk in the patient population (e.g., by monitoring patient selection or avoiding a concomitant treatment)
- Availability of alternative therapies

The decision to provide information about an emerging drug safety issue does not necessarily mean that FDA has concluded there is a causal relationship between the drug and the adverse event described. Nor does communicating emerging drug safety information necessarily mean that FDA is advising health care professionals to limit their prescribing of the drug at issue. Rather, the communications are intended to further inform prescribing and assist health care professionals in making individualized treatment decisions with their patients, based on the balance of potential benefits and risks of the drug for that patient.

At times, decisions to communicate about important drug safety issues are affected by information the public has received from sources other than FDA, such as the mainstream media. In these cases, the safety of a particular drug or drug class may be publicly questioned based on information provided by these other sources that may be incorrect, incomplete, or misleading. In such cases, FDA may issue a statement or engage in other methods of communication to clarify or correct information and respond to public interest.

FDA strives to keep all communications clear and understandable. We also consider elements of human behavior in our communications. We realize, for instance, that risk information provided without context may alarm patients, causing them to discontinue needed medication. With all drug safety communications, FDA now makes a concerted effort to communicate the benefits of a drug along with its risk. Whenever possible and appropriate, when we communicate drug safety information, we include specific advice to patients who use the drug on its safe and effective use to facilitate discussions with their health care practitioners.

4. How Does FDA Communicate Important Drug Safety Information to the Public?

FDA has created effective and ongoing relationships with a wide array of trade and professional associations, patient advocacy and consumer groups, safety organizations, media, and other entities. When drug safety issues arise, we reach out to these groups and work with them to communicate the safety issue to their constituencies.

FDA uses various tools and methods to communicate drug safety information to the public. Important tools used in this effort include, but are not limited to, FDA-approved prescribing information (i.e., drug labeling) and a postmarket communication tool called a *Drug Safety Communication* (DSC), both discussed in the following questions, along with other important tools and methods we use to communicate drug safety information to the public.

5. What is FDA-Approved Labeling?

FDA-approved prescribing information for health care professionals — and patient package inserts and Medication Guides for patients — is the primary source of established information about a drug's safety and efficacy; it summarizes the essential scientific information needed for

the safe and effective use of the drug. The prescribing information for prescription drugs contains sections directed to health care professionals, and may also include sections that are intended for patients.[9]

For some prescription drugs, such as oral contraceptives and estrogens, FDA long ago determined that the safe and effective use of the drug required additional information in nontechnical language to be distributed directly to patients by their health care practitioner or pharmacist (21 CFR 310.501 and 310.515). These *patient package inserts* also may be provided voluntarily by manufacturers for other drugs and are regulated by FDA as labeling.

When patient-directed information is considered necessary for proper use of a drug, FDA requires patient-oriented information in nontechnical language in the form of *Medication Guides* (MedGuides). These have been required for certain prescription drugs that pose a serious and significant public health concern and for which FDA-approved patient information is necessary for safe and effective use of the drug. MedGuides are required if FDA determines that one or more of the following circumstances exist:

- Patient-focused information (*patient labeling*) could help prevent serious adverse effects.
- A drug product has serious risk(s) (relative to benefits) of which patients should be made aware because information concerning the risk(s) could affect a patient's decision to use, or to continue to use, the product.
- A drug product is important to health, and patient adherence to directions for use is crucial to the drug's effectiveness.[10]

In addition, over-the-counter (OTC) drugs bear a *Drug Facts* label that conveys information in a clear, standardized format to enable consumer self-selection of an appropriate drug and enhance the safe and effective use of the drug by consumers.[11]

FDA-approved prescribing information for CDER-regulated drug products is available on the FDA Web site at *Drugs@FDA*. FDA-approved prescribing information for CBER-regulated products is available on the FDA Web site.[12] In addition, FDA facilitates the availability of up-to-date drug prescribing information in an easily accessible electronic format on the National Library of Medicine Web site at *DailyMed*.[13] See also question 10.

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[9] In the *Federal Register* of January 24, 2006 (71 FR 3922), FDA published a final rule, "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products," designed to improve the usefulness of prescribing information for prescription drugs approved after June 30, 2001 (for further information, see http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm). Labeling for these drugs is currently being converted to the new content and format according to a schedule determined at the time of publication of the final rule, and is expected to facilitate the safe and optimal use of prescription drugs.

[10] See 21 CFR 208.1.

[11] See 21 CFR 201.66 (format and content requirements for over-the-counter (OTC) drug product labeling).

[12] See http://www.fda.gov/BiologicsBloodVaccines/ucm121134.htm.

[13] See http://dailymed.nlm.nih.gov/dailymed/about.cfm.

6. What is a CDER Drug Safety Communications (DSC)?

A *Drug Safety Communication* (DSC) is a specific tool used by FDA to communicate to the public important information about safety issues, including emerging safety information, about marketed drugs. DSCs are standardized electronic communications posted on the FDA Web site.[14] Written as clearly as possible, DSCs are targeted to both health care professionals and patients. DSCs generally communicate the following information:

- A summary of the safety issue and the nature of the risk being communicated
- The established benefit or benefits of the drug being discussed
- Recommended actions for health care professionals and patients, when appropriate
- A summary of the data reviewed or being reviewed by FDA

The DSC is FDA's primary safety communication tool for important postmarket drug safety issues. In the past, and at the time our March 2007 guidance was released on this topic, safety communications were issued by FDA in a variety of formats. They were issued under different titles and targeted to different audiences. For instance, in August 2007, FDA began issuing *Early Communications about Ongoing Safety Reviews* (ECs) to keep health care professionals and the general public informed of postmarket safety issues under evaluation by FDA. Safety communications have also been issued under the titles *Public Health Advisory*, *Patient Information Sheet*, *Healthcare Professional Sheet*, and *Alerts on Patient Information and Healthcare Professional Sheets*, and, as these titles suggest, have targeted different audiences. To improve the clarity of our communications, FDA began using a single communication vehicle — the *Drug Safety Communication* — in early 2010.

Some DSCs are related to drug safety issues that continue to develop as more information is obtained. FDA disseminates follow-up DSCs to keep the public informed of new information pertaining to a previously communicated DSC. In addition, some emerging safety information may take a long time to evaluate (if, for example, there is a need for additional clinical trial or epidemiological data to further assess the risk). During the evaluation period, FDA may issue a follow-up DSC as a public reminder, even if no additional information is available since the original DSC was issued.

Note: Although a DSC communicates important safety issues about marketed drugs, it is ***not*** a crisis communication document. If a drug product is defective or tainted, or poses some other form of immediate danger, FDA uses other communication tools, such as *Public Health Alerts*, press releases, stakeholder calls, and media briefings, to inform the public rapidly and protect public health.

7. How Does CBER Communicate Safety Information?

FDA's Center for Biologics Evaluation and Research (CBER) communicates important postmarket safety information regarding biological products to the public using the most

[14] See at http://www.fda.gov/Drugs/DrugSafety/ucm199082.htm.

appropriately targeted communication, taking into consideration the type of product (e.g., vaccine, blood product, or cell therapy), safety issue, and audience. Examples of communication tools include Public Health Notifications, press releases, and safety information updates. These safety communications, like DSCs noted above, include the following important information: (1) a summary of the safety issue and FDA's current understanding of the risk; (2) a summary of information, including the source of the information, reviewed by FDA; (3) information on the benefits and risks of the product involved; and (4) when available and appropriate, recommendations for health care professionals and/or patients and caregivers. Follow-up information is disseminated to keep the public informed of new information pertaining to a previously communicated safety issue. CBER may issue a follow-up as a public reminder, even if no additional information is available since the original communication was issued.

As with CDER-regulated products, if a CBER-regulated biological product is defective or tainted, or poses some other form of immediate danger, FDA may choose from a variety of other communication tools and channels to rapidly inform the public and protect public health.

8. What Other Safety Information Does FDA Post on Its Web Site?

In accordance with requirements of the Food and Drug Administration Amendments Act of 2007 (FDAAA) and to further our transparency objectives, FDA posts various other types of drug safety information, in addition to DSCs, on its Web site, including the following:[15]

- Since 2008, as required by section 921 of FDAAA, FDA has posted on its Web site reports of potential safety issues with drugs[16] identified as a result of our reviews of reports to FDA's Adverse Event Reporting System (AERS). The appearance of a drug on this list, which is updated quarterly, means that FDA has identified a potential safety issue (i.e., new safety information or a potential signal of a serious risk), but it does not mean that FDA has concluded there is a causal relationship between the drug and the risk described.[17]

- Since June 16, 2010, FDA has been posting the results of evaluations performed in accordance with section 915 of FDAAA. Section 915 requires FDA to evaluate marketed drugs 18 months after approval or after 10,000 individuals have used the drug, whichever is later. These evaluations are conducted using various sources of available safety information about marketed drugs to determine whether there are any new serious adverse events not previously identified during development, known side effects reported

[15] This is not an all inclusive list but highlights some new categories of drug safety information we have begun to post as required by FDAAA.

[16] See http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/UCM082196.

[17] FDA has used the term *safety signal* to refer to a concern about an excess of adverse events compared to what would be expected to be associated with a product's use. See FDA guidance for industry, *Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment*, available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

in an unusual number of patients, or potential new safety concerns now that the drugs are being used in the general population.[18]

- In accordance with section 915 of FDAAA, FDA maintains a list of drugs that have been approved with Risk Evaluation and Mitigation Strategies (REMS) and copies of those REMS on its Web site.[19]

9. What Other Methods Are Used to Communicate Drug Safety Information?

In addition to written communications, FDA uses other communication tools, including webinars, broadcasts, and conference calls, to disseminate drug safety information. FDA uses various forms of electronic social media to communicate some safety issues and is continuing to assess additional ways to communicate effectively with the public using these vehicles.

Consistent with FDA's commitment to the expansion of existing communication channels to provide targeted drug safety information to the public, FDA is exploring additional methods of communication, including concise advisories and other Internet postings; more detailed short articles; articles in trade and professional journals; a standardized, one-document solution for patient medication information (PMI); and background papers. If new communication tools are adopted, we intend to update this guidance.

Drug sponsors also use various methods to communicate drug safety information. For example, a sponsor might distribute a Dear Health Care Provider Letter (sometimes referred to as a *Dear Doctor* letter) to convey important information about a marketed drug. A sponsor can issue a Dear Health Care Provider Letter on its own initiative or following a request or requirement by FDA. A sponsor can be required to issue a Dear Health Care Provider Letter or other communication that is approved as part of a communication plan of a REMS. Dear Health Care Provider letters can be used to disseminate information regarding a significant hazard to health, to announce important changes in prescribing information, or to emphasize corrections to prescription drug advertising or prescribing information. Depending on the issue and whether the communication is tied to a regulatory action, FDA may notify the public when sponsors issue a Dear Health Care Provider Letter.

10. Where Is FDA's Drug Safety Information Located?

All of the drug safety information FDA communicates is available via links found on FDA's Web site (e.g., links to the Index to Drug-Specific Information Web page, Drugs@FDA, Safety and Availability [Biologics] and MedWatch Web pages), as described below.

FDA's Web site provides an easily accessible link to the Index to Drug-Specific Information Web page (http://www.fda.gov/cder/drug/DrugSafety/DrugIndex.htm) from which the public can access information about drugs that are the subject of a DSC regarding an important, and often

[18] See http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/ucm204091.htm.

[19] See http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm.

emerging, drug safety issue, as well as established drug safety information. This Index contains links to available Drug Information Pages for specific drugs (identified by both trade name and nonproprietary name) that contain approved drug prescribing information, consumer-friendly information sheets, when available, and other drug information. Drug Information Pages generally are available for drugs that are new molecular entities, or that have been the subject of recent safety communications.

For drugs without a Drug Information Page, the Web page links consumers to Drugs@FDA, which contains drug prescribing information and other regulatory information related to approved drugs (see http://www.accessdata.fda.gov/scripts/cder/drugsatfda).

FDA's Web site contains the Safety & Availability [Biologics] page from which the public can access information about CBER-regulated drugs that are the subject of an important safety communication. (http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/default.htm). In addition, product information pages for licensed biological products include links to related safety information.

The MedWatch program augments FDA and manufacturer communication of drug safety information by distributing MedWatch Safety Alerts to individual subscribers and through its MedWatch Partners Program. Safety information about medical products (including drugs, biologics, devices, and dietary supplements), such as selected information that is the subject of Drug Safety Communications, Dear Health Care Provider Letters, press releases, and market withdrawals, also is available through MedWatch Safety Alerts. This information is available to the general public on the MedWatch Web site (http://www.fda.gov/medwatch/safety), which contains archived information dating back to 1996.

MedWatch, in addition to sending out individual medical product alerts, posts Monthly Safety Labeling Changes on the Web and also distributes them via an alert.[20] This posting includes clinically important prescribing information updates to the following sections of the prescribing information:

- Boxed Warnings
- Contraindications
- Warnings and Precautions
- Adverse Reactions
- Patient Package Insert & Medication Guide

11. How Is Drug Safety Information Updated?

The public can access the most current safety information about a drug through the Index to Drug-Specific Information and Safety & Availability [Biologics] Web pages. FDA intends to update the information available on these Web pages on a periodic basis to reflect new information that becomes available.

[20] See http://www.fda.gov/Safety/MedWatch/SafetyInformation/Safety-RelatedDrugLabelingChanges/default.htm.

Emerging drug safety information presented as a DSC is identified by the month and year in which the information is posted on the Index to Drug-Specific Information Web page. We intend to update DSCs to describe important new information relevant to the emerging drug safety issue after the emerging drug safety issue is addressed through revision of prescribing information, approval of a REMS, request for voluntary withdrawal from the market, or other regulatory action. We plan to identify updated information with the month and year in which it was added to the Web site or communicated by other methods. After an emerging safety issue has been addressed through regulatory action, it is permanently archived (as are all DSCs) on the FDA Web site.

If data become available that provide sufficient evidence that a drug is not associated with the safety concern previously described by FDA as an emerging drug safety issue, FDA intends to update the information accordingly. In these instances, we plan to issue a new update of comparable prominence to the DSC to reflect this new information. Updated DSCs, like all DSCs, are permanently archived on the Web site.

Some important drug safety information may have utility independent of any regulatory action. For example, sometimes a sponsor may be required to conduct a long-term study or clinical trial related to an emerging drug safety issue.[21] This is one reason why DSCs remain permanently archived.

FDA recognizes that evaluation of some emerging drug safety issues may not be accomplished quickly. This may be because of the complexity of an issue or the need for studies or clinical trials of adequate duration to evaluate a potential risk with a long latency period.[22] In these cases, archived DSCs create a permanent record of the continued evaluation of the issue. This will help ensure that important information about ongoing safety issues that may affect a health care professional's decision to prescribe, or a patient's or consumer's decision to use, a medication will continue to be communicated.

For CBER-regulated products, emerging drug safety information is presented on FDA's Web page Safety & Availability [Biologics] by the year in which the information is posted. Updates are provided as new information becomes available.

12. How Does FDA Handle Confidential Information About a Drug Safety Issue?

Most of the information currently posted on the Index to Drug-Specific Information Web page is information that is prepared for public disclosure and contains no confidential information. FDA may publish related information on the Web page that was not specifically prepared for public disclosure, such as FDA scientific reviews. This information is reviewed before publication to ensure that disclosure of this information is in accordance with applicable disclosure laws and FDA regulations.

[21] See 21 U.S.C. 355(o)(3).

[22] See draft guidance, *Classifying Significant Postmarket Drug Safety Issues*.

13. Does FDA Involve Sponsors Before Making Emerging Drug Safety Information Public?

Our communication of emerging drug safety information is intended to represent FDA's independent analysis of emerging information and FDA's scientific judgment as to the appropriate communication of this emerging drug safety information to the public. FDA may solicit sponsor input when appropriate, for example, to confirm the accuracy of factual information. FDA strives to notify the relevant sponsor at least 24 hours before the first public communication that emerging safety information about its drug will be posted on the FDA Web site.

For purposes of this guidance, the relevant sponsor generally is the new drug application (NDA), biologics license application (BLA), or abbreviated new drug application (ANDA) holder(s) for the drug or drug class that is the subject of a DSC containing an important drug safety issue. We recognize that over-the-counter (OTC) drugs subject to one or more final OTC monographs, rather than approved under an NDA or ANDA, may be manufactured by multiple entities and thus have multiple relevant sponsors. FDA continues to consider appropriate mechanisms to facilitate timely notification of affected entities marketing OTC drugs and welcomes comment on this issue.

Note: Sponsors are required to report certain adverse drug experience information to FDA in accordance with the U.S. Food, Drug, and Cosmetic Act (FDCA) and our regulations[23] and may provide FDA with additional information relevant to a drug safety issue at any time. A sponsor also may request that the Agency update its communication of emerging drug safety information if the sponsor provides additional information supporting the request.[24]

14. Can FDA Risk Communication Be Used in Prescription Drug Promotion?

FDA recognizes that some sponsors may consider making promotional comparisons between their drugs and drugs for which emerging drug safety information has been provided by FDA. We remind sponsors that all safety and effectiveness claims made in prescription drug promotion,[25] including claims based on Government materials available from the Index to Drug-Specific Information, must be supported by substantial evidence or substantial clinical experience and must not be otherwise false or misleading (21 U.S.C. 355 and 352; 21 CFR 202.1(e)).

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[23] Sponsors of approved NDAs or ANDAs, manufacturers of marketed prescription drugs for human use without approved NDAs or ANDAs, and licensed manufacturers of approved BLAs are required to report adverse experiences to the FDA under 21 CFR 310.305, 314.80, 314.98, and 600.80. Manufacturers of OTC products subject to monographs are required to report serious adverse experiences to the FDA under FDCA section 760.

[24] Any such request should be made in accordance with standard procedures for submitting information concerning a particular drug to FDA (e.g., directed to the appropriate division within the Office of New Drugs, the Office Generic Drugs, or the Office of Nonprescription Products, as appropriate).

[25] The Federal Trade Commission (FTC) has primary responsibility for regulating the advertising of nonprescription drug products.

Neither the fact that FDA has communicated emerging drug safety information for a drug nor the specific information posted about that drug will generally constitute (either separately or collectively) substantial evidence or substantial clinical experience that would support a comparative safety or effectiveness claim. Therefore, comparative claims made in prescription drug promotion based on an FDA communication of emerging drug safety information (e.g., "Our drug is safer because of the emerging drug safety information posted by the FDA about a competitor's drug") may be considered false or misleading.

Representations that minimize the implications of emerging drug safety information communicated by FDA also may be considered false or misleading. For those seeking to explain to health care professionals what emerging drug safety information means, we refer to the sections of this guidance that discuss the purpose of disseminating emerging drug safety information and the nature of the information to be posted on the Index to Drug-Specific Information Web page.

SUMMARY

FDA plays a critical role in detecting and managing safety issues that are identified after a drug is approved for marketing, including a critical role in communicating information to the public. The actions we take depend on many factors, including the characteristics of the adverse events, the frequency of the reports, the seriousness of the diseases or conditions for which the drug provides a benefit, the availability of alternative therapies, and the consequences of not treating the disease. Despite working toward systematic methods of identifying and disseminating information about drug safety issues, communicating about drug safety issues will always require a significant amount of judgment about whether to communicate in a given case and, if so, what to communicate.

It is our goal is to make the most up-to-date drug safety information available to the public in a timely manner so that health care professionals and patients can consider the information when making decisions about medical treatment, yet be aware of uncertainties in the data. FDA is committed to providing accurate, clear, reliable, and useful drug safety information.

EXHIBIT G

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

Media:

Jeremy Kahn (mailto:jeremy.kahn@fda.hhs.gov)

301-796-8671

Consumer:

888-INFO-FDA

More Press Announcements (/news-events/newsroom/press-announcements)

EXHIBIT H

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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Inquiries

Media:

Sarah Peddicord (mailto:sarah.peddicord@fda.hhs.gov)

301-796-2805

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)

More Press Announcements (/news-events/newsroom/press-announcements)

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EXHIBIT I

NDA 021698/S-031

SUPPLEMENT APPROVAL

Sanofi US Services Inc.
Attention: Doris Sincak MS
Senior Manager, North America and Global Regulatory Affairs
55 Corporate Drive
Bridgewater, NJ 08807

Dear Ms. Sincak:

Please refer to your supplemental new drug application (sNDA) dated and received April 22, 2019, and your amendment, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Maximum Strength Zantac 150 (ranitidine hydrochloride) tablet,150 mg.

This "Prior Approval" supplemental new drug application provides for discontinuation of the Consumer Information Leaflet (CIL) and addition of the "Tips for Managing Heartburn" information to the outer carton for all stock-keeping units.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

We remind you of your commitment to increase the size of the statement of identity by May 2020.

LABELING

Submit final printed labeling (FPL), as soon as they are available, but no more than 30 days after they are printed. The FPL must be identical to the enclosed labeling and must be in the "Drug Facts" format (21 CFR 201.66), where applicable.

MAXIMUM STRENGTH ZANTAC 150 TABLETS

Submitted Labeling	Date Submitted
3-count hangtag carton (blister) – origin Mexico	June 21, 2019

3-count hangtag carton (blister) – origin Spain	June 21, 2019
8-count carton (blister) – origin Mexico	April 22, 2019
8-count carton (blister) – origin Spain	April 22, 2019
24-count carton (blister) – origin Mexico	April 22, 2019
24-count carton (blister) – origin Spain	April 22, 2019
32-count *Bonus! 8 Free Tablets* carton (blister) – origin Mexico	April 22, 2019
32-count *Bonus! 8 Free Tablets* carton (blister) – origin Spain	April 22, 2019
40-count carton (bottle) – origin Mexico	April 22, 2019
40-count carton (bottle) – origin Spain	April 22, 2019
50-count carton (bottle) – origin Mexico	April 22, 2019
50-count carton (bottle) – origin Spain	April 22, 2019
65-count carton (bottle) – origin Mexico	April 22, 2019
65-count carton (bottle) – origin Spain	April 22, 2019
78-count *Bonus! 13 Free Tablets* carton (bottle) – origin Mexico	April 22, 2019
78-count *Bonus! 13 Free Tablets* carton (bottle) – origin Spain	April 22, 2019
80-count dispenser (pouch) – origin Mexico	April 22, 2019
80-count dispenser (pouch) – origin Spain	April 22, 2019
90-count “VALUE SIZE 90 TABLETS” carton (bottle) - *Mexico*	April 22, 2019

90-count "VALUE SIZE 90 TABLETS" carton (bottle) - *Spain*	April 22, 2019
140-count (2x70) Club backer card (bottle)	April 22, 2019
Submitted Labeling	**Date Submitted**
ZANTAC 150 COOL MINT	
8-count carton *Cool Mint* (blister) – origin Mexico	April 22, 2019
24-count carton *Cool Mint* (blister) – origin Mexico	April 22, 2019
32-count *Bonus! 8 Free Tablets* carton *Cool Mint* (blister) – origin Mexico	April 22, 2019
40-count carton *Cool Mint* (bottle) – origin Mexico	April 22, 2019
50-count carton *Cool Mint* (bottle) – origin Mexico	April 22, 2019
65-count carton *Cool Mint* (bottle) – origin Mexico	April 22, 2019
78-count *Bonus! 13 Free Tablets* carton *Cool Mint* (bottle) – origin Mexico	April 22, 2019
90-count "VALUE SIZE 90 TABLETS" carton *Cool Mint* (bottle) - *Mexico*	April 22, 2019

The FPL should be submitted electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*.[1] For administrative purposes, designate this submission "**Final Printed Labeling for approved NDA 021698/S-031**." Approval of this submission by FDA is not required before the labeling is used.

[1] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

DRUG REGISTRATION AND LISTING

All drug establishment registration and drug listing information is to be submitted to FDA electronically, via the FDA automated system for processing structured product labeling (SPL) files (eLIST). At the time that you submit your final printed labeling (FPL), the content of labeling (Drug Facts) should be submitted in SPL format as described at FDA.gov.[2] Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Dr. Helen Lee, Regulatory Project Manager, at 301-796-6848.

Sincerely,

{See appended electronic signature page}

Valerie Pratt, MD
Deputy Director, Safety
Division of Nonprescription Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Carton and Container Labeling

[2] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

VALERIE S PRATT
09/18/2019 02:41:47 PM

EXHIBIT J

Zantac 150 3ct Carton
06.13.19

ZAN_150_3ct_CTN_0140048-01_Mex_2019_FDA_DSN3

Sanofi Regulatory Specifications			Verified Date: 06/13/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9.0 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9.0 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	5.8 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.070 in
PDP dimensions (in millimeters)			H 60mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 8.81 pt. H 0.00 pt
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 61 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

AA0415

Zantac 150 3ct Carton
06.13.19

ZAN_150_3ct_CTN_0140047-01_Spain_2019_FDA_DSN3

Sanofi Regulatory Specifications			Verified Date: 06/13/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9.0 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9.0 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	5.8 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.070 in
PDP dimensions (in millimeters)			H 60mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 8.81 pt. H 0.00 pt
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 61 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity pt.) (Divided by Largest Logo Copy (pt.)			V 15% H 0%

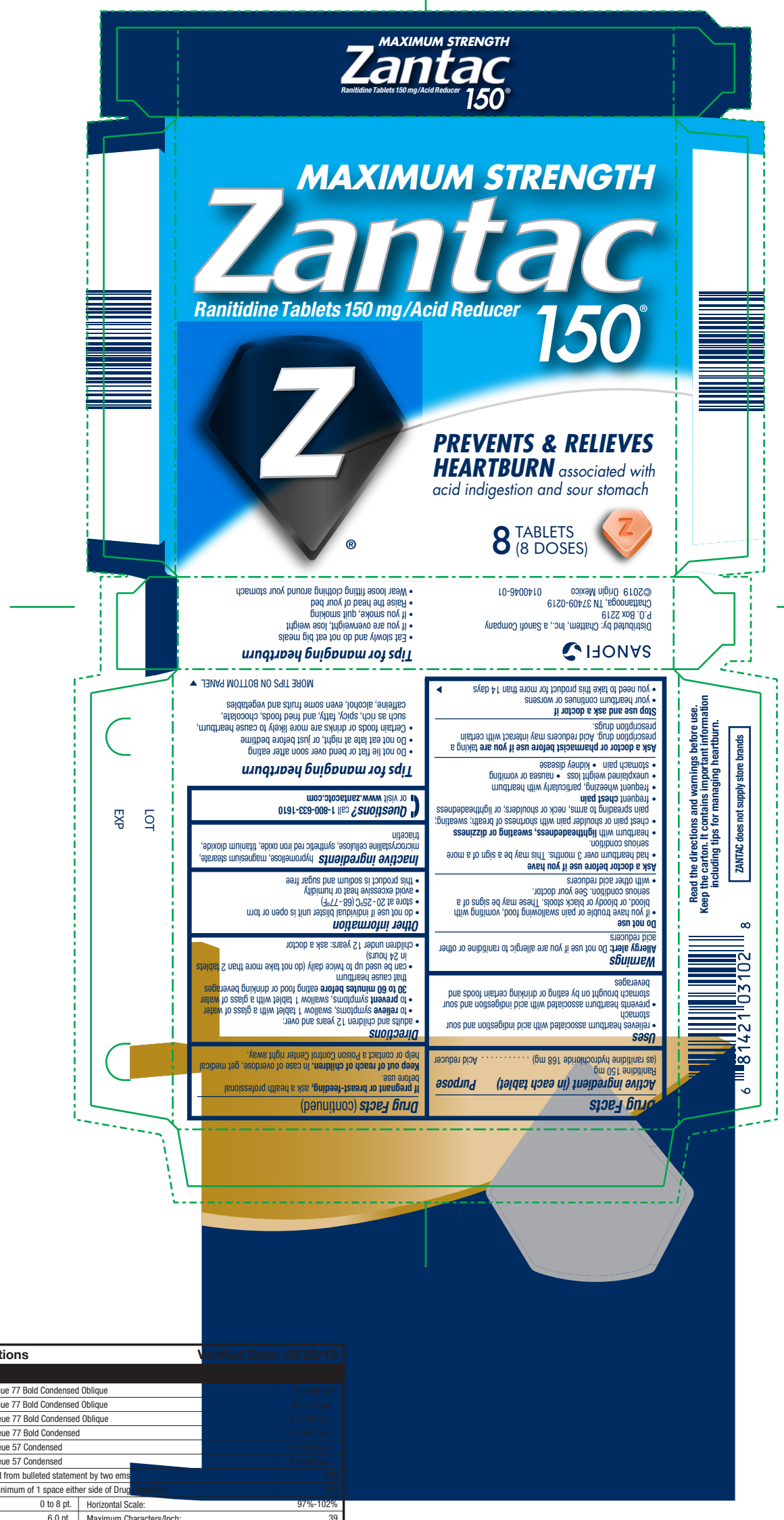
Reference ID: 4493200

AA0416

AA0417

Zantac 150 8ct Carton
03.28.19

ZAN_150_8ct_CTN_0140046-01_Mex_2019_FDA_DSN2



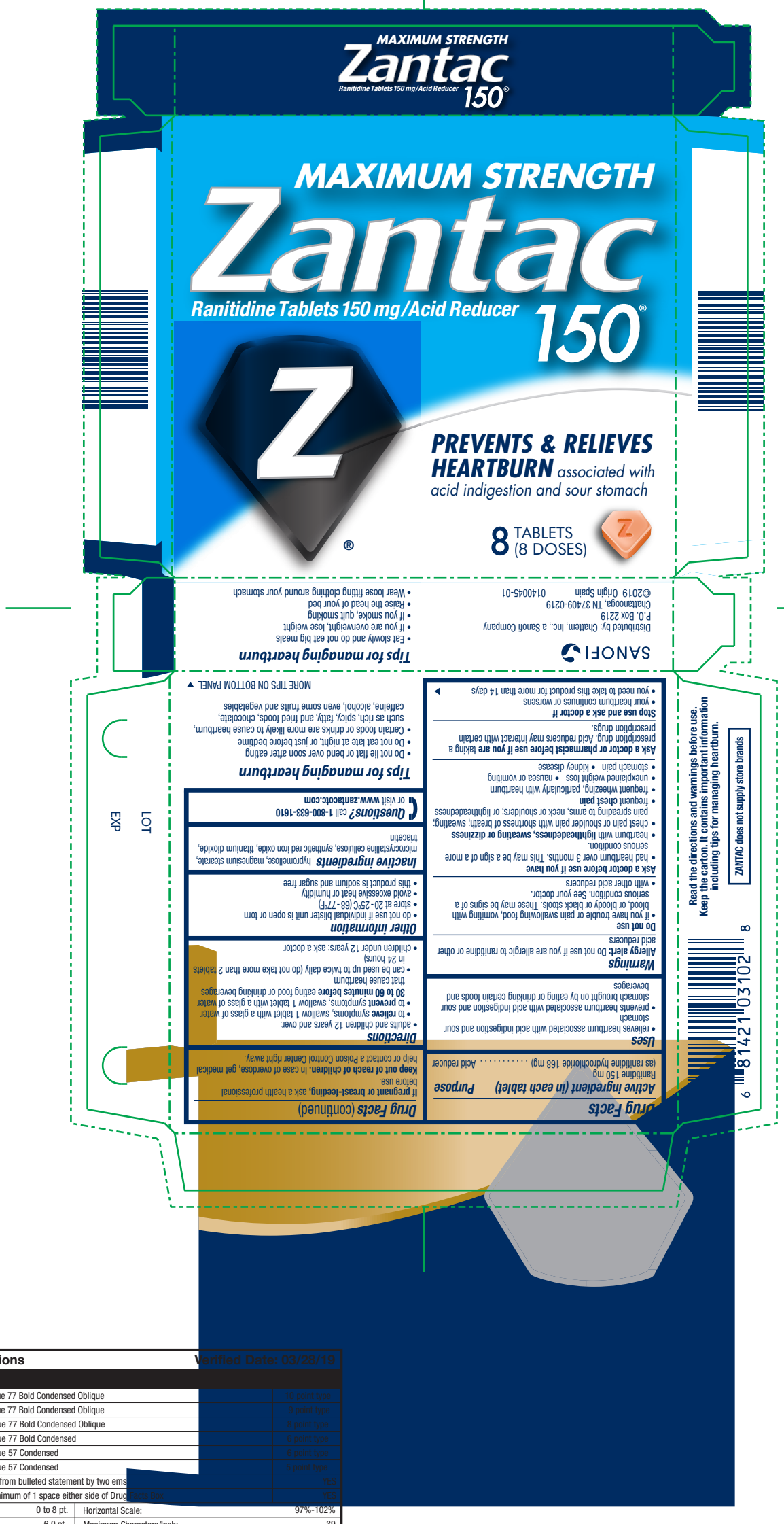
Sanofi Regulatory Specifications		Verified Date: 03/28/19	
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		8 point type
Bullets	Font name: Helvetica Neue 57 Condensed		8 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

AA0418

Zantac 150 8ct Carton
03.28.19

ZAN_150_8ct_CTN_0140045-01_Spain_2019_FDA_DSN3



Sanofi Regulatory Specifications			Verified Date: 03/28/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		8 point type
Bullets	Font name: Helvetica Neue 57 Condensed		8 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

Zantac 150 24ct Carton
03.18.19

ZAN_150_24ct_CTN_0140044-01_Mex_2019_FDA_DSN2

AA0419

Sanofi Regulatory Specifications			Verified Date: 03/18/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	5.9 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

Zantac 150 24ct Carton
03.14.19

ZAN_150_24ct_CTN_0140043-01_Spain_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	5.9 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 150 32ct Carton
03.14.19

ZAN_150_32ct_Bonus_CTN_0140074-01_Mex_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	5.9 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Sanofi Regulatory Specifications — **Verified Date: 03/06/19**

Drug Facts Info		
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique	10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique	9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique	8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed	6 point type
Body Text	Font name: Helvetica Neue 57 Condensed	6 point type
Bullets	Font name: Helvetica Neue 57 Condensed	5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems		YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box		YES

Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	5.9 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.

Principal Display Panel Info	
Font size of Net Quantity of Contents (Smallest character height in inches)	0.088 in
PDP dimensions (in millimeters)	H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")	V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")	V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP	
Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)	V 15% H 0%

Zantac 150 32ct Carton
03.06.19

ZAN_150_32ct_Bonus_CTN_0140077-01_Spain_2019_FDA_DSN2

Zantac 150 40ct Carton
03.14.19

ZAN_150_40ct_CTN_ 0140071-01_Mex_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) / (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

AA0423

Zantac 150 40ct Carton
03.14.19

ZAN_150_40ct_CTN_0140070-01_Spain_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) / (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

AA0424

Zantac 150 50ct Carton
03.14.19

ZAN_150_50ct_CTN_0140042-01_Mex_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) / (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

AA0425

Zantac 150 50ct Carton
03.14.19

ZAN_150_50ct_CTN_0140041-01_Spain_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) / (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

AA0426

Zantac 150 65ct Carton
02.28.19

ZAN_150_65ct_CTN_0140039-01_Mex_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 02/28/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) / (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

AA0427

Zantac 150 65ct Carton
03.14.19

ZAN_150_65ct_CTN_0140040-01_Spain_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) / (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

AA0428

Zantac 150 78ct Carton
02.28.19

ZAN_150_78ct_Bonus_CTN_0140036-01_Mex_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 02/28/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) / (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 150 78ct Carton
03.14.19

ZAN_150_78ct_Bonus_CTN_0140072-01_Spain_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 150 1ct Sachet/Pouch Dispenser (80ct)
03.18.19
ZAN_150_80ct_Dispenser_0140081-01_Mex_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/18/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		11.5 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		9.25 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		7 point type
Body Text	Font name: Helvetica Neue 57 Condensed		7 point type
Bullets	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.5 pt.	Maximum Characters/Inch:	30
Barlines:	2.5 pt.	Hairlines:	.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			.0903 in
PDP dimensions (in inches)			H 4.00 in W 4.75 in
Font size of Statement of Identity (if not live text, to be measured in Helvetica capital "M")			V 13 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 94 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

MAXIMUM STRENGTH
Zantac 150®
Ranitidine Tablets 150 mg/Acid Reducer

PREVENTS & RELIEVES HEARTBURN associated with acid indigestion and sour stomach

Drug Facts

Active ingredient (in each tablet) — **Purpose**
Ranitidine 150 mg (as ranitidine hydrochloride 168 mg) ..... Acid reducer

Uses
- relieves heartburn associated with acid indigestion and sour stomach
- prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain foods and beverages

Warnings
Allergy alert: Do not use if you are allergic to ranitidine or other acid reducers

Do not use
- if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.
- with other acid reducers

Ask a doctor before use if you have
- had heartburn over 3 months. This may be a sign of a more serious condition
- heartburn with **lightheadedness, sweating or dizziness**
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**
- frequent wheezing, particularly with heartburn
- unexplained weight loss • nausea or vomiting
- stomach pain • kidney disease

Ask a doctor or pharmacist before use if you are taking a prescription drug. Acid reducers may interact with certain prescription drugs.

Stop use and ask a doctor if
- your heartburn continues or worsens
- you need to take this product for more than 14 days ▸

Drug Facts (continued)

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions
- adults and children 12 years and over:
  - to **relieve** symptoms, swallow 1 tablet with a glass of water
  - to **prevent** symptoms, swallow 1 tablet with a glass of water **30 to 60 minutes before** eating food or drinking beverages that cause heartburn
  - can be used up to twice daily (do not take more than 2 tablets in 24 hours)
- children under 12 years: ask a doctor

Other information
- do not use if individual foil pouch is open or torn
- store at 20-25°C (68-77°F)
- avoid excessive heat or humidity
- this product is sodium and sugar free

Inactive ingredients hypromellose, magnesium stearate, microcrystalline cellulose, synthetic red iron oxide, titanium dioxide, triacetin

Questions? call **1-800-633-1610** or visit **www.zantacotc.com**

Tips for managing heartburn
- Do not lie flat or bend over soon after eating
- Do not eat late at night, or just before bedtime
- Certain foods or drinks are more likely to cause heartburn, such as rich, spicy, fatty, and fried foods, chocolate, caffeine, alcohol, even some fruits and vegetables
- Eat slowly and do not eat big meals
- If you are overweight, lose weight
- If you smoke, quit smoking
- Raise the head of your bed
- Wear loose fitting clothing around your stomach

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0140081-01

6 81421 03112 7

Do not discard this carton.
It contains important consumer information.

80 POUCHES
1 TABLET (1 DOSE)

TO OPEN
PUSH IN TAB AND PULL OUT

Zantac 150 1ct Sachet/Pouch Dispenser (80ct)
03.12.19
ZAN_150_80ct_Dispenser_0140080-01_Spain_2019_FDA_DSN3

Sanofi Regulatory Specifications			Verified Date: 03/12/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		11.5 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		9.25 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		7 point type
Body Text	Font name: Helvetica Neue 57 Condensed		7 point type
Bullets	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.5 pt.	Maximum Characters/Inch:	30
Barlines:	2.5 pt.	Hairlines:	.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			.0903 in
PDP dimensions (in inches)			H 4.00 in W 4.75 in
Font size of Statement of Identity (if not live text, to be measured in Helvetica capital "M")			V 13 pt. H 0.00 pt.
Font size of Logo/Largest Copy on POP (If not live text, to be measured in Helvetica capital "M")			V 94 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on POP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

MAXIMUM STRENGTH
Zantac 150®
Ranitidine Tablets 150 mg/Acid Reducer

PREVENTS & RELIEVES HEARTBURN associated with acid indigestion and sour stomach

Drug Facts

Active ingredient (in each tablet) — **Purpose**
Ranitidine 150 mg (as ranitidine hydrochloride 168 mg) ..... Acid reducer

Uses
- relieves heartburn associated with acid indigestion and sour stomach
- prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain foods and beverages

Warnings
Allergy alert: Do not use if you are allergic to ranitidine or other acid reducers

Do not use
- if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.
- with other acid reducers

Ask a doctor before use if you have
- had heartburn over 3 months. This may be a sign of a more serious condition.
- heartburn with **lightheadedness, sweating or dizziness**
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**
- frequent wheezing, particularly with heartburn
- unexplained weight loss • nausea or vomiting
- stomach pain • kidney disease

Ask a doctor or pharmacist before use if you are taking a prescription drug. Acid reducers may interact with certain prescription drugs.

Stop use and ask a doctor if
- your heartburn continues or worsens
- you need to take this product for more than 14 days ▶

Drug Facts (continued)

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions
- adults and children 12 years and over:
  - to **relieve** symptoms, swallow 1 tablet with a glass of water
  - to **prevent** symptoms, swallow 1 tablet with a glass of water **30 to 60 minutes before** eating food or drinking beverages that cause heartburn
  - can be used up to twice daily (do not take more than 2 tablets in 24 hours)
- children under 12 years: ask a doctor

Other information
- do not use if individual foil pouch is open or torn
- store at 20-25°C (68-77°F)
- avoid excessive heat or humidity
- this product is sodium and sugar free

Inactive ingredients hypromellose, magnesium stearate, microcrystalline cellulose, synthetic red iron oxide, titanium dioxide, triacetin

Questions? call **1-800-633-1610** or visit **www.zantacotc.com**

Tips for managing heartburn
- Do not lie flat or bend over soon after eating
- Do not eat late at night, or just before bedtime
- Certain foods or drinks are more likely to cause heartburn, such as rich, spicy, fatty, and fried foods, chocolate, caffeine, alcohol, even some fruits and vegetables
- Eat slowly and do not eat big meals
- If you are overweight, lose weight
- If you smoke, quit smoking
- Raise the head of your bed
- Wear loose fitting clothing around your stomach

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0140080-01

6 81421 03112 7

Do not discard this carton.
It contains important consumer information.

80 POUCHES
1 TABLET (1 DOSE)
TO OPEN
PUSH IN TAB AND PULL OUT

Zantac 150 90ct Carton
03.14.19

ZAN_150_90ct_Bonus_CTN_0140038-01_Mex_2019_FDA_DSN

AA0433

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) / Brand/Logo/Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

Zantac 150 90ct Carton
03.14.19

ZAN_150_90ct_Bonus_CTN_0140037-01_Spain_2019_FDA_DSN

AA0434

Sanofi Regulatory Specifications

Drug Facts Info

Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.

Principal Display Panel Info

Font size of Net Quantity of Contents (Smallest character height in inches)	0.088 in
PDP dimensions (in millimeters)	H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")	V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")	V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) / Reduction/Largest Logo Copy (pt.)	V 15% H 0%

Reference ID: 4493200

AA0435

Zantac 150 Twin Card (140ct)

03.25.19

ZAN_150_TWIN_140CT_Card_0140082-01_2019_FDA_DSN5

Twin Pack 2 Bottles x 70ct = 140ct

MAXIMUM STRENGTH

Zantac 150®

Ranitidine Tablets 150 mg/Acid Reducer

140
TABLETS
(140 DOSES)

PREVENTS & RELIEVES HEARTBURN
associated with acid indigestion and sour stomach

KO Varnish
Lot Code

8 81421 03160 6

Drug Facts

Active ingredient (in each tablet)	Purpose
Ranitidine 150 mg (as ranitidine hydrochloride 168 mg)	Acid reducer

Uses
- relieves heartburn associated with acid indigestion and sour stomach
- prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain foods and beverages

Warnings
Allergy alert: Do not use if you are allergic to ranitidine or other acid reducers

Do not use
- if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.
- with other acid reducers

Ask a doctor before use if you have
- had heartburn over 3 months. This may be a sign of a more serious condition.
- heartburn with **lightheadedness, sweating or dizziness**, chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**
- frequent wheezing, particularly with heartburn
- unexplained weight loss • nausea or vomiting
- stomach pain • kidney disease

Ask a doctor or pharmacist before use if you are taking a prescription drug. Acid reducers may interact with certain prescription drugs.

Stop use and ask a doctor if
- your heartburn continues or worsens
- you need to take this product for more than 14 days

Drug Facts (continued)

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions
- adults and children 12 years and over:
  - to **relieve** symptoms, swallow 1 tablet with a glass of water
  - to **prevent** symptoms, swallow 1 tablet with a glass of water **30 to 60 minutes before** eating food or drinking beverages that cause heartburn
- can be used up to twice daily (do not take more than 2 tablets in 24 hours)
- children under 12 years: ask a doctor

Other information
- do not use if printed foil under bottle cap is open or torn
- store at 20-25°C (68-77°F)
- avoid excessive heat or humidity
- this product is sodium and sugar free

Inactive ingredients
hypromellose, magnesium stearate, microcrystalline cellulose, synthetic red iron oxide, titanium dioxide, triacetin

Questions? call **1-800-633-1610** or visit **www.zantacotc.com**

Tips for managing heartburn
- Do not lie flat or bend over soon after eating
- Do not eat late at night, or just before bedtime
- Certain foods or drinks are more likely to cause heartburn, such as rich, spicy, fatty, and fried foods, chocolate, caffeine, alcohol, even some fruits and vegetables
- Eat slowly and do not eat big meals
- If you are overweight, lose weight
- If you smoke, quit smoking
- Raise the head of your bed
- Wear loose fitting clothing around your stomach

Read the directions and warnings before use. Keep the card. It contains important information including tips for managing heartburn.

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0140082-01

MAXIMUM STRENGTH
Zantac 150®
Ranitidine Tablets 150 mg/Acid Reducer

Sanofi Regulatory Specifications — Verified Date: 03/25/19

Drug Facts Info

Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique	11.5 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique	10 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique	9.25 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed	7 point type
Body Text	Font name: Helvetica Neue 57 Condensed	7 point type
Bullets	Font name: Helvetica Neue 57 Condensed	6 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems		YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box		YES

Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.5 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	.5 pt.

Principal Display Panel Info

Font size of Net Quantity of Contents (Smallest character height in inches)	.0903 in
PDP dimensions (in inches)	H 6.75 in W 7.75 in
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")	V 13 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")	V 94 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)	V 15% H 0%

Zantac 150 Cool Mint 8ct Carton
03.28.19

ZAN_150_CoolMint_8ct_CTN_0140069-01_Mex_2019_FDA_DSN3

Sanofi Regulatory Specifications			Verified Date: 03/28/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 150 Cool Mint 24ct Carton
03.14.19

ZAN_150_CoolMint_24ct_CTN_0140068-01_Mex_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	5.9 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital “M”)			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital “M”)			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 150 Cool Mint 32ct Carton
03.06.19

ZAN_150_CoolMint_32ct_Bonus_CTN_0140075-01_Mex_2019_FDA_DSN2

Sanofi Regulatory Specifications			Verified Date: 03/06/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	5.9 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 150 Coolmint 40ct Carton
02.28.19

ZAN_150_Coolmint_40ct_CTN_0140063-01_MEX_2019_FDA_DSN.ai

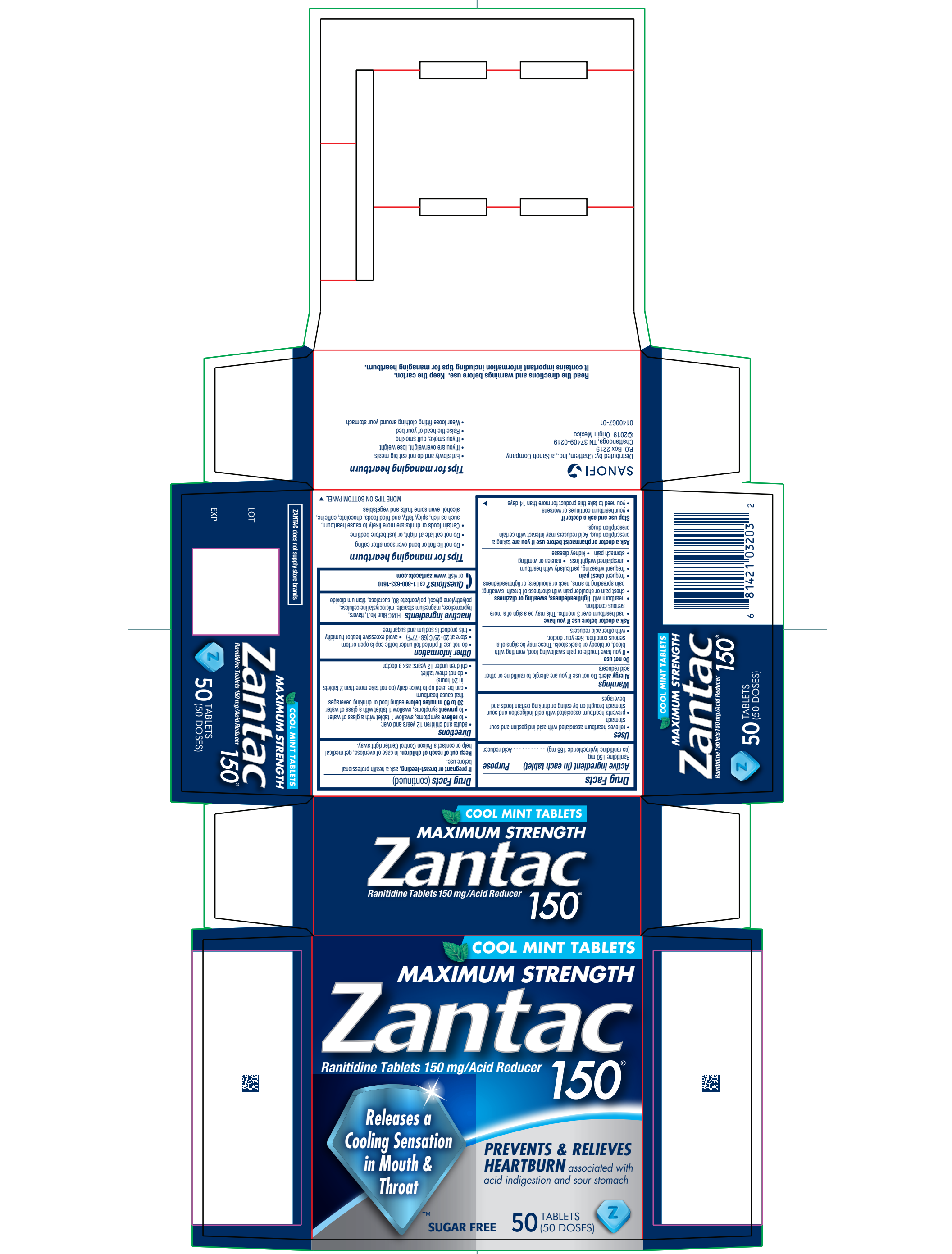
Sanofi Regulatory Specifications			Verified Date: 02/28/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

AA0439

Zantac 150 Coolmint 50ct Carton
03.14.19

ZAN_150_CoolMint_50ct_CTN_0140067-01_Mex_2019_FDA_DSN



Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) Divided by Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

AA0440

Zantac 150 Coolmint 65ct Carton
03.14.19

ZAN_150_Coolmint_65ct_CTN_0140066-01_Mex_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) Divided by Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

AA0441

Zantac 150 Coolmint 78ct Carton
03.14.19

ZAN_150_Coolmint_78ct_Bonus_CTN_0140065-01_Mex_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) / (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493200

AA0442

Zantac 150 Coolmint 90ct Carton
03.14.19

ZAN_150_Coolmint_90ct_Value_CTN_0140064-01_Mex_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

VALERIE S PRATT
09/18/2019 02:41:47 PM

EXHIBIT K

NDA 020520/S-038

SUPPLEMENT APPROVAL

Sanofi US Services Inc.
Attention: Doris Sincak MS
Senior Manager, North America and Global Regulatory Affairs
55 Corporate Drive
Bridgewater, NJ 08807

Dear Ms. Sincak:

Please refer to your supplemental new drug application (sNDA) dated April 23, 2019, and your amendment, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zantac 75 (ranitidine hydrochloride) tablet, 75 mg.

This "Prior Approval" supplemental new drug application provides for discontinuation of the Consumer Information Leaflet (CIL) and addition of the "Tips for managing heartburn" information to the outer carton for all stock-keeping units.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

We remind you of your commitment to increase the size of the statement of identity by May 2020.

LABELING

Submit final printed labeling (FPL), as soon as they are available, but no more than 30 days after they are printed. The FPL must be identical to the table below. The final printed label must be in the "Drug Facts" format (21 CFR 201.66), where applicable.

Zantac 75 tablets

Submitted Labeling	Date Submitted
2-count "*On-The-Go Packs*" carton (pouch) – origin Mexico	June 21, 2019
2-count "*On-the-Go Packs*" carton (pouch) – origin Spain	June 21, 2019

10-count carton (blister) – origin Mexico	April 23, 2019
10-count carton (blister) – origin Spain	April 23, 2019
30-count carton (blister) – origin Mexico	April 23, 2019
30-count carton (blister) – origin Spain	April 23, 2019
40-count *Bonus! 10 Free Tablets* carton (blister) – origin Mexico	April 23, 2019
40-count *Bonus! 10 Free Tablets* carton (blister) – origin Spain	April 23, 2019
60-count carton (bottle) – origin Mexico	April 23, 2019
60-count carton (bottle) – origin Spain	April 23, 2019
80-count carton (bottle) – origin Mexico	April 23, 2019
80-count carton (bottle) – origin Spain	April 23, 2019
96-count *Bonus! 16 Free Tablets* carton (bottle) – origin Mexico	April 23, 2019
96-count *Bonus! 16 Free Tablets* carton (bottle) – origin Spain	April 23, 2019
100-count dispenser (pouch) – origin Mexico	April 23, 2019
100-count dispenser (pouch) – origin Spain	April 23, 2019

The FPL should be submitted electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*.[1] For administrative purposes, designate this submission "**Final Printed Labeling for approved NDA 020520/S-038**." Approval of this submission by FDA is not required before the labeling is used.

DRUG REGISTRATION AND LISTING

All drug establishment registration and drug listing information is to be submitted to FDA electronically, via the FDA automated system for processing structured product labeling (SPL) files (eLIST). At the time that you submit your final printed labeling (FPL), the content of labeling (Drug Facts) should be submitted in SPL format as described at FDA.gov.[2] Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Dr. Helen Lee, Regulatory Project Manager, at 301-796-6848.

Sincerely,

{See appended electronic signature page}

Valerie Pratt, MD
Deputy Director, Safety
Division of Nonprescription Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Carton and Container Labeling

[1] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

[2] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

VALERIE S PRATT
09/18/2019 04:35:47 PM

EXHIBIT L

Zantac 75 2ct Carton
06.13.19
ZAN_75_2ct_CTN_0140050-01_Mex_2019_FDA_DSN3

AA0451

Sanofi Regulatory Specifications			Verified Date: 06/13/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9.0 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9.0 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	5.8 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.070 in
PDP dimensions (in millimeters)			H 60mm W 97mm
Font size of Statement of Identity (if not live text, to be measured in Helvetica capital "M")			V 8.81 pt. H 0.00 pt
Font size of Logo/Largest Copy on PDP (if not live text, to be measured in Helvetica capital "M")			V 61 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 75 2ct Carton
06.13.19

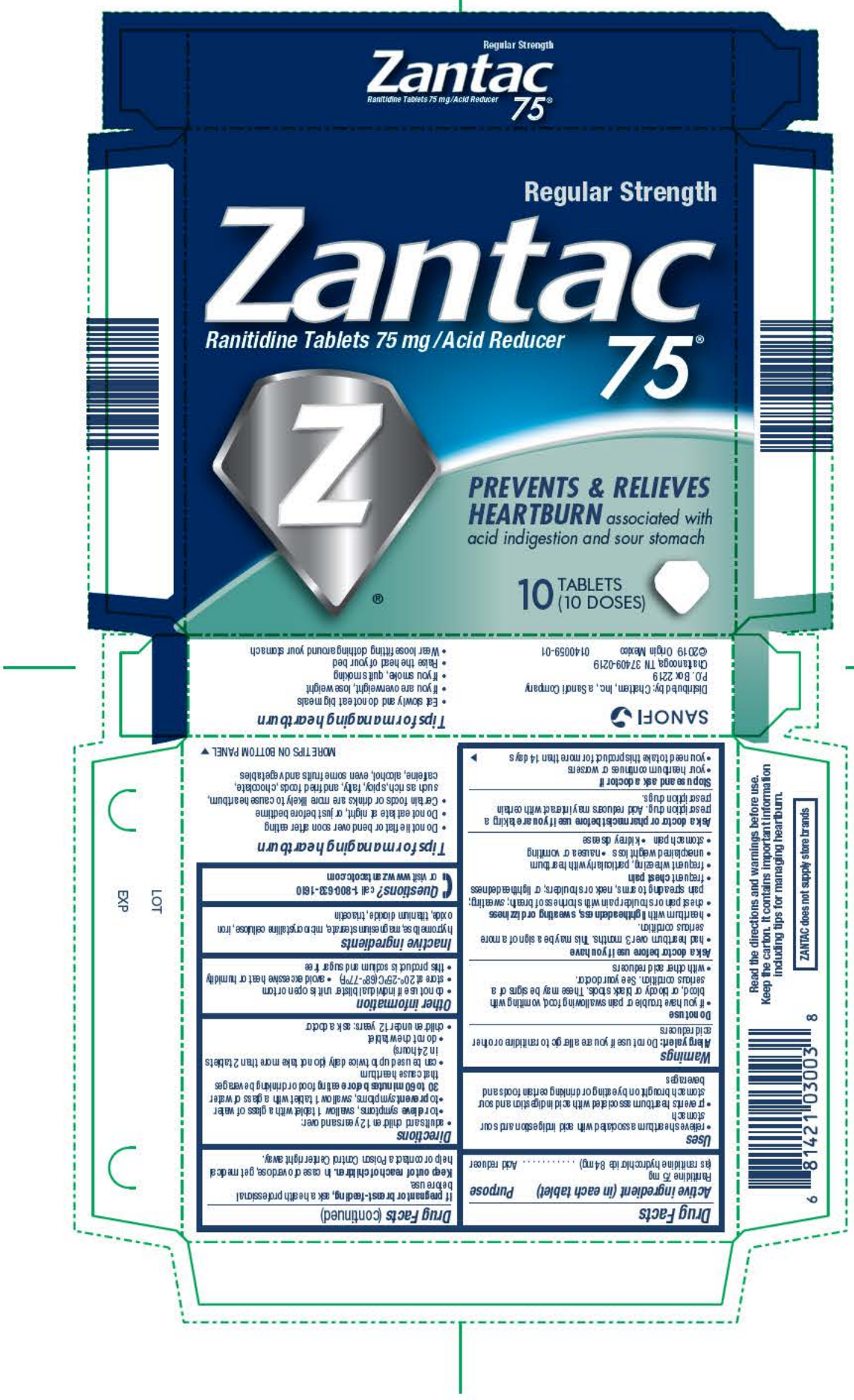
ZAN_75_2ct_CTN_0140049-01_Spain_2019_FDA_DSN2

AA0452

Sanofi Regulatory Specifications			Verified Date: 06/13/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9.0 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		NA point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	5.8 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.070 in
PDP dimensions (in millimeters)			H 60mm W 97mm
Font size of Statement of Identity (if not live text, to be measured in Helvetica capital "M")			V 8.81 pt. H 0.00 pt
Font size of Logo/Largest Copy on PDP (if not live text, to be measured in Helvetica capital "M")			V 61 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 75 10ct Carton
03.28.19

ZAN_75_10ct_CTN_0140059-01_Mex_2019_FDA_DSN3



Sanofi Regulatory Specifications			Verified Date: 03/28/19
Drug Facts Info			
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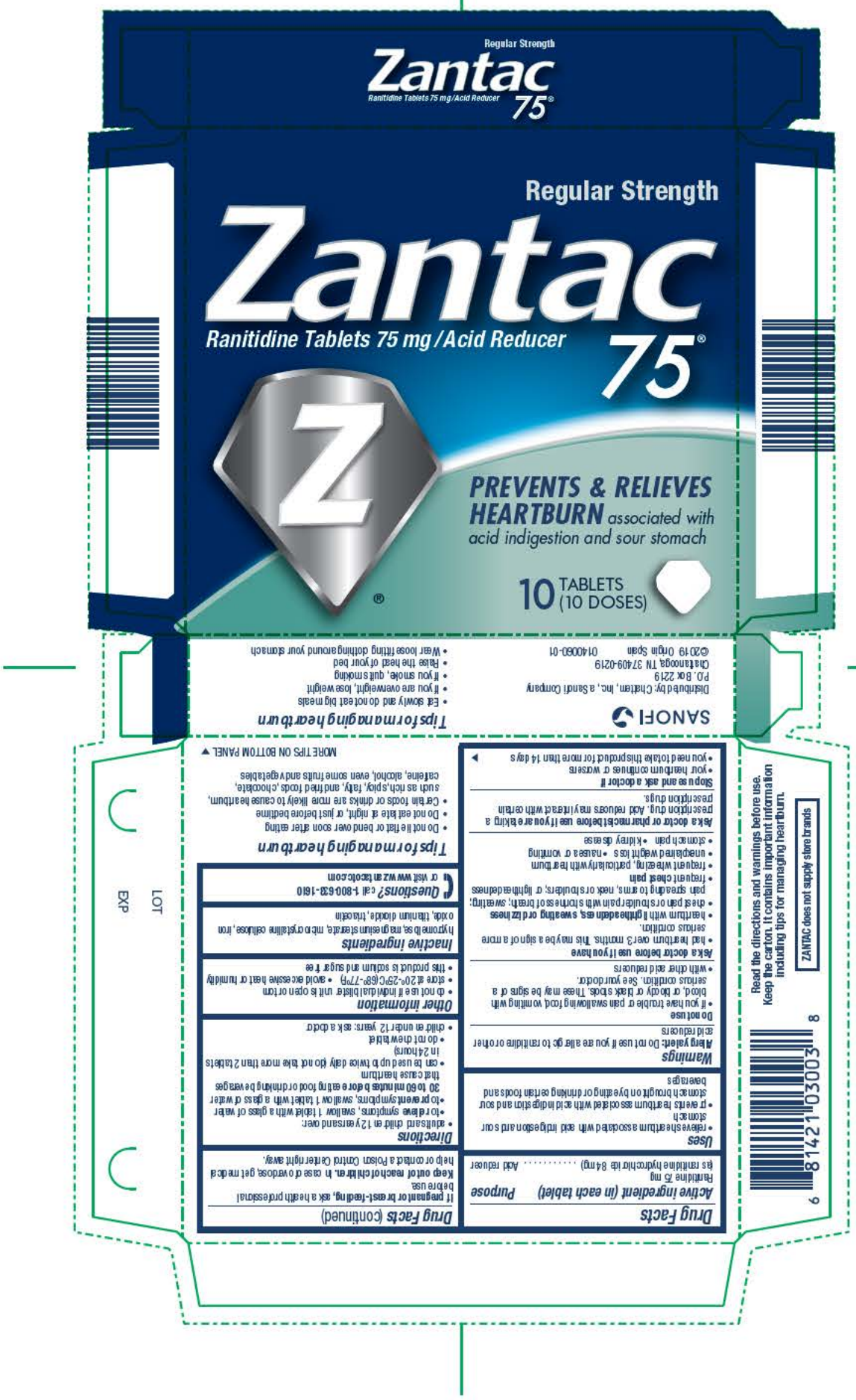
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 75 10ct Carton
03.28.19
ZAN_75_10ct_CTN_0140060-01_Spain_2019_FDA_DSN2



Sanofi Regulatory Specifications			Verified Date: 03/28/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 75 30ct Carton
03.18.19

ZAN_75_30ct_CTN_0140058-01_Mex_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/18/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 75 30ct Carton
03.18.19

ZAN_75_30ct_CTN_0140057-01_Spain_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/18/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 75 40ct Carton
03.06.19

ZAN_75_40ct_Bonus_CTN_0140073-01_Mex_2019_FDA_DSN2

Sanofi Regulatory Specifications			Verified Date: 03/06/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 75 40ct Carton
03.14.19

ZAN_75_40ct_Bonus_CTN_0140076-01_Spain_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
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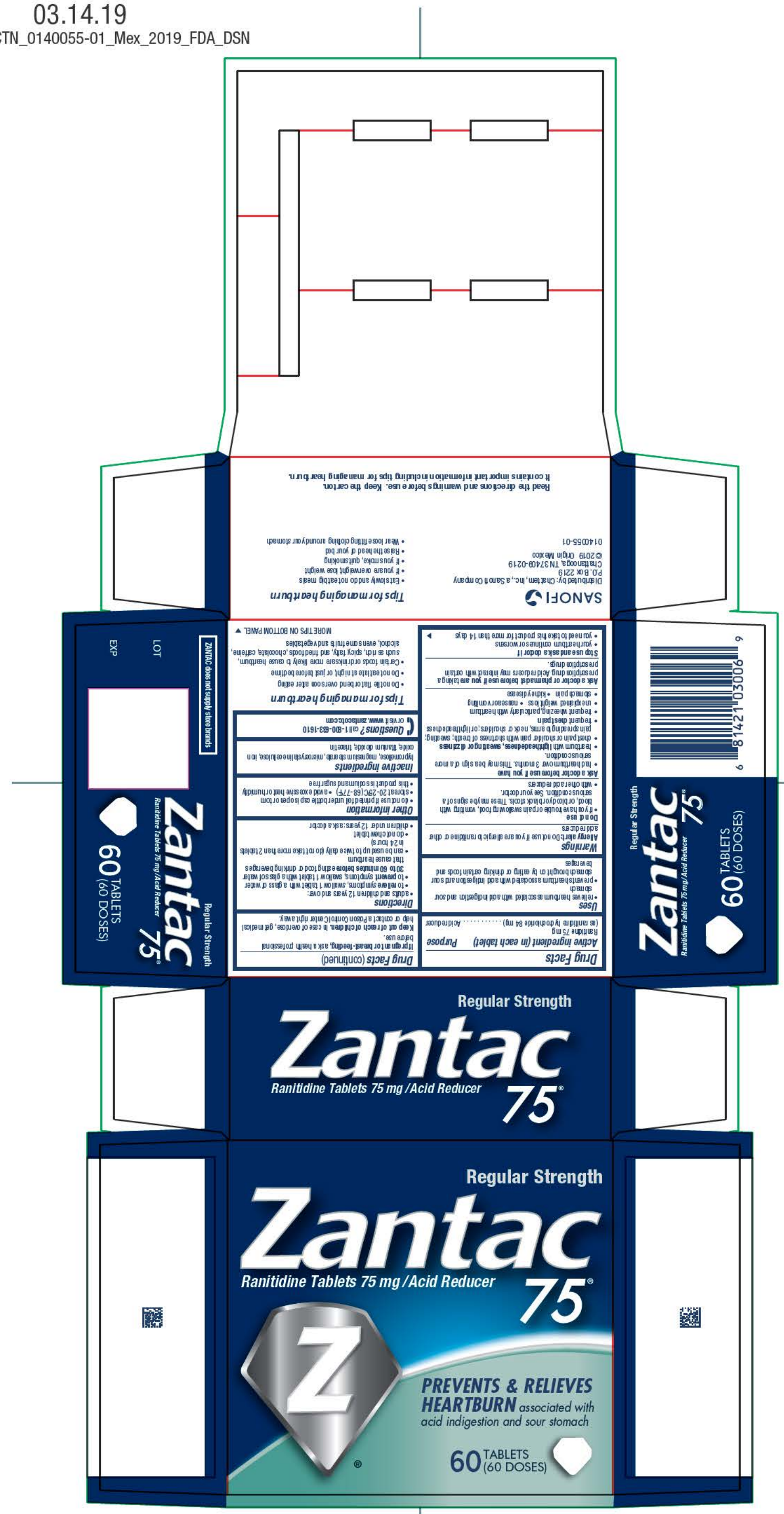
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Zantac 75 60ct Carton
03.14.19
ZAN_75_60ct_CTN_0140055-01_Mex_2019_FDA_DSN

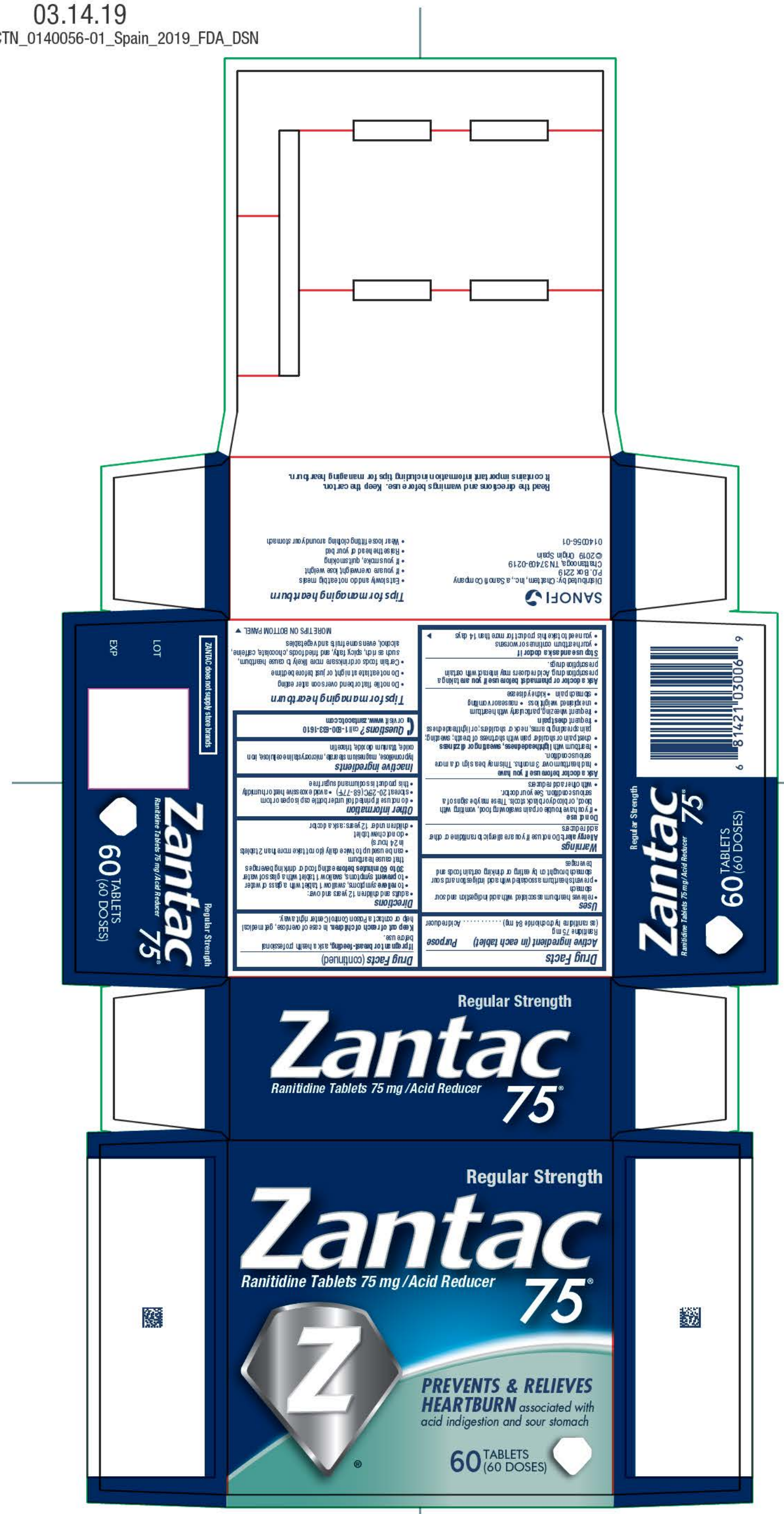


Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
Drug Facts (Title)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493295

AA0459

Zantac 75 60ct Carton
03.14.19
ZAN_75_60ct_CTN_0140056-01_Spain_2019_FDA_DSN



Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
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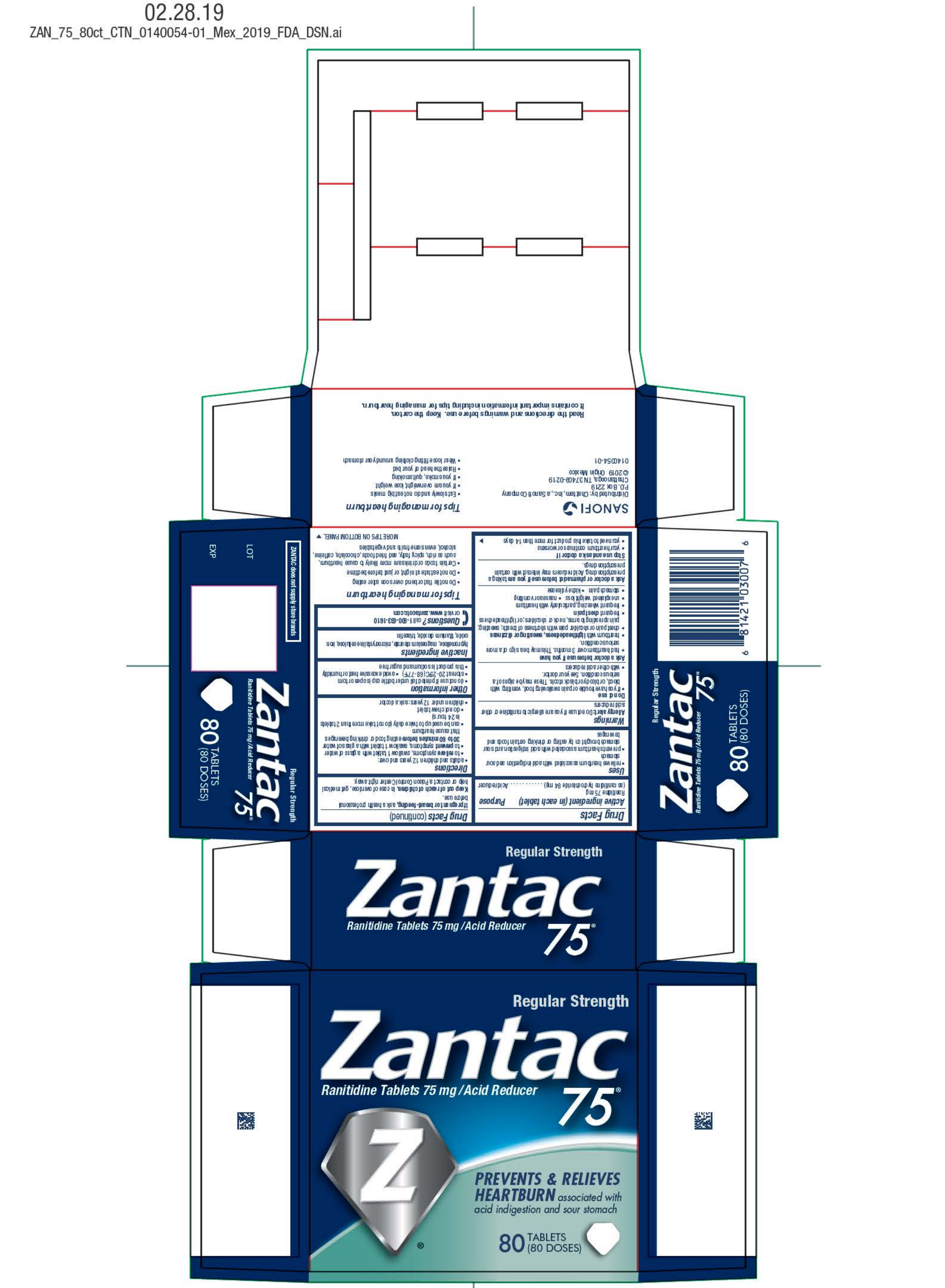
Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493295

AA0460

Zantac 75 80ct Carton
02.28.19
ZAN_75_80ct_CTN_0140054-01_Mex_2019_FDA_DSN.ai



Sanofi Regulatory Specifications			Verified Date: 02/28/19
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Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		8 point type
Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
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Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493295

AA0461

Zantac 75 80ct Carton
03.14.19

ZAN_75_80ct_CTN_0140053-01_Spain_2019_FDA_DSN.ai

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
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Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
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Subheadings	Font name: Helvetica Neue 77 Bold Condensed		6 point type
Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
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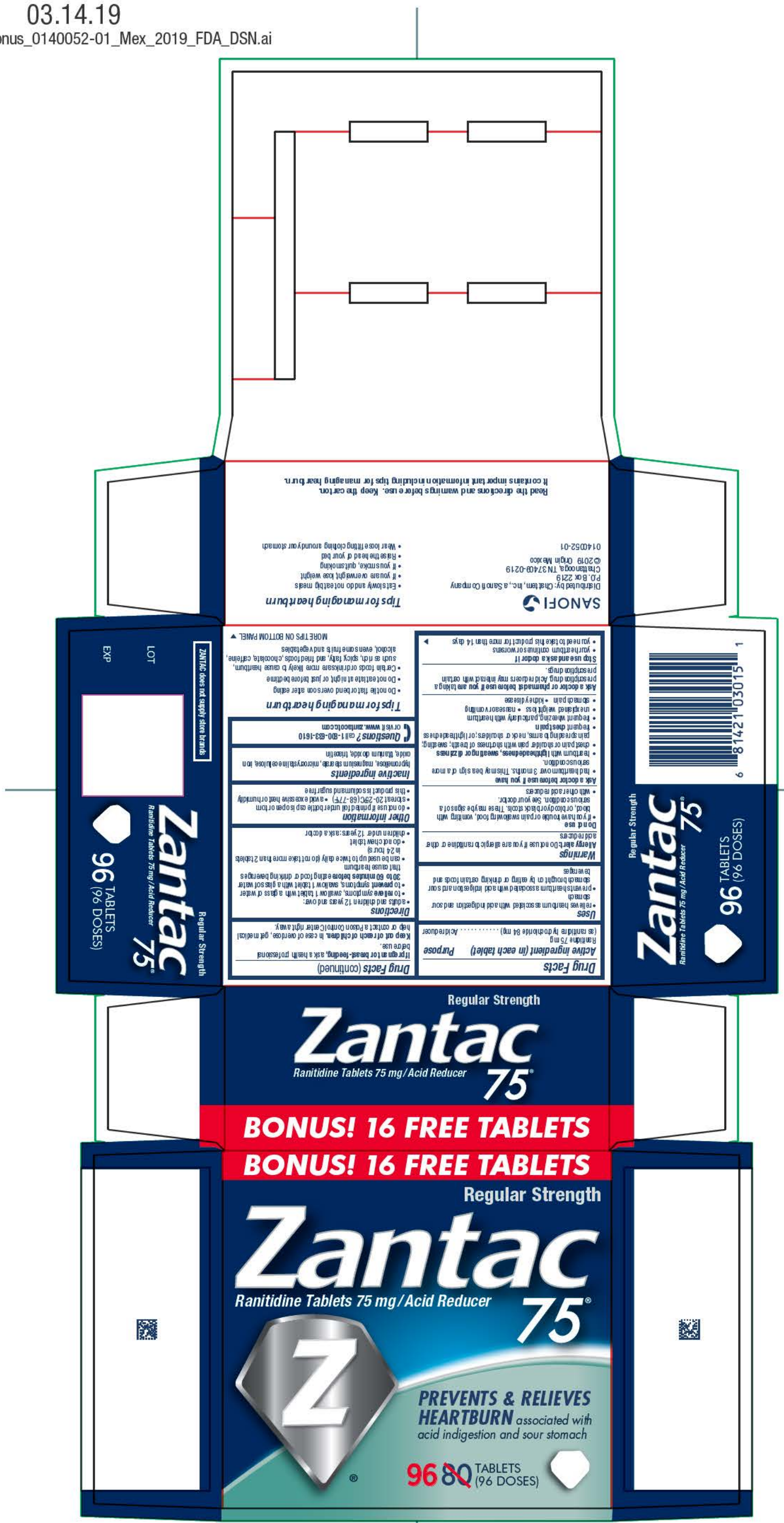
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4493295

AA0462

Zantac 75 96ct Carton
03.14.19

ZAN_75_96ct_Bonus_0140052-01_Mex_2019_FDA_DSN.ai



Sanofi Regulatory Specifications			Verified Date: 03/14/19
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Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
Barlines:	2.5 pt.	Hairlines:	0.5 pt.
Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			0.088 in
PDP dimensions (in millimeters)			H 89mm W 97mm
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 11.5 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4491291

AA0463

Zantac 75 96ct Carton
03.14.19

ZAN_75_96ct_Bonus_0140051-01_Spain_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
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Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		9 point type
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Body Text	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets	Font name: Helvetica Neue 57 Condensed		5 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
Leading (Minimum space in body of Drug Facts):	6.0 pt.	Maximum Characters/Inch:	39
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Principal Display Panel Info			
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PDP dimensions (in millimeters)			H 89mm W 97mm
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Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 82 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Reference ID: 4494291

AA0464

Zantac 75 1ct Sachet/Pouch Dispenser (100ct)
03.14.19
ZAN_75_100ct_Dispenser_0140079-01_Mex_2019_FDA_DSN

Sanofi Regulatory Specifications			Verified Date: 03/14/19
Drug Facts Info			
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Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
Headings	Font name: Helvetica Neue 77 Bold Condensed Oblique		9.25 point type
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Body Text	Font name: Helvetica Neue 57 Condensed		7 point type
Bullets	Font name: Helvetica Neue 57 Condensed		6 point type
Bullets on same lines: end of statement separated from bulleted statement by two ems			YES
Spacing of the hairlines from edge of box – i.e. Minimum of 1 space either side of Drug Facts Box			YES
Tracking:	0 to 8 pt.	Horizontal Scale:	97%-102%
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Principal Display Panel Info			
Font size of Net Quantity of Contents (Smallest character height in inches)			.0903 in
PDP dimensions (in inches)			H 4.00 in W 4.75 in
Font size of Statement of Identity (If not live text, to be measured in Helvetica capital "M")			V 13 pt. H 0.00 pt.
Font size of Logo/Largest Copy on PDP (If not live text, to be measured in Helvetica capital "M")			V 94 pt. H 0.00 pt.
Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

Regular Strength
Zantac 75®
Ranitidine Tablets 75 mg / Acid Reducer

PREVENTS & RELIEVES HEARTBURN associated with acid indigestion and sour stomach

Drug Facts

Active ingredient (in each tablet) — **Purpose**
Ranitidine 75 mg (as ranitidine hydrochloride 84 mg) ..... Acid reducer

Uses
- relieves heartburn associated with acid indigestion and sour stomach
- prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain foods and beverages

Warnings
Allergy alert: Do not use if you are allergic to ranitidine or other acid reducers

Do not use
- if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.
- with other acid reducers

Ask a doctor before use if you have
- had heartburn over 3 months. This may be a sign of a more serious condition.
- heartburn with **lightheadedness, sweating or dizziness**
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**
- frequent wheezing, particularly with heartburn
- unexplained weight loss • nausea or vomiting
- stomach pain • kidney disease

Ask a doctor or pharmacist before use if you are taking a prescription drug. Acid reducers may interact with certain prescription drugs.

Stop use and ask a doctor if
- your heartburn continues or worsens
- you need to take this product for more than 14 days ▸

Drug Facts (continued)

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions
- adults and children 12 years and over:
  - to **relieve** symptoms, swallow 1 tablet with a glass of water
  - to **prevent** symptoms, swallow 1 tablet with a glass of water **30 to 60 minutes before** eating food or drinking beverages that cause heartburn
  - can be used up to twice daily (do not take more than 2 tablets in 24 hours)
  - do not chew tablet
- children under 12 years: ask a doctor

Other information
- do not use if individual foil pouch is open or torn
- store at 20-25°C (68-77°F)
- avoid excessive heat or humidity
- this product is sodium and sugar free

Inactive ingredients
hypromellose, magnesium stearate, microcrystalline cellulose, iron oxide, titanium dioxide, triacetin

Questions? call **1-800-633-1610** or visit **www.zantacotc.com**

Tips for managing heartburn
- Do not lie flat or bend over soon after eating
- Do not eat late at night, or just before bedtime
- Certain foods or drinks are more likely to cause heartburn, such as rich, spicy, fatty, and fried foods, chocolate, caffeine, alcohol, even some fruits and vegetables
- Eat slowly and do not eat big meals
- If you are overweight, lose weight
- If you smoke, quit smoking
- Raise the head of your bed
- Wear loose fitting clothing around your stomach

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Chattanooga, TN 37409-0219
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0140079-01

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Do not discard this carton.
It contains important consumer information.

100 POUCHES
1 TABLET (1 DOSE)
TO OPEN
PUSH IN TAB AND PULL OUT

Zantac 75 1ct Sachet/Pouch Dispenser (100ct)
03.07.19
ZAN_75_100ct_Dispenser_0140078-01_Spain_2019_FDA_DSN2

Sanofi Regulatory Specifications			Verified Date: 03/07/19
Drug Facts Info			
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Drug Facts (continued)	Font name: Helvetica Neue 77 Bold Condensed Oblique		10 point type
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Body Text	Font name: Helvetica Neue 57 Condensed		7 point type
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Ratio of Statement of Identity to Logo/Largest Copy on PDP Statement of Identity (pt.) (Divided by) Largest Logo Copy (pt.)			V 15% H 0%

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

VALERIE S PRATT
09/18/2019 04:35:47 PM

EXHIBIT M

Guidance for Industry

Changes to an Approved NDA or ANDA

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
April 2004
CMC

Revision 1

Guidance for Industry

Changes to an Approved NDA or ANDA

Additional copies are available from:

Office of Training and Communications
Division of Drug Information, HFD-240
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857
(Tel) 301-827-4573
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)
April 2004
CMC

Revision 1

AA0470

TABLE OF CONTENTS

*Contains Nonbinding Recommendations**

Guidance for Industry[1]

Changes to an Approved NDA or ANDA

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.** You can use an alternative approach if it 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.

** Insofar as this guidance adjusts reporting categories pursuant to section 506A of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.70, it does have binding effect. If you have any questions about the effect of any portion of this guidance, contact the Office of Pharmaceutical Science, Center for Drug Evaluation and Research (HFD-003), Food and Drug Association, 5600 Fishers Lane, Rockville, MD 20857.

I. INTRODUCTION AND BACKGROUND

This guidance provides recommendations to holders of new drug applications (NDAs) and abbreviated new drug applications (ANDAs) who intend to make postapproval changes in accordance with section 506A of the Federal Food, Drug, and Cosmetic Act (the Act) and § 314.70 (21 CFR 314.70). The guidance covers recommended reporting categories for postapproval changes for drugs other than specified biotechnology and specified synthetic biological products. It supersedes the guidance of the same title published November 1999. Recommendations are provided for postapproval changes in (1) components and composition, (2) manufacturing sites, (3) manufacturing process, (4) specifications, (5) container closure system, and (6) labeling, as well as (7) miscellaneous changes and (8) multiple related changes.

Recommendations on reporting categories for changes relating to specified biotechnology and specified synthetic biological products regulated by CDER are found in the guidance for industry

[1] This guidance has been prepared under the direction of the Chemistry, Manufacturing and Controls Coordinating Committee in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA).

Paperwork Reduction Act Public Burden Statement: This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3520). The collection(s) of information in this guidance were approved under OMB Control No. 0910-0538 (until August 31, 2005).

* Insofar as this guidance adjusts reporting categories pursuant to section 506A of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.70, it does have binding effect.

entitled *Changes to an Approved Application for Specified Biotechnology and Specified Synthetic Biological Products* (July 1997).[2]

On November 21, 1997, the President signed the Food and Drug Administration Modernization Act of 1997 (the Modernization Act).[3] Section 116 of the Modernization Act amended the the Act by adding section 506A, which provides requirements for making and reporting manufacturing changes to an approved application and for distributing a drug product made with such changes. The FDA has revised its regulations on supplements and other changes to an approved application (21 CFR 314.70) to conform to section 506A of the Act.

This guidance does not provide recommendations on the specific information that should be developed by an applicant to assess the effect of the change on the identity, strength (e.g., assay, content uniformity), quality (e.g., physical, chemical, and biological properties), purity (e.g., impurities and degradation products), or potency (e.g., biological activity, bioavailability, bioequivalence) of a drug product as these factors may relate to the safety or effectiveness of the drug product. An applicant should consider all relevant CDER guidance documents for recommendations on the information that should be submitted to support a given change.[4]

CDER has published guidances, including the SUPAC (scale-up and postapproval changes) guidances, that provide recommendations on reporting categories. To the extent that the recommendations on ***reporting categories*** in this guidance are found to be inconsistent with guidances published before this guidance was finalized, the recommended reporting categories in such previously published guidances are superseded by this guidance. This guidance does not provide extensive recommendations on reporting categories for components and composition changes (see section V). Therefore, recommended reporting categories for components and composition changes provided in previously published guidances, such as the SUPAC guidances, still apply. Section 506A of the Act and § 314.70(c) provide for two types of changes-being-effected supplements (see section II), while previously there was only one type. It is important for applicants to use this guidance to determine which type of changes-being-effected supplement is recommended. CDER intends to update the previously published guidances to make them consistent with this guidance.

If guidance for either recommended reporting categories or information that should be submitted to support a particular change is not available, the appropriate CDER chemistry or microbiology review staff can be consulted for advice.

FDA's guidance documents, in general, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required. Insofar as this guidance adjusts reporting categories pursuant to section 506A of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.70, it does have binding effect. If you

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[2] FDA is currently revising the 1997 guidance and intends to issue it in draft for public comment.

[3] Public Law 105-115.

[4] A list of CDER guidances is available on the Internet at http://www.fda.gov/cder/guidance/index.htm.

* Insofar as this guidance adjusts reporting categories pursuant to section 506A of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.70, it does have binding effect.

have any questions about the effect of any portion of this guidance, contact the Office of Pharmaceutical Science, Center for Drug Evaluation and Research (HFD-003), Food and Drug Association, 5600 Fishers Lane, Rockville, MD 20857.

II. REPORTING CATEGORIES

Section 506A of the Act and § 314.70 provide for four reporting categories that are distinguished in the following paragraphs.

A ***major change*** is a change that has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product. A major change requires the submission of a supplement and approval by FDA prior to distribution of the drug product made using the change. This type of supplement is called, and should be clearly labeled, a ***Prior Approval Supplement*** (§ 314.70(b)). An applicant may ask FDA to expedite its review of a prior approval supplement for public health reasons (e.g., drug shortage) or if a delay in making the change described in it would impose an extraordinary hardship on the applicant. This type of supplement is called, and should be clearly labeled, a *Prior Approval Supplement - Expedited Review Requested* (§ 314.70(b)(4)).[5] FDA is most likely to grant requests for expedited review based on extraordinary hardship for manufacturing changes made necessary by catastrophic events (e.g., fire) or by events that could not be reasonably foreseen and for which the applicant could not plan.

A ***moderate change*** is a change that has a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product. There are two types of moderate change. One type of moderate change requires the submission of a supplement to FDA at least 30 days before the distribution of the drug product made using the change. This type of supplement is called, and should be clearly labeled, a ***Supplement - Changes Being Effected in 30 Days*** (§ 314.70(c)(3)). The drug product made using a moderate change cannot be distributed if FDA informs the applicant within 30 days of receipt of the supplement that a prior approval supplement is required (§ 314.70(c)(5)(i)). For each change, the supplement must contain information determined by FDA to be appropriate and must include the information developed by the applicant in assessing the effects of the change (§ 314.70(a)(2) and (c)(4)). If FDA informs the applicant within 30 days of receipt of the supplement that information is missing, distribution must be delayed until the supplement has been amended to provide the missing information (§ 314.70(c)(5)(ii)).

FDA may identify certain moderate changes for which distribution can occur when FDA receives the supplement (§ 314.70(c)(6)). This type of supplement is called, and should be clearly labeled, a ***Supplement - Changes Being Effected***. If, after review, FDA disapproves a changes-being-effected-in-30-days supplement or changes-being-effected supplement, FDA may order the

[5] Internal Agency policies and procedures relating to processing requests for expedited review of supplements to approved ANDAs and NDAs are documented in CDER's Manual of Policies and Procedures (MAPP) at 5240.1 and 5310.3, respectively. MAPPs can be located on the Internet at http://www.fda.gov/cder/mapp.htm.

* Insofar as this guidance adjusts reporting categories pursuant to section 506A of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.70, it does have binding effect.

manufacturer to cease distribution of the drug products made using the disapproved change (§ 314.70(c)(7)).

A ***minor change*** is a change that has minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product. The applicant must describe minor changes in its next ***Annual Report*** (§ 314.70(d)).

Under § 314.70(e), an applicant can submit one or more protocols (i.e., comparability protocols) describing tests, studies, and acceptance criteria to be achieved to demonstrate the absence of an adverse effect from specified types of changes. A comparability protocol can be used to reduce the reporting category for specified changes. A proposed comparability protocol that was not approved as part of the original application must be submitted as a prior approval supplement (314.70(e)). On February 25, 2003, FDA issued a draft guidance on comparability protocols entitled *Comparability protocols - Chemistry, Manufacturing, and Controls Information*.

III. GENERAL REQUIREMENTS

Other than for editorial changes in previously submitted information (e.g., correction of spelling or typographical errors, reformatting of batch records), an applicant must notify FDA about each change in each condition established in an approved application beyond the variations already provided for in the application (§ 314.70(a)(1)).

A supplement or annual report must include a list of all changes contained in the supplement or annual report. On the list, FDA recommends that the applicant describe each change in enough detail to allow FDA to quickly determine whether the appropriate reporting category has been used. For supplements, this list must be provided in the cover letter (§ 314.70(a)(6)). In annual reports, the list should be included in the summary section (§ 314.81(b)(2)(i)). The applicant must describe each change fully in the supplement or annual report (§ 314.70(a)(1)).

An applicant making a change to an approved application under section 506A of the Act must also conform to other applicable laws and regulations, including current good manufacturing practice (CGMP) requirements of the Act (21 U.S.C. 351(a)(2)(B)) and applicable regulations in Title 21 of the *Code of Federal Regulations* (e.g., 21 CFR parts 210, 211, 314). For example, manufacturers must comply with relevant CGMP validation and recordkeeping requirements and ensure that relevant records are readily available for examination by authorized FDA personnel during an inspection.

A changes-being-effected supplement providing for labeling changes under § 314.70(c)(6)(iii) must include 12 copies of the final printed labeling (§ 314.70(c)(1)). In accordance with

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§ 314.70(a)(4), an applicant also must promptly revise all promotional labeling and drug advertising to make it consistent with any labeling change implemented in accordance with § 314.70(b) or (c).

Except for supplements providing only for a change in labeling, an applicant must include in each supplement and amendment to a supplement a statement certifying that a field copy has been provided in accordance with 21 CFR 314.440(a)(4)[6] (§ 314.70(a)(5)).

IV. ASSESSING THE EFFECT OF MANUFACTURING CHANGES

A. Assessment of the Effects of the Change

The holder of an approved application under section 505 of the Act ***must assess the effects of the change before distributing a drug product made with a manufacturing change*** (§ 314.70(a)(2)).[7] For each change, the supplement or annual report must contain information determined by FDA to be appropriate and must include the information developed by the applicant in assessing the effects of the change (section 506A(b), (c)(1), (d)(2)(A), and (d)(3)(A) of the Act). The type of information that must be included in a supplemental application or an annual report is specified in § 314.70(b)(3), (c)(4), and (d)(3).

1. Conformance to Specifications

An assessment of the effects of a change on the identity, strength, quality, purity, and potency of the drug product should include a determination that the drug substance intermediates, drug substance, in-process materials, and/or drug product affected by the change conform to the approved specifications.[8] A *specification* is a quality standard (i.e., tests, analytical procedures, and acceptance criteria) provided in an approved application to confirm the quality of drug substances, drug products, intermediates, raw materials, reagents, components, in-process materials, container closure systems, and other materials used in the production of a drug substance or drug product. *Acceptance criteria* are numerical limits, ranges, or other criteria for the tests described (§ 314.3(b)). Conformance to a specification means that the

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[6] Mailing information for field copies is provided in 21 CFR 314.440(a)(4). FDA recommends that the *applicant's home FDA district office* referred to in the regulations be the district office where the applicant's headquarters is located.

[7] *Assess the effects of the change* means to evaluate the effects of a manufacturing change on the identity, strength, quality, purity, and potency of a drug product as these factors relate to the safety or effectiveness of the drug product. The terms *assess* or *assessment* as used in this guidance are not the same as validation. Certain validation information, such as for sterilization processes, is considered information that is needed to assess the effect of the change as specified in § 314.70(a)(2) and should be submitted in an NDA or ANDA. Unless otherwise specified by FDA, validation (e.g., process, equipment) data need not be submitted in the application, but should be retained at the facility and be available for review by FDA at the Agency's discretion under CGMPs.

[8] If a specification needs to be revised as a result of the change, this would be considered a multiple change (see sections VIII and XII).

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material, when tested according to the analytical procedures listed in the specification, will meet the listed acceptance criteria.

2. Additional Testing

In addition to confirming that the material affected by manufacturing changes continues to meet its specification, we recommend that the applicant perform additional testing, when appropriate, to assess whether the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product have been or will be affected. The assessment should include, as appropriate, evaluation of any changes in the chemical, physical, microbiological, biological, bioavailability, and/or stability profiles. This additional assessment could involve testing of the postchange drug product itself or, if appropriate, the material directly affected by the change. The type of additional testing that an applicant should perform would depend on the type of manufacturing change, the type of drug substance and/or drug product, and the effect of the change on the quality of the drug product. For example:

- Evaluation of changes in the impurity or degradant profile could first involve profiling using appropriate chromatographic techniques and then, depending on the observed changes in the impurity profile, toxicology tests to qualify a new impurity or degradant or to qualify an impurity that is above a previously qualified level.[9]

- Evaluation of the hardness or friability of a tablet after certain changes.

- Assessment of the effect of a change on bioequivalence when required under 21 CFR part 320 could include, for example, multipoint and/or multimedia dissolution profiling and/or an in vivo bioequivalence study.

- Evaluation of extractables from new packaging components or moisture permeability of a new container closure system.

An applicant should refer to all relevant CDER guidance documents for recommendations on the information that should be submitted to support a given change. If guidance for information that should be submitted to support a particular change is not available, applicants can consult the appropriate CDER chemistry or microbiology review staff for advice.

B. Equivalence

When testing is performed, the applicant should usually assess the extent to which the manufacturing change has affected the identity, strength, quality, purity, and potency of the

[9] Recommendations on identifying, qualifying, and reporting impurities can be found in relevant guidances (e.g., ICH Q3B *Impurities in New Drug Products* (November 1996)).

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drug product. Typically this is accomplished by comparing test results from pre- and postchange material and determining if the test results are equivalent. Simply stated: Is the drug product made after the change equivalent to the drug product made before the change? An exception to this general approach is that when bioequivalence is redocumented for certain ANDA postapproval changes, FDA recommends that the comparator be the reference listed drug. Equivalence comparisons frequently have a criterion for comparison with calculation of confidence intervals relative to a predetermined equivalence interval. For this, as well as for other reasons, *equivalent* does not necessarily mean *identical*. Equivalence may also relate to maintenance of a quality characteristic (e.g., stability) rather than a single performance of a test.

C. Adverse Effect

Some manufacturing changes have an adverse effect on the identity, strength, quality, purity, or potency of the drug product. In many cases, the applicant chooses not to implement these manufacturing changes, but sometimes the applicant wishes to do so. If an assessment indicates that a change has adversely affected the identity, strength, quality, purity, or potency of the drug product, FDA recommends that ***the change be submitted in a prior approval supplement regardless of the recommended reporting category for the change*.** For example, a process change recommended for a changes-being-effected-in-30-days supplement could cause the formation of a new degradant that requires qualification and/or identification.[10] The applicant's degradation qualification procedures may indicate that there are no safety concerns relating to the new degradant. Even so, we recommend that the applicant submit this change in a prior approval supplement with appropriate information to support the continued safety and effectiveness of the drug product. During the review of the prior approval supplement, the FDA will assess the impact of any adverse effect on the drug product as this change may relate to the safety or effectiveness of the drug product.

Applicants are encouraged to consult with the appropriate CDER chemistry or microbiology review staff if there are any questions on whether a change in a characteristic would be viewed by CDER as adversely affecting the identity, strength, quality, purity, or potency of the drug product.

V. COMPONENTS AND COMPOSITION

Changes in the qualitative or quantitative formulation, including inactive ingredients, as provided in the approved application, are considered major changes requiring a prior approval supplement, unless exempted by regulation or guidance (§ 314.70(b)(2)(i)). The deletion or reduction of an ingredient intended to affect only the color of the drug product may be reported in an annual report (§ 314.70(d)(2)(ii)). Guidance on changes in components and composition that may be submitted in a changes-being-effected supplement or annual report is not included in this document because

[10] Recommendations on identifying, qualifying, and reporting impurities can be found in relevant guidances.

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of the complexity of the recommendations, but may be covered in one or more guidance documents describing postapproval changes (e.g., SUPAC documents).

VI. MANUFACTURING SITES[11]

A. General Considerations

CDER must be notified when a manufacturer changes to a manufacturing site that is different from those specified in the approved application (314.70(a)). Sites can include those used by an applicant to (1) manufacture or process drug products,[12] in-process materials, drug substances, or drug substance intermediates, (2) package drug products, (3) label drug products, and (4) test components, drug product containers, closures, packaging materials, in-process materials, or drug products. Sites include those owned by the applicant or contract sites used by an applicant. Testing sites include those performing physical, chemical, biological, and microbiological testing to monitor, accept, or reject materials, as well as those performing stability testing. Sites used to label drug products are considered those that perform labeling of the drug product's primary or secondary packaging components. Sites performing operations that place identifying information on the dosage form itself (e.g., ink imprint on a filled capsule) are considered to be facilities that manufacture or process the drug product. FDA recommends that the supplement or annual report identify whether the proposed manufacturing site is an alternative to or replacement for the site or sites provided for in the approved application.

FDA recommends that a move to a different manufacturing site, when it is a type of site routinely subject to FDA inspection, be submitted as a prior approval supplement if the site does not have a ***satisfactory CGMP inspection***[13] for the ***type of operation***[14] being moved (see sections VI.B.1 and 2).

For labeling, secondary packaging, and testing site changes, the potential for adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product is considered to be independent of the type of drug product dosage form or specific type of operation being performed. Therefore, the recommended reporting category for any one of these manufacturing site changes will be the same for all types of drug products and operations. For manufacturing sites used to (1) manufacture or process drug products, in-process materials, drug substances, or drug substance intermediates or (2) perform primary packaging operations,

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[11] See Attachment A for a discussion of the definition of *same manufacturing site* and *different manufacturing site.*

[12] Manufacturing or processing drug product would also include the preparation (e.g., sterilization, depyrogenation, irradiation, washing) by the applicant or applicant's contractor of container closure systems or packaging components. Changes in the site used to fabricate packaging components (e.g., bottles) or manufacture packaging materials (e.g., resins) need not be reported to CDER if there are no other changes (e.g., dimensions, compositions, processing aids). If other changes occur, the reporting category should be based on the recommended reporting categories for these changes (i.e., the manufacturing site change does not need to be considered when determining the appropriate reporting category).

[13] See Glossary for a definition of *satisfactory CGMP inspection*.

[14] See Attachment B for a discussion of the term *type of operation*.

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the potential for adverse effect depends on factors such as the type of drug substance or drug product and operation being performed. Therefore, recommended reporting categories may differ depending on the type of drug product and operations.

Except for the situations described in sections VI.B.4, VI.C.1.b, and VI.D.5, construction activities at a manufacturing site or moving production operations within a building or between buildings at the same manufacturing site do not have to be reported to CDER.

We recommend that a move to a manufacturing site that involves other changes (e.g., process, equipment) be evaluated as a multiple related change (see section XII) to determine the appropriate reporting category.

B. Major Changes (Prior Approval Supplement)

The following are examples of changes considered to have a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

1. A move to a different manufacturing site, except one used to manufacture or process a drug substance intermediate, when the new manufacturing site has never been inspected by FDA for the type of operation that is being moved or the move results in a restart at the new manufacturing site of a type of operation that has been discontinued for more than two years.

2. A move to a different manufacturing site, except one used to manufacture or process a drug substance intermediate, when the new manufacturing site does not have a satisfactory CGMP inspection for the type of operation being moved.

3. A move to a different manufacturing site for (1) the manufacture, processing, or primary packaging of drug products when the primary packaging components control the dose delivered to the patient or the formulation modifies the rate or extent of availability of the drug, or (2) the manufacture or processing of in-process materials with modified-release characteristics. Examples of these types of drug products include modified-release solid oral dosage forms,[15] transdermal systems, liposomal drug products, depot drug products, oral and nasal metered-dose inhalers (MDIs), dry powder inhalers (DPIs), and nasal spray pumps.

4. Transfer of the manufacture of an aseptically processed sterile drug substance or aseptically processed sterile drug product to (1) a newly constructed or refurbished aseptic processing facility or area or (2) an existing aseptic processing facility or area that does not manufacture similar (including container types and sizes) approved drug products. An example

[15] Certain operations relating to the manufacture, processing, or primary packaging of modified-release solid oral dosage form drug products need not be reported in a prior approval supplement (see sections VI.C.1.c and VI.D.6).

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would be transferring the manufacture of a lyophilized drug product to an existing aseptic process area where no approved lyophilized drug products are manufactured or where the approved lyophilized drug products being manufactured have different container types and/or sizes than the container of the drug product being transferred. See section VI.C.1.b for recommendations for other manufacturing site changes relating to aseptically processed sterile drug substance or aseptically processed sterile drug product.

5. Transfer of the manufacture of a finished drug product sterilized by terminal processes to a newly constructed facility at a different manufacturing site. Once this change has been approved, subsequent site changes to the facility for similar drug product types and processes may be submitted as a changes-being-effected-in-30-days supplement (see section VI.C.1.a).

C. Moderate Changes (Supplement - Changes Being Effected)

The following are examples of changes considered to have a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product. If the new site does not have a satisfactory CGMP inspection for the type of operation being moved (see sections VI.B.1 and 2), then FDA recommends that the changes listed below (excluding changes relating to drug substance intermediate manufacturing sites) be submitted in a prior approval supplement.

1. Supplement - Changes Being Effected in 30 Days

a. A move to a different manufacturing site for the manufacture or processing of any drug product, in-process material, or drug substance that is not otherwise provided for in this guidance.

b. For aseptically processed sterile drug substance or aseptically processed sterile drug product, a move to an aseptic processing facility or area at the same or different manufacturing site except as provided for in section VI.B.4.

c. A move to a different manufacturing site for the primary packaging of (1) any drug product that is not otherwise listed as a major change and (2) modified-release solid oral dosage form drug products.

d. A move to a different manufacturing site for testing if (1) the test procedures approved in the application or procedures that have been implemented via an annual report are used, (2) all postapproval commitments made by the applicant relating to the test procedures have been fulfilled (e.g., providing methods validation

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samples), and (3) the new testing facility has the capability to perform the intended testing.

2. Supplement - Changes Being Effected

A move to a different manufacturing site for the manufacture or processing of the final intermediate.

D. Minor Changes (Annual Report)

The following are examples of changes considered to have a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product. If the new site does not have a satisfactory CGMP inspection for the type of operation being moved, then FDA recommends that the changes listed below (excluding changes relating to drug substance intermediate manufacturing sites) be submitted in a prior approval supplement (see sections VI.B.1 and 2).

1. A move to a different manufacturing site for secondary packaging.

2. A move to a different manufacturing site for labeling.

3. A move to a different manufacturing site for the manufacture or processing of drug substance intermediates other than the final intermediate.

4. A change in the contract sterilization site for packaging components when the process is not materially different from that provided for in the approved application

5. A transfer of the manufacture of a finished product sterilized by terminal processes to a newly constructed building or existing building at the same manufacturing site.

6. A move to a different manufacturing site for the ink imprinting of solid oral dosage form drug products.

VII. MANUFACTURING PROCESS

A. General Considerations

The potential for adverse effects on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product depends on the type of manufacturing process and the changes being instituted for the drug substance or drug product. In some cases, there may be a substantial potential for adverse effect regardless of direct testing of the drug substance or drug product for conformance with the approved specification. When there is a substantial potential for adverse effects, a change must be submitted in a prior approval supplement (section 506A(c) of the Act).

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B. Major Changes (Prior Approval Supplement)

The following are examples of changes considered to have a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

1. Changes that may affect the controlled (or modified) release, metering or other characteristics (e.g., particle size) of the dose delivered to the patient, including the addition or deletion of a code imprint by embossing, debossing, or engraving on a modified-release solid oral dosage form.

2. Changes that may affect drug product sterility assurance including, where appropriate, process changes for sterile drug substances and sterile packaging components. These include:

   - Changes in the sterilization method (e.g., gas, dry heat, irradiation). These include changes from sterile filtered or aseptic processing to terminal sterilization, or vice versa.
   - Addition, deletion, or substitution of sterilization steps or procedures for handling sterile materials in an aseptic processing operation.
   - Replacing sterilizers that operate by one set of principles with sterilizers that operate by another principle (e.g., substituting a gravity displacement steam process with a process using superheated water spray).
   - Addition to an aseptic processing line of new equipment made of different materials (e.g., stainless steel versus glass, changes between plastics) that will come in contact with sterilized bulk solution or sterile drug components, or deletion of equipment from an aseptic processing line.
   - Replacing a Class 100 aseptic fill area with a barrier system or isolator for aseptic filling. Once this change has been approved, subsequent process changes for similar product types in the same barrier system or isolator may be submitted as a changes-being-effected-in-30-days supplement.
   - Replacement or addition of lyophilization equipment of a different size that uses different operating parameters or lengthens the overall process time.
   - Changes from bioburden-based terminal sterilization to the use of an overkill process, and vice versa.
   - Changes to aseptic processing methods, including scale, that extend the total processing, including bulk storage time, by more than 50 percent beyond the validated limits in the approved application.
   - Changes in sterilizer load configurations that are outside the range of previously validated loads.

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- Changes in materials or pore size rating of filters used in aseptic processing.

3. The following changes for a natural product:[16]

   - Changes in the virus or adventitious agent removal or inactivation methods. This applies to any material where such procedures are necessary, including drug substance, drug product, reagents, and excipients.
   - For drug substance and drug product, changes in the source material (e.g., microorganism, plant) or cell line.
   - For drug substance and drug product, establishment of a new master cell bank or seed.

4. Any fundamental change in the manufacturing process or technology from that currently used by the applicant. For example:

   a. Drug product

      - Dry to wet granulation or vice versa.
      - Change from one type of drying process to another (e.g., oven tray, fluid bed, microwave).

   b. Drug substance

      - Filtration to centrifugation or vice versa.
      - Change in the route of synthesis of a drug substance.

5. The following changes for drug substance

   - Any process change made after the final intermediate processing step in drug substance manufacture.

   - Changes in the synthesis or manufacture of the drug substance that may affect its impurity profile and/or the physical, chemical, or biological properties.

6. Addition of an ink code imprint or change to or in the ink used for an existing imprint code for a solid oral dosage form drug product when the ink as changed is not currently used on ***CDER-approved drug products***.[17]

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[16] For the purposes of this guidance, *natural product* refers to materials (e.g., drug substance, excipients) that are derived from plants, animals, or microorganisms, and that are subject to approval under section 505 of the Act. The specific recommendations for natural products are not applicable to inorganic compounds (e.g., salts, minerals).

[17] See Attachment C for a discussion of *CDER-approved drug products.*

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7. Establishing a new procedure for reprocessing a batch of drug substance or drug product that fails to meet the approved specification.

C. Moderate Changes (Supplement - Changes Being Effected)

The following are examples of changes considered to have a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

1. Supplement - Changes Being Effected in 30 Days

a. For drug products, any change in the process, process parameters, and/or equipment except as otherwise provided for in this guidance.

b. For drug substances, any change in process and/or process parameters except as otherwise provided for in this guidance.

c. For natural protein drug substances and natural protein drug products:

- Any change in the process, process parameters, and/or equipment except as otherwise provided for in this guidance (e.g., section VII.B.5, VII.D.7).
- An increase or decrease in production scale during finishing steps that involves different equipment.
- Replacement of equipment with equipment of different design that does not affect the process methodology or process operating parameters.

d. For sterile drug products, drug substances, and components, as appropriate:

- Changes in dry heat depyrogenation processes for glass container systems for drug substances and drug products that are produced by terminal sterilization processes or aseptic processing.
- Changes to filtration parameters for aseptic processing (including flow rate, pressure, time, or volume, but not filter materials or pore size rating) when additional validation studies for the new parameters should be performed.
- Filtration process changes that provide for a change from single to dual sterilizing filters in series, or for repeated filtration of a bulk.

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- Changes from one qualified sterilization chamber to another for in-process or terminal sterilization that result in changes to validated operating parameters (time, temperature, F_0, and others).
- Changes in scale of manufacturing for terminally sterilized drug products that increase the bulk solution storage time by more than 50 percent beyond the validated limits in the approved application when bioburden limits are unchanged.

e. For drug substances, redefinition of an intermediate, excluding the final intermediate, as a starting material.

2. Supplement - Changes Being Effected

a. A change in methods or controls that provides 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.

b. For sterile drug products, elimination of in-process filtration performed as part of the manufacture of a terminally sterilized drug product.

D. Minor Changes (Annual Report)

The following are examples of changes considered to have a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

1. For drug products, changes to equipment of the same design and operating principle and/or changes in scale except as otherwise provided for in this guidance (e.g., section VII.C.1.c, VII.D.7).

2. A minor change in an existing code imprint for a dosage form. For example, changing from a numeric to alphanumeric code.

3. Addition of an ink code imprint or a change in the ink used in an existing code imprint for a solid oral dosage form drug product when the ink is currently used on CDER-approved drug products.

4. Addition or deletion of a code imprint by embossing, debossing, or engraving on a solid dosage form drug product other than a modified-release dosage form.

5. A change in the order of addition of ingredients for solution dosage forms or solutions used in unit operations (e.g., granulation solutions).

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6. Changes in scale of manufacturing for terminally sterilized drug products that increase the bulk solution storage time by no more than 50 percent beyond the validated limits in the approved application when bioburden limits are unchanged.

7. For natural protein drug products and natural protein drug substances:

   - An increase or decrease in production scale during finishing steps that does not involve an equipment change.
   - Replacement of equipment with equipment of the same design, operating principle, and capacity with no change in production scale.

VIII. SPECIFICATIONS

A. General Considerations

All changes in specifications from those in the approved application must be submitted in a prior approval supplement unless otherwise exempted by regulation or guidance (§ 314.70(b)(2)(i)). *Specifications* (i.e., tests, analytical procedures, and acceptance criteria) are the quality standards provided in an approved application to confirm the quality of drug substances, drug products, intermediates, raw materials, reagents, components, in-process materials, container closure systems, and other materials used in the production of a drug substance or drug product. For the purpose of defining specifications, *acceptance criteria* are numerical limits, ranges, or other criteria for the tests described. Examples of a test, an analytical procedure, and an acceptance criterion are, respectively, an assay, a specific, fully described high pressure liquid chromatography (HPLC) procedure, and a range of 98.0–102.0 percent. The recommendations in this section also apply to specifications associated with sterility assurance that are included in NDA and ANDA submissions.[18]

A *regulatory* analytical procedure is the procedure in the approved application that is designated for use in evaluating a defined characteristic of the drug substance or drug product. Section 501(b) of the Act recognizes the analytical procedures in the *U.S. Pharmacopeia/National Formulary* (USP/NF) as the regulatory analytical procedures for compendial items. Tests and associated acceptance criteria and regulatory analytical procedures in addition to those specified in the USP/NF may be required for approving compendial items (section 505 of the Act).

The applicant may include in its application *alternatives* to the approved regulatory analytical procedures for testing the drug substance and drug product. However, for purposes of determining compliance with the Act, regulatory analytical procedures are used.

[18] See FDA guidance for industry on the *Submission of Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products* (November 1994).

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In sections B through D below, the use of the term *analytical procedure* without a qualifier such as *regulatory* or *alternative* refers to an analytical procedure used to test materials other than the drug substance or drug product.

B. Major Changes (Prior Approval Supplement)

The following are examples of changes in specifications considered to have a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

1. Relaxing an acceptance criterion except as otherwise provided for in this guidance (e.g., section VIII.C.1.b, VIII.C.1.e).

2. Deleting any part of a specification except as otherwise provided for in this guidance (e.g., section VIII.D.2).

3. Establishing a new regulatory analytical procedure including designation of an alternative analytical procedure as a regulatory procedure.

4. A change in a regulatory analytical procedure that does not provide the same or increased assurance of the identity, strength, quality, purity, or potency of the material being tested as the regulatory analytical procedure described in the approved application.

5. A change in an analytical procedure used for testing components, packaging components, the final intermediate, in-process materials after the final intermediate, or starting materials introduced after the final intermediate that does not provide the same or increased assurance of the identity, strength, quality, purity, or potency of the material being tested as the analytical procedure described in the approved application except as otherwise noted. For example, a change from an HPLC procedure that distinguishes impurities to (1) an HPLC procedure that does not, (2) another type of analytical procedure (e.g., titrimetric) that does not, or (3) an HPLC procedure that distinguishes impurities but the limit of detection and/or limit of quantitation is higher.

6. Relating to testing of raw materials for viruses or adventitious agents:[19] (1) relaxing an acceptance criterion, (2) deleting a test, or (3) a change in the analytical procedure that does not provide the same or increased assurance of the identity, strength, quality, purity, or potency of the material being tested as the analytical procedure described in the approved application.

[19] In this context, testing for adventitious agents is not considered to include tests that are found in an official compendium (e.g., USP <61>).

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C. Moderate Changes (Supplement - Changes Being Effected)

The following are examples of changes in specifications considered to have a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

1. Supplement - Changes Being Effected in 30 Days

a. Any change in a regulatory analytical procedure other than those identified as major changes or editorial changes.

b. Relaxing an acceptance criterion or deleting a test for raw materials used in drug substance manufacturing, in-process materials prior to the final intermediate, starting materials introduced prior to the final drug substance intermediate, or drug substance intermediates (excluding final intermediate) except as provided for in section VIII.B.6.

c. A change in an analytical procedure used for testing raw materials used in drug substance manufacturing, in-process materials prior to the intermediate, starting materials introduced prior to the final drug substance intermediate, or drug substance intermediates (excluding final intermediate) that does not provide the same or increased assurance of the identity, strength, quality, purity, or potency of the material being tested as the analytical procedure described in the approved application except as provided for in section VIII.B.6.

d. Relaxing an in-process acceptance criterion associated with microbiological monitoring of the production environment, materials, and components that are included in NDA and ANDA submissions. For example, increasing the microbiological alert or action limits for critical processing environments in an aseptic fill facility or increasing the acceptance limit for bioburden in bulk solution intended for filtration and aseptic filling.

e. Relaxing an acceptance criterion or deleting a test to comply with an official compendium that is consistent with FDA statutory and regulatory requirements (§ 314.70(c)(2)(iii)).

2. Supplement - Changes Being Effected

a. An addition to a specification that provides 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. For example, adding a new test and associated analytical procedure and acceptance criterion.

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b. A change in an analytical procedure used for testing components, packaging components, the final intermediate, in-process materials after the final intermediate, or starting materials introduced after the final intermediate that provides the same or increased assurance of the identity, strength, quality, purity, or potency of the material being tested as the analytical procedure described in the approved application.

D. Minor Changes (Annual Report)

The following are examples of changes in specifications considered to have a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

1. Any change in a specification made to comply with an official compendium, except the changes described in section VIII.C.1.e, that is consistent with FDA statutory and regulatory requirements (§ 314.70(d)(2)(i)).

2. For drug substance and drug product, the addition or revision of an alternative analytical procedure that provides the same or increased assurance of the identity, strength, quality, purity, or potency of the material being tested as the analytical procedure described in the approved application or deletion of an alternative analytical procedure.

3. Tightening of acceptance criteria.

4. A change in an analytical procedure used for testing raw materials used in drug substance synthesis, starting materials introduced prior to the final drug substance intermediate, in-process materials prior to the final intermediate, or drug substance intermediates (excluding final intermediate) that provides the same or increased assurance of the identity, strength, quality, purity, or potency of the material being tested as the analytical procedure described in the approved application.

IX. CONTAINER CLOSURE SYSTEM

A. General Considerations

The potential for adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product when making a change to or in the container closure system is generally dependent on the route of administration of the drug product, performance of the container closure system, and the likelihood of interaction between the packaging component and the dosage form. In some cases there may be a substantial potential for adverse effect, regardless of direct drug product testing for conformance with the approved specification.

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A change to or in a packaging component will often result in a new or revised specification for the packaging component. This situation does not have to be considered a multiple related change. Only the reporting category for the packaging change needs to be considered.

B. Major Changes (Prior Approval Supplement)

The following are examples of changes considered to have a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

1. For liquid (e.g., solution, suspension, elixir) and semisolid (e.g., creams, ointments) dosage forms, a change to or in polymeric materials (e.g., plastic, rubber) of primary packaging components, when the composition of the component as changed has never been used in a CDER-approved drug product of the same dosage form and same route of administration. For example, a polymeric material that has been used in a CDER-approved topical ointment would not be considered CDER-approved for an ophthalmic ointment.

2. For liquid (e.g., solution, suspension, elixir) and semisolid (e.g., creams, ointments) dosage forms in permeable or semipermeable container closure systems, a change from an ink and/or adhesive used on the permeable or semipermeable packaging component to an ink or adhesive that has never been used in a CDER-approved drug product of the same dosage form and same route of administration ***and*** with the same type of permeable or semipermeable packaging component (e.g., low density polyethylene, polyvinyl chloride).

3. A change in the primary packaging components for any drug product when the primary packaging components control[20] the dose delivered to the patient (e.g., the valve or actuator of a metered-dose inhaler).

4. For sterile drug products, any change that may affect drug product sterility assurance, such as:[21]

    - A change from a glass ampule to a glass vial with an elastomeric closure.

[20] A container closure system that is considered to control the dose delivered to the patient is a container closure system where the system itself, rather than a person, regulates the amount of drug product ultimately delivered to a patient. A container closure system where a person controls the amount of drug product administered or that allows verification that the appropriate amount has been administered (e.g., number of tablets, milliliters of liquid) is not considered a container closure system that controls the dose delivered to the patient.

[21] Some of these identified changes, depending on the circumstances, may have to be submitted as original NDAs or ANDAs instead of as supplements. Applicants can consult the appropriate CDER chemistry division/office if there are questions.

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- A change to a flexible container system (bag) from another container system.
- A change to a prefilled syringe dosage form from another container system.
- A change from a single unit dose container to a multiple dose container system.
- Changes that add or delete silicone treatments to container closure systems (such as elastomeric closures or syringe barrels).
- Changes in the size and/or shape of a container for a sterile drug product.

5. Deletion of a secondary packaging component intended to provide additional protection to the drug product (e.g., carton to protect from light, overwrap to limit transmission of moisture or gases) or a change in the composition of, or the addition of, a secondary packaging component that may affect the impurity profile of the drug product.

6. A change to a new container closure system if the new container closure system does not provide the same or better protective properties than the approved container closure system.

C. Moderate Changes (Supplement - Changes Being Effected)

The following are examples of changes considered to have a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

1. Supplement - Changes Being Effected in 30 Days

a. A change to or in a container closure system, except as otherwise provided for in this guidance, that does not affect the quality of the drug product.

b. Changes in the size or shape of a container for a sterile drug substance.

c. A change in the number of units (e.g., tablets, capsules) or labeled amount (e.g., grams, milliliters) of a nonsterile drug product in a unit-of-use container.[22]

2. Supplement - Changes Being Effected

[22] A unit-of-use container is one that contains a specific quantity of a drug product and is intended to be dispensed to the patient without further modification except for the addition of appropriate labeling.

* Insofar as this guidance adjusts reporting categories pursuant to section 506A of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.70, it does have binding effect.

a. A change in the size and/or shape of a container for a nonsterile drug product, except for solid dosage forms (see section IX.D.2), without a change from one container closure system to another (§ 314.70(c)(6)(ii)).

b. A change in the labeled amount (e.g., grams, milliliters) of drug product for a nonsterile drug product in a multiple-unit container,[23] except for solid dosage forms (see section IX.D.3) .

c. A change in or addition or deletion of a desiccant.

D. Minor Changes (Annual Report)

The following are examples of changes considered to have a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

1. A change in the container closure system for a nonsterile drug product, based on a showing of equivalency to the approved system under a protocol approved in the application or published in an official compendium (§ 314.70(d)(2)(v)).

2. A change in the size and/or shape of a container for a nonsterile solid dosage form (§ 314.70(d)(2)(iv)).

3. A change in the number of units (e.g., tablets, capsules) or labeled amount (e.g., grams) of nonsterile solid dosage form in a multiple-unit container.

4. The following changes in the container closure system of solid oral dosage form drug products as long as the new package provides the same or better protective properties (e.g., light, moisture) and any new primary packaging component materials have been used in and been in contact with CDER-approved solid oral dosage form drug products:[24]

   - Adding or changing a child-resistant closure, changing from a metal to plastic screw cap, or changing from a plastic to metal screw cap.

[23] A multiple-unit container is a container that permits withdrawal of successive portions of the contents without changing the strength, quality, or purity of the remaining portion. This type of container is not distributed directly to patients but is used by health care practitioners who dispense the drug product in smaller amounts to a patient in accordance with a physician's instructions.

[24] For sections IX.D.4 to IX.D.7, changes in the container closure system that result in drug product contact with a component material that has never been used in any CDER-approved drug product of the same type should be submitted as a changes-being-effected-in-30-days supplement (section IX.C.1) or prior approval supplement (section IX.B.1).

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- Changing from one plastic container to another of the same type of plastic (e.g., high density polyethylene (HDPE) container to another HDPE container).
- Changes in packaging materials used to control odor (e.g., charcoal packets).
- Changes in bottle filler (e.g., change in weight of cotton or amount used) without changes in the type of filler (e.g., cotton to rayon).
- Increasing the wall thickness of the container.
- A change in or addition of a cap liner.
- A change in or addition of a seal (e.g., heat induction seal).
- A change in an antioxidant, colorant, stabilizer, or mold releasing agent for production of the container and/or closure to one that is used at similar levels in the packaging of CDER-approved solid oral dosage form drug products.
- A change to a new container closure system when the container closure system is already approved in the NDA or ANDA for other strengths of the drug product.

5. The following changes in the container closure system of nonsterile liquid drug products as long as the new package provides the same or better protective properties and any new primary packaging component materials have been used in and been in contact with CDER-approved liquid drug products with the same route of administration (i.e., the material in contact with a liquid topical should already have been used with other CDER-approved liquid topical drug products):

   - Adding or changing a child-resistant closure, changing from a metal to plastic screw cap, or changing from a plastic to metal screw cap.
   - Increasing the wall thickness of the container.
   - A change in or addition of a cap liner.
   - A change in or addition of a seal (e.g., heat induction seal).

6. A change in the container closure system of unit dose packaging (e.g., blister packs) for nonsterile solid dosage form drug products as long as the new package provides the same or better protective properties and any new primary packaging component materials have been used in and been in contact with CDER-approved drug products of the same type (e.g., solid oral dosage form, rectal suppository).

7. The following changes in the container closure system of nonsterile semisolid drug products as long as the new package provides the same or

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better protective properties and any new primary packaging component materials have been used in and been in contact with CDER-approved semisolid drug products:

- Changes in the closure or cap.
- Increasing the wall thickness of the container.
- A change in or addition of a cap liner.
- A change in or addition of a seal.
- A change in the crimp sealant.

8. A change in the flip seal cap color as long as the cap color is consistent with any established color coding system for that class of drug products.

X. LABELING

A. General Considerations

A drug product labeling change includes changes in the package insert, package labeling, or container label. In accordance with § 314.70(a)(4), an applicant must promptly revise all promotional labeling and drug advertising to make it consistent with any labeling change implemented in accordance with paragraphs (b) or (c) of § 314.70. All labeling changes for ANDA drug products must be consistent with section 505(j) of the Act.

B. Major Changes (Prior Approval Supplement)

Any proposed change in the labeling, except changes designated as moderate or minor by regulation or guidance, must be submitted as a prior approval supplement (§ 314.70(b)(2)(v)(A)). If applicable, any change to a Medication Guide required under 21 CFR part 208, except for changes in the information specified in § 208.20(b)(8)(iii) and (b)(8)(iv), must be submitted in a prior approval supplement (§ 314.70(b)(v)(B)). The following list contains some examples of changes currently considered by CDER to fall into this reporting category.

1. Changes based on postmarketing study results, including, but not limited to, labeling changes associated with new indications and usage.

2. Change in, or addition of, pharmacoeconomic claims based on clinical studies.

3. Changes to the clinical pharmacology or the clinical study section reflecting new or modified data.

4. Changes based on data from preclinical studies.

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5. Revision (expansion or contraction) of population based on data.

6. Claims of superiority to another drug product.

7. Change in the labeled storage conditions, unless exempted by regulation or guidance.

C. Moderate Changes (Supplement - Changes Being Effected)

Under § 314.70(c)(6)(iii), a changes-being-effected supplement must be submitted for any labeling change that (1) adds or strengthens a contraindication, warning, precaution, or adverse reaction, (2) adds or strengthens a statement about drug abuse, dependence,

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psychological effect, or overdosage, (3) adds or strengthens an instruction about dosage and administration that is intended to increase the safe use of the drug product, (4) deletes false, misleading, or unsupported indications for use or claims for effectiveness, or (5) normally requires a supplement submission and approval prior to distribution of the drug product that FDA specifically requests be submitted under this provision. A changes-being-effected supplement that provides for a labeling change under §§ 314.70(c)(6)(iii) must include 12 copies of final printed labeling (§ 314.70(c)(1)). The following list includes some examples of changes currently considered by CDER to fall into this reporting category.

1. Addition of an adverse event due to information reported to the applicant or Agency.

2. Addition of a precaution arising out of a postmarketing study.

3. Clarification of the administration statement to ensure proper administration of the drug product.

D. Minor Changes (Annual Report)

Labeling with editorial or similar minor changes or with a change in the information concerning the description of the drug product or information about how the drug is supplied that does not involve a change in the dosage strength or dosage form should be described in an annual report (§ 314.70(d)(2)(ix) and (d)((2)(x)) . The following list includes some examples currently considered by CDER to fall into this reporting category.

1. Changes in the layout of the package or container label that are consistent with FDA regulations (e.g., 21 CFR part 201) without a change in the content of the labeling.

2. Editorial changes, such as adding a distributor's name.

3. Foreign language versions of the labeling if no change is made to the content of the approved labeling and a certified translation is included.

4. Labeling changes made to comply with an official compendium.

XI. MISCELLANEOUS CHANGES

A. Major Changes (Prior Approval Supplement)

The following are examples of changes considered to have a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

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1. Changes requiring completion of studies in accordance with 21 CFR part 320 to demonstrate equivalence of the drug product to the drug product as manufactured without the change or to the reference listed drug (§ 314.70(b)(2)(ii)).

2. Addition of a stability protocol or comparability protocol.

3. Changes to an approved stability protocol or comparability protocol unless otherwise provided for in this guidance (e.g., VIII.C, VIII.D, XI.C.2).

4. An extension of an expiration dating period based on (1) data obtained under a new or revised stability testing protocol that has not been approved in the application or (2) full shelf life data on pilot scale batches using an approved protocol.

5. Changes to a drug product under an application that is subject to a validity assessment because of significant questions regarding the integrity of the data supporting that application (§ 314.70(b)(2)(viii)).

B. Moderate Changes (Supplement - Changes Being Effected)

The following are examples of changes considered to have a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

1. Supplement - Changes Being Effected in 30 Days

Reduction of an expiration dating period to provide increased assurance of the identity, strength, quality, purity, or potency of the drug product. Extension of an expiration date that has previously been reduced under this provision should be submitted in a changes-being-effected-in-30-days supplement even if the extension is based on data obtained under a protocol approved in the application.

2. Supplement - Changes Being Effected

No changes have been identified.

C. Minor Changes (Annual Report)

The following are examples of changes considered to have a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

1. An extension of an expiration dating period based on full shelf life data on production batches obtained under a protocol approved in the application (§ 314.70(d)(2)(vi)).

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2. Addition of time points to the stability protocol or deletion of time points beyond the approved expiration dating period.

3. A change from previously approved stability storage conditions to storage conditions recommended in International Conference on Harmonisation (ICH) guidances.

4. Non-USP reference standards:

   - Replacement of an in-house reference standard or reference panel (or panel member) according to procedures in an approved application.
   - Tightening of acceptance criteria for existing reference standards to provide greater assurance of drug product purity and potency.

XII. MULTIPLE RELATED CHANGES

Multiple related changes involve various combinations of individual changes. For example, a site change may also involve equipment and manufacturing process changes or a components and composition change may necessitate a change in a specification. For multiple related changes where the recommended reporting categories for the individual changes differ, CDER recommends that the submission be in accordance with the most restrictive of the categories recommended for the individual changes. When the multiple related changes all have the same recommended reporting category, CDER recommends that the submission be in accordance with the reporting category for the individual changes.

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ATTACHMENT A: MANUFACTURING SITES

All owners or operators of all drug establishments (not exempt by regulation) that engage in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs are required to register with the FDA (21 CFR 207.20). An *establishment* means a place of business under one management at one general physical location (§ 207.3(a)(7)). A *general physical location* is reasonably construed to include separate buildings within the same city ***if*** the activities in the buildings are closely related to the same business enterprise, are under the supervision of the same local management, and are all inspected at the same time (ORA Field Management Directive No. 132).

For the purposes of determining the reporting category for moves between buildings, the terms *same manufacturing site* and *different manufacturing site* mean:

Domestic Establishments

Same manufacturing site:

- The new and old buildings are included under the same drug establishment registration number[25]

and

- The same FDA district office is responsible for inspecting the operations in both the new and old buildings.

Different manufacturing site:

- The new and old buildings have different drug establishment registration numbers

or

- Different FDA district offices are responsible for inspecting operations in the new and old buildings.

For domestic establishments, the terms *same manufacturing site* and *different manufacturing site* supersede the terms *contiguous campus*, *same campus*, and *different campus* as used in the SUPAC guidances.

Foreign Establishments

[25] The registration number is the number assigned to the establishment as part of the registration process (e.g., ORA Field Management Directive No. 92).

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Foreign establishments are not currently required to register with the FDA. On May 14, 1999, FDA published a proposed rule to require registration of foreign establishments (64 FR 26330). Until registration of foreign establishments is required, same and different manufacturing sites mean:

Same manufacturing site:

- A contiguous or unbroken site or a set of buildings in adjacent city blocks.

Different manufacturing site:

- The new and old buildings are not on a contiguous site or not in adjacent city blocks.

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ATTACHMENT B: TYPE OF OPERATION AND CGMP INSPECTIONS

Section VI states that a change to a different manufacturing site should be submitted in a prior approval supplement when (1) the new manufacturing site has never been inspected by FDA for the type of operation being moved, (2) the move results in a restart at the new manufacturing site of a type of operation that has been discontinued for more than two years, or (3) the new manufacturing site does not have a satisfactory current good manufacturing practice (CGMP) inspection for the type of operation being moved.

A *profile class system* is used by FDA to assist in (1) managing the CGMP inspection process, (2) evaluating the findings and the compliance follow-up needed, and (3) communicating the results of inspections. A profile class can relate to the manufacture of a particular dosage form (e.g., large volume parenterals, oral liquids), type of drug substance (e.g., sterile bulk by chemical synthesis), or specific function performed at a site (e.g., control testing laboratory). There are profile class codes for major categories of drug substance processes, dosage forms, and manufacturing functions (see table below). However, the system is not comprehensive for all operations performed in the pharmaceutical industry (see not elsewhere classified (NEC) profile class code).

The term *type of operation* refers to the specialized or even unique conditions and practices that are employed to manufacture a class or category of drug substance or drug product or to perform a limited segment of the manufacturing process. These conditions and practices exist and are performed within the framework of CGMPs, along with general conditions and practices that contribute to the manufacture of all drug products at a given manufacturing site. The conditions and practices, both general and specific, are inspected to evaluate the CGMP acceptability of a manufacturing site. A wide variety of classes or categories of drug substances and drug products may be produced at a manufacturing site, or the manufacturing site may only produce a single class of drug substance and/or drug product or perform a limited segment of a manufacturing process. Each type of operation is represented by a ***profile class code.***

Generally, a satisfactory CGMP status for a profile class code is used to communicate a satisfactory CGMP clearance for all of the products and for all of the operations included within the category that code represents. Thus the profile class code for a particular dosage form or type of drug substance is used to communicate the CGMP status for all aspects of manufacturing, processing, packing, or holding that are performed at the specific manufacturing site relating to that particular dosage form or type of drug substance, including packaging and labeling operations, testing, and quality control. The profile class code for a particular dosage form or type of drug substance is also used to communicate the CGMP status for manufacturing sites that produce in-process material (e.g., controlled-release beads), package drug products, or label drug products, even if these are stand-alone (e.g., contractor) operations.

A few profile class codes that describe certain types of operations (see items in boldface in table) are provided to report the CGMP status for contractor firms whose only function in the manufacturing process is to perform this operation. If one of these operations (e.g., steam sterilization process) is performed at the manufacturing site involved in producing the drug product/drug substance, the CGMP status for that operation is reported as part of the profile class code for the particular dosage form or type of drug substance. For example, a manufacturing site

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producing a terminally sterilized small volume parenteral drug product would be reported with the profile class code for the dosage form (SVT), not by the profile code for the sterilization process (SSP).

Certain inspections may be required by program priorities even if the rating for a profile class code indicates an acceptable CGMP status. The current profile codes/classes for human drugs are:

ADM	Aerosol dispensed medication	NEC	Not elsewhere classified (when using this class, specific drug products are noted)
CBI	Biotechnology crude drug	OIN	Ointment, nonsterile (includes cream, jelly, paste)
CEX	Plant/animal extraction crude drug	POW	Powders (includes oral and topical)
CFS	Sterile bulk by fermentation crude drug	RAD	Radiopharmaceutical
CFN	Nonsterile bulk by fermentation crude drug	**RSP**	**Radiation sterilization process**
CHG	Capsule, prompt release	SNI	Sterile noninjectable
CRU	Crude bulk drugs-nonsynthesized	SOP	Soap
CSG	Capsules, soft gelatin	**SSP**	**Steam sterilization process**
CSN	Nonsterile bulk by chemical synthesis	SUP	Suppositories
CSP	**Chemical sterilization process**	SVL	Small volume parenterals (lyophilized)
CSS	Sterile bulk by chemical synthesis	SVS	Sterile-filled small volume parenterals
CTL	**Control testing laboratories**	SVT	Terminally sterilized small volume parenteral
CTR	Capsules, modified-release	TCM	Tablets, prompt-release
GAS	Medical gas (includes liquid oxygen and other)	TCT	Tablets, delayed-release
GSP	**Gas sterilization process**	TDP	Transdermal patches
HSP	**Dry heat sterilization process**	**TSP**	**Fractional (tyndallization) sterilization process**
LIQ	Liquid (includes solutions, suspension, elixirs, and tinctures)	TTR	Tablets, extended-release
LVP	Large volume parenterals	**WSP**	**Water sterilization process**

CGMP inspectional status, based on the profile class, is available through FDA's Freedom of Information (FOI) Office. (See Glossary under Satisfactory Current Good Manufacturing Practice (CGMP) Inspection for more information regarding FOI requests.)

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Examples of postapproval manufacturing site changes and recommended reporting categories:

- An applicant wants to move the manufacture of an immediate-release tablet (TCM) to a different manufacturing site that currently manufactures, and has satisfactory CGMP status for, capsules (CHG) and powders for oral solution (POW). This manufacturing site change should be submitted in a prior approval supplement because the new manufacturing site does not have a satisfactory CGMP inspection for immediate-release tablets.
- An applicant wants to contract out packaging operations for immediate-release tablets (TCM) and capsules (CHG) and modified-release capsules (CTR). The potential contract packager has a satisfactory CGMP status for immediate-release and modified-release capsules but has never packaged immediate-release tablets. The packaging site change for the immediate-release tablet drug products should be submitted in a prior approval supplement. The packaging site change for the capsule drug products should be submitted as recommended in section VI of this guidance for packaging sites with a satisfactory CGMP inspection.
- An applicant wishes to consolidate product testing to a single analytical laboratory at a manufacturing site. This manufacturing site produces various solid oral dosage form drug products, has an operational analytical laboratory currently at the site, and satisfactory CGMP inspections for the manufacturing occurring at the facility. Some of the drug products that will be tested at the analytical laboratory when the consolidation occurs are not solid oral dosage form products. Unlike most other production operations, testing laboratories (and other operations in boldface in the table) are not inspected on a dosage form/type of drug substance specific basis. The satisfactory CGMP inspection of the analytical laboratory, which was performed as part of the CGMP inspection for manufacture of the solid oral dosage form drug products, is considered to apply to all dosage forms, including those not actually produced at the site. The consolidation can be submitted in a changes-being-effected-in-30-days supplement if the change is consistent with the recommendations in section VI.C.1.d.

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ATTACHMENT C: CDER-APPROVED DRUG PRODUCTS

In several places throughout the guidance, different reporting categories are proposed for changes to or the addition of certain components based on whether the component/material has been used in and has been in contact with CDER-approved drug products. Different reporting categories are recommended once CDER has reviewed certain components/materials in association with a drug product approval because similar subsequent changes then have a reduced potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product. For example, certain changes in the container closure systems of solid oral dosage form drug products may be included in an annual report as long as the new package provides the same or better protective properties and any new primary packaging component materials have been used in and been in contact with CDER-approved solid oral dosage form drug products (see section IX.D.4). If the new primary packaging component material has not been used in or has not been in contact with CDER-approved solid oral dosage form drug products, then submission of the change in an annual report is not recommended.

CDER-approved drug products are considered those drug products subject to an approved NDA or ANDA. Some information on which components/materials are used in CDER-approved products is available from the Agency (e.g., FDA, CDER, *Inactive Ingredient Guide*, 1996, Division of Drug Information Resources). When information is not available, an applicant should use reliable sources of information to determine that the component or material has been used in and has been in contact with a CDER-approved drug product of the same dosage form and route of administration, as appropriate. The applicant should identify in the supplement or annual report the basis for the conclusion that the component or material is used in a CDER-approved drug product.

If an applicant cannot confirm that a component or material has been used in and has been in contact with a CDER-approved drug product of the same dosage form and route of administration, the applicant has the option of submitting the change for a single NDA or ANDA using the higher recommended reporting category and, after approval, submitting similar changes for other NDAs and ANDAs using the lower recommended reporting category.

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GLOSSARY

Acceptance Criteria: Numerical limits, ranges, or other criteria for the tests described (21 CFR 314.3(b)).

Active Ingredient/Drug Substance: Any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of a disease, or to affect the structure or any function of the human body, but does not include intermediates used in the synthesis of such ingredient. The term includes those components that may undergo chemical change in the manufacture of the drug product and are present in the drug product in a modified form intended to furnish the specified activity or effect (21 CFR 210.3(b)(7) and 314.3(b)).

Assess the Effects of the Change: To evaluate the effects of a manufacturing change on the identity, strength, quality, purity, and potency of a drug product as these factors may relate to the safety or effectiveness of the drug product (21 CFR 314.3(b)).

Container Closure System: The sum of packaging components that together contain and protect the dosage form. This includes primary packaging components and secondary packaging components if the latter are intended to provide additional protection to the drug product.

Component: Any ingredient intended for use in the manufacture of a drug product, including those that may not appear in such drug product (21 CFR 210.3(b)(3)).

Drug Product: A finished dosage form, for example, tablet, capsule, or solution, that contains an active ingredient generally, but not necessarily, in association with inactive ingredients (21 CFR 210.3(b)(4)).

Final Intermediate: The last compound synthesized before the reaction that produces the drug substance. The final step forming the drug substance involves covalent bond formation or breakage; ionic bond formation (i.e., making the salt of a compound) does not qualify. Consequently, when the drug substance is a salt, the precursors to the organic acid or base, rather than the acid or base itself, should be considered the final intermediate.

Inactive Ingredient: Any intended component of the drug product other than an active ingredient.

In-process Material: Any material fabricated, compounded, blended, or derived by chemical reaction that is produced for, and used in, the preparation of the drug product (21 CFR 210.3(b)(9)). For drug substance, in-process materials are considered those materials that are undergoing change (e.g., molecular, physical).

Intermediate: A material that is produced during steps of the synthesis of a drug substance and undergoes further molecular change before it becomes a drug substance.

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Package: The container closure system and labeling, associated components (e.g., dosing cups, droppers, spoons), and external packaging (e.g., cartons, shrink wrap).

Packaging Component: Any single part of a container closure system.

Primary Packaging Component: A packaging component that is or may be in direct contact with the dosage form.

Reference Listed Drug: The listed drug identified by FDA as the drug product on which an applicant relies in seeking approval of its abbreviated application (21 CFR 314.3(b)).

Satisfactory Current Good Manufacturing Practice (CGMP) Inspection: A satisfactory CGMP inspection is an FDA inspection during which (1) no objectionable conditions or practices were found (No Action Indicated (NAI)) or (2) objectionable conditions were found, but voluntary corrective action is left to the firm and the objectionable conditions will not be the subject of further administrative or regulatory actions (Voluntary Action Indicated (VAI)).

Information about the CGMP status of a firm may be obtained by requesting a copy of the Quality Assurance Profile (QAP) from the FDA's Freedom of Information (FOI) Office. The QAP contains information on the CGMP compliance status of firms that manufacture, package, assemble, repack, relabel, or test human drugs, devices, biologics, and veterinary drugs. All FOI requests must be in writing (21 CFR 20.40(a)) and should be prepared following the instructions found in the reference entitled *A Handbook for Requesting Information and Records from FDA.* An electronic version of this reference is available on the Internet at http://www.fda.gov/opacom/backgrounders/foiahand.html.

Secondary Packaging Component: A packaging component that is not and will not be in direct contact with the dosage form.

Specification: The quality standard (i.e., tests, analytical procedures, and acceptance criteria) provided in an approved application to confirm the quality of drug substances, drug products, intermediates, raw materials, reagents, components, in-process materials, container closure systems, and other materials used in the production of a drug substance or drug product (21 CFR 314.3(b)).

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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 February 25, 2021, I served a copy of the within document(s):

DECLARATION OF GREG G. SPERLA IN SUPPORT OF DEFENDANTS' 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 February 25, 2021, at Sacramento, California.

Selena Paradee

SERVICE LIST

Mark Todzo Joseph Mann Lexington Law Group 503 Divisadero Street San Francisco, CA 94117 mtodzo@lexlawgroup.com jmann@lexlawgroup.com	*Plaintiff* Center for Environmental Health
Dennis Raglin Danielle Vallone Steptoe & Johnson LLP 633 West Fifth St., Suite 1900 Los Angeles, CA 90071 draglin@steptoe.com dvallone@steptoe.com	*Defendant* Perrigo Company
Jeffrey B. Margulies Lauren A. Shoor Andy Guo Norton Rose Fulbright US LLP 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Telephone: (213) 892-9200 Facsimile: (213) 892-9494 jeff.margulies@nortonrosefulbright.com lauren.shoor@nortonrosefulbright.com andy.guo@nortonrosefulbright.com	*Defendant* Target Corporation
Cheryl S. Chang Erika R. Schulz Blank Rome LLP 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Chang@BlankRome.com ESchulz@BlankRome.com	*Defendant* Apotex Corp.
Megan E. Grossman Lewis Brisbois Bisgaard & Smith LLP 550 E. Swedesford Road, Suite 270 Wayne, PA 19087 Megan.Grossman@lewisbrisbois.com	*Defendant* Granules USA, Inc.

Will Wagner
Greenberg Traurig LLP
1201 K Street, Suite 1100
Sacramento, CA 94111
wagnerw@gtlaw.com

Trenton H. Norris
Arnold & Porter Kaye Scholer LLP
Three Embarcadero Center, 10th Floor
San Francisco, CA 94111
trent.norris@arnoldporter.com

Defendant
7-Eleven, Inc.

Exhibit 21

By Fax

COPY

GEORGE GIGOUNAS (Bar No. CA-209334)
george.gigounas@dlapiper.com
GREGORY SPERLA (Bar No. CA-278062)
greg.sperla@dlapiper.com
SEAN NEWLAND (Bar No. CA-300928)
sean.newland@dlapiper.com
DLA PIPER LLP (US)
555 Mission Street
Suite 2400
San Francisco, California 94105-2933
Tel: 415.836.2500
Fax: 415.836.2501

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

REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S 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

Pursuant to California Evidence Code §§ 450 *et seq.*, Defendants Chattem, Inc. and Sanofi-Aventis U.S. LLC (collectively "Defendants") submit this Request for Judicial Notice in Support of their Demurrer to the Second Amended Complaint Pursuant to California Code of Civil Procedure Sections 410.30 and 418.10 filed by Plaintiff on January 4, 2021.

Each document Defendants seek notice of relate to U.S. Food and Drug Administration (the "FDA") authorizations. Pursuant to Evidence Code § 452(c), the Court may take judicial notice of "[o]fficial acts of the legislative, executive, and judicial departments of the United States and of any state of the United States." An FDA authorization is a formal act by a department of the executive branch of the United States and, accordingly, is a proper subject for judicial notice.

Judicial notice is also appropriate under California Evidence Code § 452(h). Section 452(h) authorizes judicial notice of "[f]acts and propositions that are not reasonably subject to dispute and are capable of immediate and accurate determination by resort to courses of reasonable accuracy." Each document for which judicial notice is sought is a common FDA record or resource, is thus not reasonably subject to dispute, and can be immediately and accurately verified on the FDA's website.

In light of the above, Defendants request that the Court take judicial notice of the following exhibits attached to the Declaration of Greg Sperla concurrently filed with this request:

Exhibit A: December 19, 1995 letter from the FDA approving Zantac's 75mg formulation as an over-the-counter ("OTC') drug.

Exhibit B: August 31, 2004 letter from the FDA approving Zantac's 150mg formulation as an OTC drug.

Exhibit C: The FDA website's drug information page for Zantac's 75mg OTC formulation listing, among other information, the formulation's NDA and FDA approval date.

Exhibit D: The FDA website's drug information page for Zantac's 150mg OTC formulation listing, among other information, the formulation's NDA and FDA approval date.

Exhibit E: A copy of a document publicly available on the FDA website titled Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book"). The Orange Book lists all drugs approved by the FDA and the companies, including Defendants, authorized to manufacture and sell each listed drug by way of an approved New Drug, or for generics Abbreviated

New Drug, Application.

Exhibit F: FDA guidance document titled "Guidance: Draft Safety Information – FDA's Communication to the Public" dated March 2012.

Exhibit G: FDA Statement: FDA advising patients and health care professionals of NDMA found in samples of ranitidine, Food and Drug Administration (September 13, 2019).

Exhibit H: FDA News Release: FDA Requests Removal of All Ranitidine Products (Zantac) from the Market, Food and Drug Administration (April 1, 2020).

Exhibit I: September 18, 2019 letter from the FDA approving Sanofi's supplemental new drug application ("sNDA") concerning revised labeling for Zantac 150.

Exhibit J: A copy of the Zantac 150 labeling approved by the FDA on September 18, 2019 (*see* Exhibit H).

Exhibit K: September 18, 2019 letter from the FDA approving Sanofi's sNDA concerning revised labeling for Zantac 75.

Exhibit L: A copy of the Zantac 75 labeling approved by the FDA on September 18, 2019 (*see* Exhibit J).

Exhibit M: FDA guidance document titled "Guidance for Industry, Changes to An Approved NDA or ANDA" dated April 2004.

Dated: February 25, 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

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 February 25, 2021, I served a copy of the within document(s):

REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF DEFENDANTS CHATTEM, INC. AND SANOFI-AVENTIS U.S. LLC'S 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 February 25, 2021, at Sacramento, California.

Selena Paradee

SERVICE LIST

Mark Todzo Joseph Mann Lexington Law Group 503 Divisadero Street San Francisco, CA 94117 mtodzo@lexlawgroup.com jmann@lexlawgroup.com	*Plaintiff* Center for Environmental Health
Dennis Raglin Danielle Vallone Steptoe & Johnson LLP 633 West Fifth St., Suite 1900 Los Angeles, CA 90071 draglin@steptoe.com dvallone@steptoe.com	*Defendant* Perrigo Company
Jeffrey B. Margulies Lauren A. Shoor Andy Guo Norton Rose Fulbright US LLP 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Telephone: (213) 892-9200 Facsimile: (213) 892-9494 jeff.margulies@nortonrosefulbright.com lauren.shoor@nortonrosefulbright.com andy.guo@nortonrosefulbright.com	*Defendant* Target Corporation
Cheryl S. Chang Erika R. Schulz Blank Rome LLP 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Chang@BlankRome.com ESchulz@BlankRome.com	*Defendant* Apotex Corp.
Megan E. Grossman Lewis Brisbois Bisgaard & Smith LLP 550 E. Swedesford Road, Suite 270 Wayne, PA 19087 Megan.Grossman@lewisbrisbois.com	*Defendant* Granules USA, Inc.

Will Wagner
Greenberg Traurig LLP
1201 K Street, Suite 1100
Sacramento, CA 94111
wagnerw@gtlaw.com

Trenton H. Norris
Arnold & Porter Kaye Scholer LLP
Three Embarcadero Center, 10th Floor
San Francisco, CA 94111
trent.norris@arnoldporter.com

Defendant
7-Eleven, Inc.

Exhibit 22

GEORGE GIGOUNAS (Bar No. CA-209334)
george.gigounas@dlapiper.com
GREGORY SPERLA (Bar No. CA-278062)
greg.sperla@dlapiper.com
SEAN NEWLAND (Bar No. CA-300928)
sean.newland@dlapiper.com
DLA PIPER LLP (US)
555 Mission Street
Suite 2400
San Francisco, California 94105-2933
Tel: 415.836.2500
Fax: 415.836.2501

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 SECOND AMENDED COMPLAINT**

[PROPOSED] ORDER

Defendants Chattem, Inc. and Sanofi-Aventis U.S. LLC ("Defendants") Demurrer to Plaintiff Center for Environmental Health's ("Plaintiff") Second Amended Complaint, came on regularly for hearing before the Honorable Winifred Y. Smith on April 30, 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 and having heard the arguments of counsel, and with good cause appearing, **IT IS HEREBY ORDERED** that:

1. Defendants' Demurrer to Plaintiff's Second Amended Complaint is **SUSTAINED WITHOUT LEAVE TO AMEND**.

2. Defendants to give notice.

Dated:_____

_____
Honorable Winifred Y. Smith
Alameda County Superior Court Judge

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 February 25, 2021, I served a copy of the within document(s):

[PROPOSED] ORDER SUSTAINING DEMURRER TO 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 February 25, 2021, at Sacramento, California.

Selena Paradee

SERVICE LIST

Mark Todzo Joseph Mann Lexington Law Group 503 Divisadero Street San Francisco, CA 94117 mtodzo@lexlawgroup.com jmann@lexlawgroup.com	*Plaintiff* Center for Environmental Health
Dennis Raglin Danielle Vallone Steptoe & Johnson LLP 633 West Fifth St., Suite 1900 Los Angeles, CA 90071 draglin@steptoe.com dvallone@steptoe.com	*Defendant* Perrigo Company
Jeffrey B. Margulies Lauren A. Shoor Andy Guo Norton Rose Fulbright US LLP 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Telephone: (213) 892-9200 Facsimile: (213) 892-9494 jeff.margulies@nortonrosefulbright.com lauren.shoor@nortonrosefulbright.com andy.guo@nortonrosefulbright.com	*Defendant* Target Corporation
Cheryl S. Chang Erika R. Schulz Blank Rome LLP 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Chang@BlankRome.com ESchulz@BlankRome.com	*Defendant* Apotex Corp.
Megan E. Grossman Lewis Brisbois Bisgaard & Smith LLP 550 E. Swedesford Road, Suite 270 Wayne, PA 19087 Megan.Grossman@lewisbrisbois.com	*Defendant* Granules USA, Inc.

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wagnerw@gtlaw.com

Trenton H. Norris
Arnold & Porter Kaye Scholer LLP
Three Embarcadero Center, 10th Floor
San Francisco, CA 94111
trent.norris@arnoldporter.com

Defendant
7-Eleven, Inc.

Exhibit 23

Brian M. Ledger (SBN 156942)
bledger@grsm.com
GORDON REES SCULLY MANSUKHANI, LLP
101 W. Broadway, Suite 2000
San Diego, CA 92101
Telephone: (619) 696-6700
Facsimile: (619) 696-7124

Attorneys for Defendants
DR. REDDY'S LABORATORIES, INC. AND
DR. REDDY'S LABORATORIES LOUISIANA, LLC

SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

DR. REDDY'S 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, *et. al.*,

Defendants.

Case No. RG 20054985

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

NOTICE OF DEFENDANTS DR. REDDY'S LABORATORIES, INC. AND DR. REDDY'S LABORATORIES LOUISIANA, LLC'S DEMURRER AND DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT

[*Filed concurrently with Joint Memorandum of Points and Authorities; Joint Request for Judicial Notice; Declaration of Brian M. Ledger; and [Proposed] Order*]

RESERVATION NO.: R-2240276

Hearing Date	**April 30, 2021**
Hearing Time	**10:00 a.m.**
Location	**Dept. 21**
Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

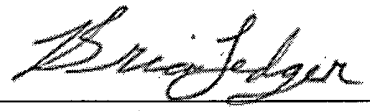
TO THE COURT, ALL PARTIES AND THEIR ATTORNEYS OF RECORD:

PLEASE TAKE NOTICE that on **April 30, 2021**, at 10:00 a.m., or as soon as the matter can be heard, in Department 21 of the Alameda County Superior Court, located at 1221 Oak Street, Oakland, California, Defendants Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories Louisiana, LLC (collectively, "Dr. Reddy's") will demur to Plaintiffs' Second Amended Complaint pursuant to California Code of Civil Procedure, Sections 430.10(e) and 430.30, on the grounds that it fails to state a cause of action against Dr. Reddy's.

Dr. Reddy's Demurrer will be based on this Notice of Demurrer and Demurrer, the accompanying Joint Memorandum of Points and Authorities by the Generic Defendants, the Generic Defendants' Joint Request for Judicial Notice, and the Declaration of Brian M. Ledger, as well as such other evidence the Court may consider.

Dated: February 19, 2021

GORDON REES SCULLY MANSUKHANI LLP

By: 

Brian M. Ledger
Attorney for Defendants
Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories Louisiana, LLC

GENERAL DEMURRER

The Second Amended Complaint against Dr. Reddy's fails to state facts sufficient to constitute a case of actions pursuant to Code of Civil Procedure Sections 430.10(e) and 430.30.

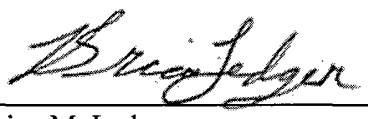
Demurrer to Plaintiffs' First Cause of Action for Injunctive Relief and Civil Penalties

1. Plaintiff's First Cause of Action alleging a violation of Health & Safety Code Section 25249.6, *et seq*, does not contain facts sufficient to state a cause of action against Dr. Reddy's because Plaintiff's claim that Dr. Reddy's failed to include a Proposition 65 warning with its over-the-counter drug ranitidine in violation of this section is preempted by federal law. (California Code of Civil Procedure Sections 430.10(e), 430.)

WHEREFORE, Dr. Reddy's prays that this demurrer be granted without leave to amend, that Plaintiff take nothing by its Second Amended Complaint, and that Dr. Reddy's be awarded judgment for its costs and all other proper relief.

Dated: February 19, 2021

GORDON REES SCULLY MANSUKHANI LLP

By: 

Brian M. Ledger
Attorney for Defendants
Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories Louisiana, LLC

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 **February 19, 2021**, I served the following listed document(s), by method indicated below, on the parties in this action: **NOTICE OF DEFENDANTS DR. REDDY'S LABORATORIES, INC. AND DR. REDDY'S LABORATORIES LOUISIANA, LLC'S DEMURRER AND 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.

☐ **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 **February 19, 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

Mark N. Todzo, Esq. mtodzo@lexlawgroup.com Joseph Mann, Esq. jmann@lexlawgroup.com **LEXINGTON LAW GROUP** 503 Divisadero Street San Francisco, CA 94117 Tel: 415.913.7800 Fax: 415.759.4112	Attorneys for Plaintiff CENTER FOR ENVIRONMENTAL HEALTH
Jeffrey Margulies, Esq. Jeff.margulies@nortonrosefulbright.com Lauren Shoor, Esq. lauren.shoor@nortonrosefulbright.com Andrew Guo, Esq. andy.guo@nortonrosefulbright.com **NORTON ROSE FULBRIGHT US LLP** 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Tel: 213 892 9225 Fax: 213.892.9494	Attorneys for Defendant TARGET CORPORATION
Paul Desrochers, Esq. Paul.desrochers@lewisbrisbois.com **LEWIS BRISBOIS BISGAARD & SMITH LLP** 333 Bush Street, Suite 100 San Francisco, CA 94104 Tel: 415.438.6615 Fax: 415.434.0882	Attorneys for Defendant GRANULES USA, INC.
Cheryl Chang, Esq. chang@blankrome.com Erika Schulz, Esq. eschulz@blankrome.com **BLANKROME LLP** 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Tel: 424.239.3400 Fax: 424.239.3434	Attorneys for Defendant APOTEX CORP.

Brian Ledger, Esq. bledger@gordonrees.com **GORDON REESE SCULLY MANSUKHANI LLP** 101 W. Broadway, Suite 1600 San Diego, CA 92102-8271 Tel: 619.696.6700 Fax: 619.696.7124	Attorneys for Defendants DR. REDDY'S LABORATORIES, INC. DR. REDDY'S LABORATORIES LOUISIANA, LLP
George Gigounas, Esq. George.gigounas@dlapiper.com Greg Sperla, Esq. Greg.sperla@dlapiper.com **DLA PIPER** 400 Capitol Mall, Suite 2400 Sacramento, CA 95814-4428 Tel: 916.930.3200 Fax: 916.930.3201	Attorneys for Defendants SANOFI-AVENTIS U.S. LLC CHATTEM INC.
Will Wagner, Esq. wagnerw@gtlaw.com **GREENBERG TRAURIG, LLP** 1201 K Street, Suite 1100 Sacramento, CA 95814 Tel: 916.442.1111 Fax: 916.448.1709 Trenton H. Norris trent.norris@arnoldporter Vanessa C. Adriance vanessa.adriance@arnoldporter.com **ARNOLD & PORTER** Three Embarcadero Center, 10th Floor San Francisco, CA 94111-4075 Tel: (415) 471-3303 Fax: (415) 471-3400	Attorneys for Defendant 7-ELEVEN, INC.

Exhibit 24

Brian M. Ledger (SBN156942)
bledger@grsm.com
GORDON REES SCULLY MANSUKHANI, LLP
101 W. Broadway, Suite 2000
San Diego, CA 92101
Telephone: (619) 696-6700
Facsimile: (619) 696-7124

Attorneys for Defendants
DR. REDDY'S LABORATORIES, INC. AND
DR. REDDY'S LABORATORIES LOUISIANA, LLC

SUPERIOR COURT OF STATE OF CALIFORNIA

FOR THE COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

vs.

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, *et. al.*,

Defendants.

CASE NO. RG20054985

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

DECLARATION OF BRIAN M. LEDGER IN SUPPORT OF DEFENDANTS DR. REDDY'S LABORATORIES, INC. AND DR. REDDY'S LABORATORIES LOUISIANA, LLC'S DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT

[Filed Concurrently With Notices of Demurrers; Joint Memorandum of Points and Authorities; Joint Request for Judicial Notice; and [Proposed] Order]

RESERVATION NO. R-2240276

Hearing Date:	**April 30, 2021**
Hearing Time:	**10:00 a.m.**
Location:	**Dept. 21**
Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

I, Brian M. Ledger, hereby declare:

1. I am an attorney at Gordon Rees Scully Mansukhani, LLP, counsel of record in the above-entitled matter for Defendants Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories Louisiana, LLC (collectively, "Dr. Reddy's"). I am admitted to the bar of the State of California and am an active member of the California State Bar in good standing. Except where otherwise stated, I have personal knowledge of the matters stated herein, and if sworn as a witness could and would testify competently thereto.

2. I met and conferred with Plaintiff by contacting Mark Todzo, counsel for Plaintiff, by telephone and discussing the matters raised by Dr. Reddy's demurrer. We did not reach an agreement resolving the matters raised by Dr. Reddy's demurrer.

3. Since meet and confer efforts did not resolve the dispute, Dr. Reddy's is proceeding with the filing of the demurrer.

I declare under penalty of the perjury laws of California that the foregoing is true and correct and that this declaration was executed on February 19, 2021, in San Diego, California.

By: 

Brian M. Ledger
Attorney for Defendants
Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories Louisiana, LLC

Gordon Rees Scully Mansukhani, LLP
101 W. Broadway, Suite 2000
San Diego, CA 92101

Gordon Rees Scully Mansukhani, LLP
101 W. Broadway, Suite 2000
San Diego, CA 92101

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 **February 19, 2021** I served the following listed document(s), by method indicated below, on the parties in this action: **DECLARATION OF BRIAN M. LEDGER IN SUPPORT OF DEFENDANTS DR. REDDY'S LABORATORIES, INC. AND DR. REDDY'S LABORATORIES LOUISIANA, LLC'S DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT**

SERVICE LIST ATTACHED

☐ **BY U.S. MAIL**
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/s/ Carmen Markarian
Carmen Markarian

SERVICE LIST

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

Matter No.: 26550-0005

Mark N. Todzo, Esq. mtodzo@lexlawgroup.com Joseph Mann, Esq. jmann@lexlawgroup.com **LEXINGTON LAW GROUP** 503 Divisadero Street San Francisco, CA 94117 Tel: 415.913.7800 Fax: 415.759.4112	Attorneys for Plaintiff CENTER FOR ENVIRONMENTAL HEALTH
Jeffrey Margulies, Esq. Jeff.margulies@nortonrosefulbright.com Lauren Shoor, Esq. lauren.shoor@nortonrosefulbright.com Andrew Guo, Esq. andy.guo@nortonrosefulbright.com **NORTON ROSE FULBRIGHT US LLP** 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Tel: 213 892 9225 Fax: 213.892.9494	Attorneys for Defendant TARGET CORPORATION
Paul Desrochers, Esq. Paul.desrochers@lewisbrisbois.com **LEWIS BRISBOIS BISGAARD & SMITH LLP** 333 Bush Street, Suite 100 San Francisco, CA 94104 Tel: 415.438.6615 Fax: 415.434.0882	Attorneys for Defendant GRANULES USA, INC.
Cheryl Chang, Esq. chang@blankrome.com Erika Schulz, Esq. eschulz@blankrome.com **BLANKROME LLP** 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Tel: 424.239.3400 Fax: 424.239.3434	Attorneys for Defendant APOTEX CORP.

Gordon Rees Scully Mansukhani, LLP
101 W. Broadway, Suite 2000
San Diego, CA 92101

Brian Ledger, Esq. bledger@gordonrees.com **GORDON REESE SCULLY MANSUKHANI LLP** 101 W. Broadway, Suite 1600 San Diego, CA 92102-8271 Tel: 619.696.6700 Fax: 619.696.7124	Attorneys for Defendants DR. REDDY'S LABORATORIES, INC. DR. REDDY'S LABORATORIES LOUISIANA, LLP
George Gigounas, Esq. George.gigounas@dlapiper.com Greg Sperla, Esq. Greg.sperla@dlapiper.com **DLA PIPER** 400 Capitol Mall, Suite 2400 Sacramento, CA 95814-4428 Tel: 916.930.3200 Fax: 916.930.3201	Attorneys for Defendants SANOFI-AVENTIS U.S. LLC CHATTEM INC.
Will Wagner, Esq. wagnerw@gtlaw.com **GREENBERG TRAURIG, LLP** 1201 K Street, Suite 1100 Sacramento, CA 95814 Tel: 916.442.1111 Fax: 916.448.1709 Trenton H. Norris trent.norris@arnoldporter Vanessa C. Adriance vanessa.adriance@arnoldporter.com **ARNOLD & PORTER** Three Embarcadero Center, 10th Floor San Francisco, CA 94111-4075 Tel: (415) 471-3303 Fax: (415) 471-3400	Attorneys for Defendant 7-ELEVEN, INC.

Gordon Rees Scully Mansukhani, LLP
101 W. Broadway, Suite 2000
San Diego, CA 92101

Exhibit 25

Brian M. Ledger (SBN 156942)
bledger@grsm.com
GORDON REES SCULLY MANSUKHANI, LLP
101 W. Broadway, Suite 2000
San Diego, CA 92101
Telephone: (619) 696-6700
Facsimile: (619) 696-7124

Attorneys for Defendants
DR. REDDY'S LABORATORIES, INC. AND
DR. REDDY'S LABORATORIES LOUISIANA, LLC

SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF ALAMEDA

CENTER FOR ENVIRONMENTAL HEALTH, a non-profit corporation,

Plaintiff,

v.

DR. REDDY'S 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, *et. al.*,

Defendants.

Case No. RG 20054985

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

[PROPOSED] ORDER SUSTAINING DEFENDANTS DR. REDDY'S LABORATORIES, INC. AND DR. REDDY'S LABORATORIES LOUISIANA, LLC'S DEMURRER TO SECOND AMENDED COMPLAINT WITHOUT LEAVE TO AMEND

[*Filed concurrently with Notice of Demurrer; Joint Memorandum of Points and Authorities; Joint Request for Judicial Notice and Declaration of Brian M. Ledger*]

RESERVATION NO.: R-2240276

Hearing Date	**April 30, 2021**
Hearing Time	**10:00 a.m.**
Location	**Dept. 21**
Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

The Court, having considered the Demurrer of Defendants DR. REDDY'S LABORATORIES, INC. and DR. REDDY'S LABORATORIES LOUISIANA, LLC ("Defendants"), the papers filed in response thereto, all other argument and the record in this case, and for good cause shown:

1. SUSTAINS the Demurrer;

2. Finds Plaintiff's claim against Defendants, reflected in the First Cause of Action alleging a violation of Health & Safety Code Section 25249.6, *et seq*, fails to state facts sufficient to constitute a case of actions pursuant to Code of Civil Procedure Sections 430.10(e) and 430.30;

3. Orders the Second Amended Complaint DISMISSED WITH PREJUDICE from this action; and

4. Orders judgment to be entered in favor of Defendants.

IT IS SO ORDERED.

DATED:

Hon. Winifred Y. Smith
County of Alameda Superior Court

SERVICE LIST

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

Matter No.: 26550-0005

Mark N. Todzo, Esq. mtodzo@lexlawgroup.com Joseph Mann, Esq. jmann@lexlawgroup.com **LEXINGTON LAW GROUP** 503 Divisadero Street San Francisco, CA 94117 Tel: 415.913.7800 Fax: 415.759.4112	Attorneys for Plaintiff CENTER FOR ENVIRONMENTAL HEALTH
Jeffrey Margulies, Esq. Jeff.margulies@nortonrosefulbright.com Lauren Shoor, Esq. lauren.shoor@nortonrosefulbright.com Andrew Guo, Esq. andy.guo@nortonrosefulbright.com **NORTON ROSE FULBRIGHT US LLP** 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Tel: 213 892 9225 Fax: 213.892.9494	Attorneys for Defendant TARGET CORPORATION
Paul Desrochers, Esq. Paul.desrochers@lewisbrisbois.com **LEWIS BRISBOIS BISGAARD & SMITH LLP** 333 Bush Street, Suite 100 San Francisco, CA 94104 Tel: 415.438.6615 Fax: 415.434.0882	Attorneys for Defendant GRANULES USA, INC.
Cheryl Chang, Esq. chang@blankrome.com Erika Schulz, Esq. eschulz@blankrome.com **BLANKROME LLP** 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Tel: 424.239.3400 Fax: 424.239.3434	Attorneys for Defendant APOTEX CORP.

Brian Ledger, Esq. bledger@gordonrees.com **GORDON REESE SCULLY MANSUKHANI LLP** 101 W. Broadway, Suite 1600 San Diego, CA 92102-8271 Tel: 619.696.6700 Fax: 619.696.7124	Attorneys for Defendants DR. REDDY'S LABORATORIES, INC. DR. REDDY'S LABORATORIES LOUISIANA, LLP
George Gigounas, Esq. George.gigounas@dlapiper.com Greg Sperla, Esq. Greg.sperla@dlapiper.com **DLA PIPER** 400 Capitol Mall, Suite 2400 Sacramento, CA 95814-4428 Tel: 916.930.3200 Fax: 916.930.3201	Attorneys for Defendants SANOFI-AVENTIS U.S. LLC CHATTEM INC.
Will Wagner, Esq. wagnerw@gtlaw.com **GREENBERG TRAURIG, LLP** 1201 K Street, Suite 1100 Sacramento, CA 95814 Tel: 916.442.1111 Fax: 916.448.1709 Trenton H. Norris trent.norris@arnoldporter Vanessa C. Adriance vanessa.adriance@arnoldporter.com **ARNOLD & PORTER** Three Embarcadero Center, 10th Floor San Francisco, CA 94111-4075 Tel: (415) 471-3303 Fax: (415) 471-3400	Attorneys for Defendant 7-ELEVEN, INC.

Exhibit 26

Dennis Raglin (SBN 179261)
draglin@steptoe.com
Danielle Vallone (SBN 302497)
dvallone@steptoe.com
STEPTOE & JOHNSON LLP
633 West Fifth Street, Suite 1900
Los Angeles, California 90071
Telephone: 213 439 9400
Facsimile: 213 439 9599

Attorneys for Defendant,
PERRIGO COMPANY

[ADDITIONAL MOVING COUNSEL LISTED ON FOLLOWING PAGE]

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, et. al.,

Defendants.

Case No. RG20054985

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

GENERIC DEFENDANTS' JOINT MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT

[Filed concurrently with Notices of Demurrers, Declaration of Dennis Raglin; Joint Request for Judicial Notice and [Proposed] Order]

RESERVATION NO: R-2242700

Hearing Date	**April 30, 2021**
Hearing Time	**10:00 a.m.**
Location	**Dept. 21**
Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

Paul Desrochers, Esq.
paul.desrochers@lewisbrisbois.com
LEWIS BRISBOIS BISGAARD & SMITH LLP
333 Bush Street, Suite 100
San Francisco, CA 94104
Tel: 415.438.6615
Fax: 415.434.0882

Attorneys for Defendant
GRANULES USA, INC.

Brian Ledger, Esq.
bledger@gordonrees.com
GORDON REES SCULLY MANSUKHANI LLP
101 W. Broadway, Suite 1600
San Diego, CA 92102-8271
Tel: 619.696.6700
Fax: 619.696.7124

Attorneys for Defendants
DR. REDDY'S LABORATORIES, INC.
DR. REDDY'S LABORATORIES LOUISIANA, LLP

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I. INTRODUCTION

Plaintiff's private-enforcement action, under Proposition 65, cannot proceed against the defendants that market generic versions of ranitidine-containing products because federal law preempts it. Proposition 65 is a warning statute that explicitly recognizes—and yields to—federal preemption. By its own terms, the statute "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. And the Supreme Court's *Mensing* and *Bartlett* decisions[1] unambiguously hold that failure-to-warn claims against generic-drug manufacturers are preempted if, as here, it is impossible for the defendants to comply with federal- and state-law duties.

Ranitidine-containing products have been withdrawn from the market and remain off the market. The products and their labeling have always been strictly regulated by the federal Food and Drug Administration ("FDA") under the Federal Food, Drug, and Cosmetic Act ("FDCA"). In light of these facts and controlling federal-preemption law, Plaintiff has no basis to seek injunctive relief, civil penalties, and attorneys' fees under Proposition 65.

Dismissal of the Proposition 65 claim here is entirely in accord with numerous federal and California state decisions that have dismissed failure to warn claims against generic-drug manufacturers. In fact, a federal judge in a multidistrict litigation ("MDL") involving the same ranitidine-containing products at issue here recently dismissed all counts against generic-drug manufacturers as preempted. The order included dismissal with prejudice and without leave to re-plead any claims premised on labeling or warning changes.

Thus, under Proposition 65's own terms and controlling United States Supreme Court authority, federal preemption bars the claim against the generic-drug manufacturers. Generic Defendants' demurrers should be granted.

II. RELEVANT FACTUAL AND PROCEDURAL BACKGROUND

In the operative Second Amended Complaint ("SAC"), Plaintiff Center for Environmental Health ("CEH") brings only one count, accusing ten named Defendants and 1-20

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

"Doe" Defendants of violating Proposition 65. Defendants all allegedly manufacture, distribute, or sell over-the-counter ("OTC") acid-reducing medications containing ranitidine ("OTC ranitidine medications"). Perrigo Company; Granules Pharmaceuticals, Inc.; Granules USA, Inc.; Dr. Reddy's Laboratories Louisiana, LLC; and Dr. Reddy's Laboratories, Inc. (collectively "Generic Defendants") are all generic drug manufacturers, and their respective OTC ranitidine medications are **generic** drugs manufactured and marketed under FDA-approved Abbreviated New Drug Applications ("ANDAs"). Request for Judicial Notice ("RJN") ¶¶ 1-5, Ex. A-C. Plaintiff contends that Proposition 65 required Generic Defendants to directly warn consumers that using the OTC ranitidine medications allegedly exposed them to the chemical n-nitrosodimethylamine ("NDMA").

Ranitidine products are no longer sold in California—or anywhere else in the United States. Manufacturers began to voluntarily withdraw their ranitidine-containing products in September 2019. In April 2020, the FDA expanded on earlier guidance by formally recommending withdrawal of *all* ranitidine products from the market. *See In re Zantac (Ranitidine) Prods. Liab. Litig.*, No. 2924 20-MD-2924 ("*Zantac MDL*"); 2020 WL 7864213 at *2 (S.D. Fla. Dec. 31, 2020).

The well-publicized nationwide withdrawal prompted hundreds of ranitidine lawsuits, most of which have been consolidated in the federal MDL presided over by Judge Robin Rosenberg in the U.S. District Court for the Southern District of Florida. The United States Judicial Panel on Multidistrict Litigation created the *Zantac MDL*, in February 2020, and ordered all "federal lawsuits for personal injury and economic damages from the purchase and/or use of ranitidine products to be transferred to" Judge Rosenberg. *Id.* Closely managing the *Zantac MDL*, and with further support from both a Magistrate and Special Master, Judge Rosenberg appointed liaison counsel to represent the broad interests of hundreds of plaintiffs and several dozen defendants, who were categorized generally as brand manufacturers, generic-drug manufacturers, distributors, repackagers, and retailers. The close case management yielded three MDL Master Complaints: a master personal-injury action and two class actions seeking refunds for consumers and third-party payors, respectively. *Id.*

Judge Rosenberg recognized that potential federal preemption of all state-law ranitidine claims involving either brand-name or generic ranitidine products posed a critical threshold issue. She ordered the categorized parties to substantively brief the preemption issue (and other threshold issues) on pre-answer motions to dismiss during the second half of 2020. She then dedicated one of two full days of oral argument on the motions to the various parties' preemption briefs and, on December 31, 2020, issued (among other opinions) a 54-page written opinion on the generic-drug manufacturers' (and repackagers') preemption arguments.

Applying *Mensing* and *Bartlett*, the United States Supreme Court's landmark generic-drug preemption rulings, Judge Rosenberg dismissed all counts across all three Master Complaints as federally preempted. *Id.* at *14. The MDL court explained that federal law preempts, and requires dismissal with prejudice of, "Plaintiffs' claims based on alleged product and labeling defects that Defendants could not independently change while remaining in compliance with federal law." *Id.* The MDL court explained that, unlike brand-name drug manufacturers, who may have some ability to "unilaterally strengthen" their FDA-approved labeling, as explained in *Wyeth v. Levine* (2009) 555 U.S. 555, 568-59, generic-drug manufacturers are bound by the federal-law "duty of sameness" which renders it impossible for generic-drug manufacturers to change their labeling to meet state-law requirements without violating federal law. *Id.* at *14-17.

Judge Rosenberg re-affirmed the sweeping scope of the *Mensing* and *Bartlett* precedents, which preclude *all* failure-to-warn and design-defect claims against generic-drug manufacturers who meet their federal obligations, regardless of how plaintiffs may style their claims:

> Based on the *Mensing* and *Bartlett* opinions, federal courts have held that numerous categories of claims against generic drug manufacturers are pre-empted, even where plaintiffs do not couch their claims as design defect or failure to warn. For example, courts have 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.

Id. at *9 (emphasis added). The court also rejected the MDL plaintiffs' theory that preemption could be avoided merely by alleging that a product is "misbranded" under

federal law, explaining that a "claim based on an allegation that a generic drug's labeling renders the drug misbranded is a pre-empted claim because the drug's manufacturer cannot independently and lawfully change FDA-approved labeling." *Id.* at *13.

The same preemption principles apply here to preclude any California state-law failure-to-warn (and design-defect) claims against generic-drug manufacturers who used FDA-approved labeling. Plaintiff's one-count complaint alleges failure to warn under Proposition 65.

III. DEMURRER STANDARD

A demurrer challenges defects that appear on the face of the complaint. *Blank v. Kirwan* (1985) 39 Cal. 3d 311, 318. A defendant may demur because the complaint does not state facts sufficient to constitute a cause of action, Cal. Code Civ. Proc. § 430.10(e), and may rely in its demurrer on matters properly subject to judicial notice. Cal. Code Civ. Proc. § 430.70; *see also* Cal. Code Evid. § 452 (listing matters subject to judicial notice).

Because "federal preemption presents a pure question of law," it is properly resolved by demurrer. *See Farm Raised Salmon Cases* (2008) 42 Cal.4th 1077, 1082-83 & 1089 n.10; *see also King v. CompPartners, Inc.* (2018) 5 Cal.5th 1039, 1061 (affirming trial court's sustaining demurrer without leave to amend because claims were preempted).

IV. ARGUMENT

A. Proposition 65 recognizes—and yields to—federal preemption

Proposition 65—the Safe Drinking Water and Toxic Enforcement Act of 1986, Cal. Health & Safety Code §§ 25249.5-25249.14—is fundamentally a statute about warnings. It imposes no liability for **selling** products that contain chemicals known to the state of California to cause cancer or reproductive toxicity. *See id.* § 25249.6. Instead, Proposition 65 proscribes such sales only if made "without first giving clear and reasonable warning" that "clearly communicate[s]" that the "chemical . . . is known . . . to cause cancer" before exposure occurs. *See id.*, §§ 25249.6; 25249.10(b); 25601" If a manufacturer gives the warning, Proposition 65's requirements are met, even if the product's risk to consumers remains. *See, e.g., Envt'l. Law Found. v. Wykle Research, Inc.* (2005) 134 Cal. App. 4th 60, 64-71.

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But 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. Accordingly, Proposition 65 provides that the requirements stated in Section 25249.6 "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); *see also id.* § 25249.6 (noting that Proposition 65 requirements apply "except as provided in Section 25249.10"). Thus, by Proposition 65's own terms, when federal law governing product warnings has preemptive effect, Proposition 65 yields.

In assessing whether "federal law governs warning in a manner that preempts state authority," United States Supreme Court decisions are controlling precedents. *See Elliott v. Albright* (1989) 209 Cal. App. 3d 1028, 1034, 257 Cal. Rptr. 762, 765 ("Decisions of the United States Supreme Court are binding not only on all of the lower federal courts . . . . , but also on state courts when a federal question is involved.") (internal citation omitted); *Essure Products Cases,* No. JCCP 4887; 2019 WL 5873725, at *2 (October 2, 2019) (W. Smith, J.) (holding similarly). Decisions of the lower federal courts "are persuasive and entitled to great weight" by California trial courts in deciding federal questions. *Etcheverry v. Tri-Ag Serv., Inc.* (2000) 22 Cal. 4th 316, 320-21; *see also Essure Products Cases*, 2019 WL 5873725, at *2. And, "where the decisions of the lower federal courts on a federal question are both numerous and consistent, [California courts] should hesitate to reject their authority." *Id.*

Here, under the controlling authority of *Mensing*, and as persuasively applied to the facts of this case in the *Zantac MDL* (*see* Relevant Factual and Procedural Background, *supra* at 3-4, Arg. B, *infra* at 7-12), "federal law governs warning in a manner that preempts state authority." Cal. Health & Safety Code § 25249.10; *see, e.g., Com. of Dental Amalgam Alloy Mfrs. v. Henry* (S.D. Cal. 1994) 871 F. Supp. 1278 (applying federal preemption to Proposition 65 claims regarding FDA-regulated dental mercury whose labeling did not contain reproductive warning otherwise required by California law). As detailed in Part B, *Mensing* held that the federal law duty of "sameness" in generic-drug labeling requires generic-drug manufacturers to use the same

warning labeling that appears on the corresponding brand-name drug label. *Mensing* and *Bartlett* held that these federal requirements for generic drugs preempt any conflicting state law that would require generic-drug manufacturers to either add a new warning that does not appear on the brand-name label or else stop selling the product at all. That is why the *Zantac MDL* court and other federal courts have consistently held that the broad federal definition of "labeling" encompasses claims that a generic drug manufacturer should have communicated a warning to consumers through means such as letters or advertising and are preempted under *Mensing* and *Bartlett*.

This clear federal authority puts Plaintiff's claims against Generic Defendants within the Section 25249.10(a) exception: federal law governs warnings for generic drugs in a manner that preempts requiring any Proposition 65 warning for the generic OTC ranitidine medications. And, because the Section 25249.10 exception applies, it is irrelevant that Plaintiff has alleged that Generic Defendants "can reduce or eliminate NDMA from the Products by using cleaner ingredients and manufacturing processes and more careful storage techniques." SAC ¶ 24. Therefore, and for the additional reasons given below, this Court should grant Generic Defendants' demurrers and dismiss the Proposition 65 claim with prejudice.

B. Impossibility preemption bars Plaintiff's Proposition 65 claim

1. *Mensing* set a bright-line rule that failure-to-warn claims against generic-drug manufacturers are preempted

The foundation of every preemption analysis is the Supremacy Clause, which establishes that federal law "shall be the supreme Law of the Land. . . ." U.S. Const., Art. VI, cl. 2. Thus, when state and federal law directly conflict, making it is impossible for a private party to comply with both, "state law must give way." *PLIVA, Inc. v. Mensing* (2011) 564 U.S. 604, 617.

In *Mensing,* the Supreme Court explained that federal law requires companies seeking to market a novel drug product to file a new drug application ("NDA") based on "costly and lengthy" multi-phase clinical trial programs. 564 U.S. at 612 (citing 21 U.S.C. § 355(b)(1), (d)). But drug companies seeking to market *generic* versions of previously approved drugs may file an ANDA that demonstrates the product's chemical and biological equivalence to a previously

approved brand-name drug. *Id.* (citing 21 U.S.C. § 355(j)(2)(A)). The ANDA must show, among other things, that the generic drug's "labeling—which under federal law is defined expansively to include warnings and other information supplementing and explaining the drug product (even if not physically accompanying it)[2]—is "the same as the labeling approved for the [brand-name] drug." *Mensing*, 564 U.S. at 612-13 (quoting 21 U.S.C. § 355(j)(2)(A)(v) and citing *id.* at § 355(j)(4)(G) (alteration in original)). "As a result, brand-name and generic drug manufacturers have different federal drug labeling duties. A brand name manufacturer seeking new drug approval is responsible for the accuracy and adequacy of its label. A manufacturer seeking generic drug approval, on the other hand, is responsible for ensuring that its warning label *is the same as the brand name's*." *Id.* (emphasis added, internal citations omitted).

The *Mensing* Court held that those federal-law requirements for generic drugs preempt state-law failure-to-warn claims against generic-drug manufacturers. *See* 564 U.S. at 608. Like Plaintiff here, the *Mensing* plaintiffs alleged that a generic drug's FDA-approved label did not adequately warn of the drug's alleged risk. *Id.* at 610. But the Supreme Court recognized that generic-drug manufacturers cannot comply with both a state-law duty requiring them to alter a drug's label and federal law requiring them to faithfully reproduce the brand-name drug's label. *Id.* at 611-13. It characterized the generic-drug manufacturers' rigid obligation to mirror their respective brands' labeling as the federal duty of "sameness." *Id.* at 613-15. And, because "it was impossible for the Manufacturers to comply with both their state-law duty to change the label and their federal law duty to keep the label the same," federal law preempted the state-law failure-to-warn claims. *Id.* at 624.

Generic impossibility preemption, thus, is rooted in the generic-drug manufacturer's inability to unilaterally change its label. The *Mensing* Court explained that state-law failure to warn claims against a generic-drug manufacturer directly conflict with federal law if the manufacturer cannot act "unilaterally" or "independently" to satisfy state warning requirements

[2] The FDCA defines "labeling" as "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 U.S.C. § 321(m). Courts have long interpreted this statute to give the broadest possible meaning to the term "labeling." *See, e.g., Strayhorn v. Wyeth Pharm., Inc.* (6th Cir. 2013) 737 F.3d 378, 394.

without federal permission. Indeed, the sole "question for 'impossibility' [preemption] is whether the private party could *independently* do under federal law what state law requires of it[.]" *Id.* at 620 (emphasis added). If it cannot lawfully do so, the claims are preempted and must be dismissed. *See id.*; *see also Zantac MDL,* 2020 WL 784213, at *7-8.

Plaintiffs cannot sidestep impossibility preemption by proposing merely contingent plans by which a generic-drug manufacturer *potentially* could have effected a generic-label change. The *Mensing* Court held that "when a party cannot satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for pre-emption purposes." 564 U.S. at 623-24. So, arguments that a generic-drug manufacturer could have or should have gone to the FDA for help to 'improve' its label or sought its permission to alert its customers to a hazard not in its labeling are irrelevant to the preemption analysis.[3]

Thus, impossibility preemption analysis begins by recognizing that *Mensing* fundamentally distinguishes (1) failure-to-warn claims against *generic-drug* manufacturers, who cannot act unilaterally, from (2) such claims against *brand-name* manufacturers, who might be able to use the changes-being-effected ("CBE") process to unilaterally change a label. *See id.* at 614, 620, 624 (distinguishing *Wyeth* v. *Levine* (2009) 555 U.S. 555, 568). Noting that some plaintiffs may view the starkly contrasting results of preemption analysis for generic and branded versions of the same drug and label as making "little sense," the *Mensing* Court explained that "federal statutes and regulations that apply to brand-name drug manufacturers are meaningfully

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[3] This is an important distinction between *Mensing* and *Coleman v. Medtronic, Inc.* (2014) 223 Cal. App. 4th 413. *Coleman* involved the federal *express* preemption provision for Class III medical devices found at 21 U.S.C. § 360k. The *Coleman* court held that a plaintiff raising a failure-to-warn claim against a Class III medical device manufacturer could survive the §360k statutory express preemption under a theory that the manufacturer failed to file adverse event reports with the FDA. 223 Cal. App. 4th at 428-30. The court recognized that a plaintiff would face a difficult "causation hurdle" to prove that adverse-event information reported to FDA would have reached a prescribing physician and prevented the plaintiff's injury, but held that this was an insufficient basis to dismiss on preemption grounds at the pleadings stage. *Id.* at 429-430; *see also Stengel v. Medtronic Inc.* (9th Cir. 2013) 704 F.3d 1224, 1234 (concurring opinion). In sharp contrast, in *Mensing,* the Supreme Court held that a theory of failure to warn FDA was insufficient to defeat *impossibility* preemption for generic drugs. 564 U.S. at 619-24. The Court explained that if a generic-drug manufacturer had warned FDA about a risk in its product and sought FDA's help in changing its label, it might have started a "Mouse Trap game" that could have eventually led the FDA to negotiate a new label with the brand name manufacturer, which the generic-drug manufacturer could then adopt. *Id.* But the Court held that, ***as a matter of law***, such "conjectures" that are inherently "dependent on the exercise of judgment by a federal agency" are insufficient to defeat impossibility preemption, which considers only the actions that a manufacturer can "independently" take. *Id.* Thus, a failure to warn FDA theory is insufficient to overcome preemption under *Mensing.*

different than those that apply to generic drug manufacturers," even if the drugs and labels are the same. *Id.* at 625, 626. That is the regulatory regime that Congress created, and "the special, and different, regulation of generic drugs" has "allowed the generic drug market to expand, bringing more drugs more quickly and cheaply to the public." *Id.* at 626.

And it is the rule that California courts now follow. *See Trejo v. Johnson & Johnson* (2017) 13 Cal.App.5th 110, 152, fn. 22. "Generic drug manufacturers are not free to strengthen drug label warnings under 21 Code of Federal Regulations part 314.70 (2017), the FDA's 'changes being effected' (CBE) regulation, which permits a brand-name prescription drug manufacturer to strengthen a warning label while waiting for FDA approval of the change." *Id.* (citing *Wyeth v. Levine* (2009) 555 U.S. 555, 558-559; *Mensing,* 564 U.S. at 613-615). "The CBE regulations do not apply to generic prescription drug labels, which are required by federal law to be identical to brand-name labels." *Id.*

2. *Bartlett* extended *Mensing* to design-defect claims against generic-drug manufacturers.

Just two years after *Mensing*, the Supreme Court extended *Mensing*'s bright-line rule and held that federal law *also* preempts state-law *design*-defect claims against generic drug manufacturers. *Bartlett*, 570 U.S. 475-76. The *Bartlett* Court explained that the duty of sameness extends to design as well as labeling, as "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. And, once the FDA approves a generic drug's design, the manufacturer is prohibited from making changes to the "qualitative or quantitative formulation of the drug product, including active ingredients, or in the specifications provided in the approved application" unless it first seeks and obtains FDA approval for the change. *Id.* at 477 (quoting 21 C.F.R. § 314.70(b)(2)(i)). The duty of sameness was especially salient in *Bartlett* because the relevant drug's active ingredient was—like ranitidine—a single molecule and "chemically incapable of being redesigned." *Id.* at 484.

The *Bartlett* Court also squarely rejected what it referred to as a "stop-selling" argument: that a manufacturer could satisfy both its state- and federal-law duties by choosing not to make

the FDA-approved medicine at all. *Id.* at 488-90. The Court explained that its preemption jurisprudence "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." *Id.*[4]

In sum, under *Mensing* and *Bartlett,* any cause of action that would require a generic-drug manufacturer to change its drug's labeling or chemical makeup, or take any other unilateral action without FDA approval, must be dismissed as preempted. *Bartlett*, 570 U.S. at 486. This includes any claims against generic-drug manufacturers of ranitidine "for failure to communicate information to consumers" or "violation of consumer-protection statutes." *See Zantac MDL,* 2020 WL 7864213 at *9. Implied preemption further bars any state-law claims that the manufacturer should have stopped selling its generic drug to comply with state law. *Bartlett*, 570 U.S. at 486.

3. *Mensing* resolved lower courts' inconsistent decisions over whether generic drug manufacturers could be liable under state law for not warning consumers under alternative legal theories.

Before the Supreme Court decided *Mensing*, in 2011, trial and appellate courts in California's state and federal courts, and elsewhere, struggled to reliably apply impossibility preemption principles to failure-to-warn claims against generic drug manufacturers. In two pre-*Mensing* cases, one state (*McKenney*) and one federal (*Gaeta*), California trial judges correctly held that claims against generic drug manufacturers were preempted because the generic-drug manufacturers could not unilaterally change their product labeling to satisfy state law.[5] Without the benefit of the final *Mensing* opinion, both appellate courts reversed, erroneously holding that state-law claims against generic drug manufacturers were not preempted.[6] These erroneous

[4] Courts also have relied on *Bartlett* to dismiss, as preempted, claims that a manufacturer could have chosen not to market a drug in the first instance. *See Yates v. Ortho-McNeil-Janssen Pharm., Inc.* (6th Cir. 2015) 808 F.3d 281, 300 (rejecting plaintiff's "never-start selling rationale for the same reasons the Supreme Court in *Bartlett* rejected the stop-selling rationale").

[5] *See Gaeta v. Perrigo Pharms. Co.* (N.D. Cal. 2008) 562 F. Supp. 2d 1091, 1098 ("The Court finds 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 v. Perrigo Pharms. Co.* (N.D. Cal. 2009) 672 F. Supp. 2d 1017, 1022 ("The Court holds that the Supreme Court's decision in *Wyeth v. Levine* did not address the issue of whether a generic drug manufacturer may use the CBE process to unilaterally change a warning label, which is dispositive to this case. Accordingly, the Court DENIES Plaintiffs' Motion for Reconsideration in Light of *Wyeth v. Levine.*").

[6] *McKenney v. Purepac Pharmaceutical Co.* (2008) 167 Cal.App.4th 72, 77; *Gaeta v. Perrigo Pharms. Co.* (9th Cir. 2011) 630 F.3d 1225, 1232.

appellate decisions were issued in the brief period between the Supreme Court's 2009 *Wyeth v. Levine* decision—which held that inadequate-warning claims against *brand* manufacturers were not preempted if the NDA holder could use the CBE process to unilaterally change its label—and its 2011 *Mensing* decision, which explained why *generics* could *not* use the CBE process or take any other unilateral action to change the label.

Mensing brought order to this once-unpredictable area of law for California courts, expressly invalidating the initial Ninth Circuit *Gaeta* opinion and overruling *McKenney's* holding by necessary implication. *See L. Perrigo Co. v. Gaeta* (2011) 565 U.S. 973. The Ninth Circuit dutifully reversed course and affirmed the trial court's original decision finding the claims for generic drugs fully preempted, resulting in judgment being entered in favor of *generic-drug* manufacturer Perrigo. *Gaeta v. Perrigo Pharms. Co.* (9th Cir. 2012) 469 F. App'x 556, 557. Courts in California now recognize that, when generic-drug manufacturers are challenged for labeling conduct that comports with federal requirements, "any state law claims based on failure-to-warn would conflict impermissibly with federal FDA regulations, and are therefore preempted." *Ko v. Mut. Pharm. Co., Inc.* (N.D. Cal. Oct. 18, 2013) No. C-13-00890-RMW; 2013 WL 5692375, at *2 (N.D. Cal. October 18, 2013).

Indeed, a California federal court recently applied *Mensing* and *Bartlett* to grant a generic-drug manufacturer's motion to dismiss a personal injury claim involving a ranitidine product. *Davallou v. Glenmark Pharm. US Head Quarters*; No. 20-cv-00619-DMS-MDD; 2020 WL 4284965 (S.D. Cal. July 27, 2020). The court noted that "state law claims involving generic drugs labels or warning are preempted by federal law," *id.* at *3 (citing *Mensing*, 564 U.S. at 618 and *Bartlett*, 570 U.S. at 486), and that "[b]ecause ranitidine is a generic drug, Defendant is bound by federal law to use the same label, warnings, and design approved by the Federal Drug Administration ("FDA") in connection with [brand name] Zantac." *Id.* Accordingly, while the *pro se* plaintiff was allowed to replead to correct basic pleading deficiencies, the California federal district court held that to the extent that "Plaintiff alleges that Defendant should have included additional warnings on ranitidine's label, Plaintiff's claim is preempted." *Id.* at *3.

4. Courts nationwide have applied *Mensing* and *Bartlett* to preclude claims against generic-drug manufacturers, including "failure to communicate" claims.

Since 2013, dozens of courts nationwide have applied *Mensing* and *Bartlett's* bright-line preemption rules to dismiss state-law claims against generic-drug manufacturers (and others in the supply chain), no matter how styled. These include:

- *Gaeta, supra,* (9th Cir. 2012) 469 F. App'x 556, 557 (post-*Mensing* decision affirming district court's dismissal of claims against Perrigo in case involving generic OTC ibuprofen);
- *Moretti v. Wyeth, Inc.* (9th Cir. 2014) 579 F. App'x 563, 564 (affirming dismissal of claims against manufacturer of generic metoclopramide because it was impossible for the manufacturer to satisfy the state-law obligations asserted in the plaintiff's complaint to issue a new or revised warning);
- *Guarino v. Wyeth, LLC* (11th Cir. 2013) 719 F.3d 1245 (affirming dismissal of claims for negligence, strict liability, breach of warranty, misrepresentation and fraud, and negligence *per se* asserted against manufacturer of generic metoclopramide);
- *In re Darvocet, Darvon, & Propoxyphene Prods. Liab. Litig.* (6th Cir. 2014) 756 F.3d 917 (affirming dismissal of wrongful marketing, failure-to-warn, design defect, breach of express and implied warranty, fraud, misrepresentation, breach of consumer protection statutes, wrongful death, survivorship, unjust enrichment, loss of consortium, and punitive damage claims against manufacturers of generic propoxyphene);[7]
- *Davallou, supra;* No. 20-cv-00619-DMS-MDD; 2020 WL 4284965 (S.D. Cal. July 27, 2020) (granting motion to dismiss personal injury claim against generic-drug manufacturer involving ranitidine on preemption grounds);

[7] *See also Wagner v. Teva Pharm. USA, Inc.* (7th Cir. 2016) 840 F.3d 355; *Houston v. United States* (7th Cir. 2016) 638 F. App'x 508; *Yates v. Ortho-McNeil-Janssen Pharm., Inc.* (6th Cir. 2015) 808 F.3d 281; *In re Fosamax (Alendronate Sodium) Prod. Liab. Litig. (No. II)* (3d Cir. 2014) 751 F.3d 150; *Drager v. PLIVA USA, Inc.* (4th Cir. 2014) 741 F.3d 470; *Eckhardt v. Qualitest Pharm., Inc.* (5th Cir. 2014) 751 F.3d 674; *Lashley v. Pfizer, Inc.* (5th Cir. 2014) 750 F.3d 470; *Johnson v. Teva Pharm. USA, Inc.* (5th Cir. 2014) 758 F.3d 605; *Brinkley v. Pfizer, Inc.* (8th Cir. 2014) 772 F.3d 1133; *Demahy v. Schwarz Pharma, Inc.* (5th Cir. 2012) 702 F.3d 177.

- *Ko, supra*, No. C-13-00890-RMW; 2013 WL 5692375 (N.D. Cal. Oct. 18, 2013) (granting motion to dismiss state-law products liability claims involving against manufacturer of generic sulindac medication on preemption grounds);
- *Greager v. McNeil-PPC, Inc.* (N.D. Ill. 2019) 414 F. Supp. 3d 1137 (dismissing claims of defective design, failure to warn, negligence, consumer fraud, breach of implied warranty of merchantability, and willful and wanton misconduct asserted against manufacturer and retailer of generic OTC medications);

Despite the firm boundaries set by *Mensing* and *Bartlett* for claims against generic-drug manufacturers, plaintiffs still try to plead around them by suggesting that various state-law duties to communicate additional warnings (commonly referred to as a "failure to communicate") can somehow survive impossibility preemption. They cannot. *See Mensing*, 564 U.S. at 615. Following the Supreme Court's clear guidance, federal appellate courts repeatedly reject the theory. The Eleventh Circuit, in *Guarino*, explained that, because generic-drug manufacturers are "dependent on brand-names taking the lead" in communications to "consumers, doctors, or pharmacists," failure-to-communicate theories of liability against generic-drug manufacturers are "preempted by federal law." 719 F.3d at 1249 (citing *Morris v. PLIVA, Inc.* (5th Cir. 2013) 713 F.3d 774, 777).

Other federal courts have explained that the "failure to communicate" theory must be rejected because drug "labeling" is broadly construed under federal law. The Sixth Circuit, in *Strayhorn v. Wyeth Pharms., Inc.* (6th Cir. 2014) 737 F.3d 378, explained that under the FDCA, "labeling" includes not only the printed label that appears on a product or its container, but also "all labels and other written, printed, or graphic matter . . . accompanying such article." *Id.* at 394 (quoting 21 U.S.C. § 321(m)). And the United States Supreme Court has held that "[o]ne article or thing is accompanied by another when it supplements or explains it. . . . No physical attachment one to the other is necessary." *Id.* (quoting *Kordel v. United States* (1948) 335 U.S. 345, 349-50). Thus, because "advertising and promotional materials are considered labeling" under federal law, "and because labeling is limited by federal law to the information contained in the brand-name drug's labeling," the Sixth Circuit held that "all of the warranty claims against

the Generic Manufacturers based on these materials are preempted under *Mensing*." *Id.* Every other federal circuit court to consider the issue has similarly rejected "failure to communicate" claims as preempted under *Mensing*.[8]

5. The *Zantac MDL* recently applied these same precedents to find hundreds of state-law claims—including California common-law and statutory actions for not warning consumers about NDMA—preempted.

Both here and in the *Zantac MDL*, plaintiffs have claimed that generic ranitidine manufacturers failed to provide adequate warnings to consumers under state law. *See,* SAC ¶ 1 ("This Complaint seeks to remedy Defendants' continuing **failure to warn** individuals in California...") (emphasis added). As Judge Rosenberg has already held, "claims based on alleged product and labeling defects that Defendants could not independently change while remaining in compliance with federal law are dismissed with prejudice as pre-empted." *Zantac MDL*, 2020 WL 7864213, at *13. As the MDL court explained, the *Mensing* and *Bartlett* precedents preclude *all* failure-to-warn and design-defect claims against generic-drug manufacturers that require them to violate their federal duty of sameness. Regardless of how plaintiffs may style their claims, "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." *Id.* This leaves no room to find a non-preempted state-law duty to provide additional Proposition 65 warnings to consumers. *See id.*

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[8] *See also McDaniel v. Upsher-Smith Labs., Inc.* (6th Cir. 2018) 893 F.3d 941, 945-47; *Brinkley*, 772 F.3d at 1139; *In re Darvocet, Darvon, & Propoxyphene Prods. Liab. Litig.*, 756 F.3d at 932-33; *Johnson*, 758 F.3d at 612; *Lashley*, 750 F.3d at 475; *Schrock v. Wyeth, Inc.* (10th Cir. 2013) 727 F.3d 1273, 1286.

C. Generic Defendants are not asking the Court to find *express* preemption under 21 U.S.C. § 379r, and that section is irrelevant to and does not defeat *implied* preemption under *Mensing* and *Bartlett*.

1. Express and implied preemption are analytically distinct.

To be clear, this demurrer raises the issue of impossibility preemption—a form of *implied* preemption, which is analytically distinct from *express* preemption. Cases involving federal laws that expressly bar certain state-law claims, such as the Medical Device Amendments (MDA)[9] or Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)[10] would be more likely to confuse than clarify the relevant impossibility-preemption analysis here. Express preemption often implicates "parallel" state-law claims, which are not preempted if they impose state-law duties that do not conflict with "parallel federal requirements." *See, e.g., Medtronic*, 518 U.S. at 495. But implied impossibility preemption necessarily involves conflicting state and federal requirements. This demurrer raises impossibility preemption because enforcing Proposition 65 would change the generic labeling that federal law requires by adding a new warning.

Judge Rosenberg recognized that the ranitidine failure-to-warn claims, which plaintiffs tried to couch as parallel "misbranding" claims, did not escape implied preemption. *Zantac MDL*, 2020 WL 7864213, at * 10. Explaining that no "court has adopted Plaintiffs' theory that impossibility pre-emption can be avoided by showing that a drug is misbranded," the MDL court properly declined to conflate express- and implied-preemption principles to create a loophole that "would render the vast body of pre-emption caselaw in the drug context, including binding Supreme Court decisions, meaningless." *Id.* at * 13. The MDL court criticized plaintiffs' attempt to conflate disparate principles of express and implied preemption, noting plaintiffs' improper reliance upon Supreme Court decisions that "examined a statutory provision that expressly pre-empted state law" and "did not address impossibility pre-emption" *Id.* at *14.

[9] *See, e.g., Medtronic, Inc. v. Lohr* (1996) 518 U.S. 470, 481 (applying express-preemption provision of 21 U.S.C. § 360k(a)).
[10] *See, e.g., Bates v. Dow Agrosciences L.L.C.* (2005) 544 U.S. 431, 439 (applying express preemption provision of 7 U.S.C. § 136v).

Here, Generic Defendants raise this otherwise irrelevant point solely to clarify that they are **not** making an express-preemption argument in this demurrer. Thus, the Court should follow the MDL court's well-supported holding and reject any argument opposing Generic Defendants' demurrers that relies on inapt express-preemption case law.

2. California precedents show that Section 379r does not preclude implied preemption of state-law claims involving OTC products.

To promote uniform labeling of nonprescription drugs, Congress placed an express-preemption provision in Subsection (a)(2) of 21 U.S.C. § 379r, providing that "no State or political subdivision of a State may establish or continue 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)(2). But it also included a savings clause that this "section shall not apply to a State requirement adopted by a State public initiative or referendum enacted prior to September 1, 1997." *Id.* § 379r(d)(2). California's Proposition 65 meets the (d)(2) criteria, exempting it from Section 379r's restrictions. *See Dowhal v. SmithKline Beecham Consumer Healthcare* (2004) 32 Cal.4th 910, 919. A second savings clause, subsection (e), provides that nothing "in this section shall be construed to modify or otherwise affect any action or the liability of any person under the product liability law of any State." *Id.* § 379r(e). As previously noted, Generic Defendants are not basing their demurrers on section 379r or on any other express preemption.

In fact, years before the Supreme Court handed down *Mensing*, the California Supreme Court held that the "savings clause of 21 United States Code section 379r(d)(2), does not entirely exclude conflict preemption." *Dowhal* 32 Cal.4th at 926. The *Dowhal* plaintiffs, whose Proposition 65 claim involved point-of-sale warnings that they wanted for FDA-regulated OTC nicotine gum and patches, argued unsuccessfully that subsection (d)(2) shielded their Proposition 65 claim not only from express preemption under Section 379r(a) (which it did, *id.* at 919) but also implied preemption from any federal requirements outside Section 379r (which it did not). *Id.* at 924. The *Dowhal* court recognized a "general rule upholding conflict preemption even if the applicable federal law contains a savings clause" and emphasized that the "United States

Supreme Court has never interpreted a savings clause so broadly as to permit a state enactment to conflict with a federal regulation scheme." *Id.* at 926.

In *Dowhal*, the California Supreme Court applied *obstacle* preemption, a more complex, policy-based form of implied-conflict preemption, which sometimes preempts actions even when it is not impossible for the defendant to simultaneously satisfy state and federal law. *See id.* at 929. But *Mensing's* holding that *impossibility* preemption preempts failure-to-warn claims against generic-drug manufacturers for following their federal duty of sameness simplifies the relevant analysis immensely.

Post-*Mensing*, California appellate courts have held that the savings clauses in Section 379r do not extend beyond that section to preclude the federal implied-preemption principles in *Mensing* and *Bartlett*. In *Trejo v. Johnson & Johnson,* the Court of Appeal surveyed not only the few California decisions on the scope of Section 379r savings clauses but also cases nationally and agreed that California followed the majority view that Section 379r did not foreclose impossibility preemption for OTC products:

> Because the savings clause expressly refers to "this section"—that is, 21 United States Code section 379r(e)—. . . the savings clause does not foreclose the possibility that conflict preemption may arise from federal sources other than 21 United States Code section 379r. We therefore examine whether impossibility preemption applies. We conclude that it does under *Bartlett*.

13 Cal. App. 5th 110, 150-151. Courts in other jurisdictions agree that the "saving clause of § 379r(e) merely saves state-law product liability claims from the express preemption provision of § 379r(a), not from preemption generally." *Greager v. McNeil-PPC, Inc.* (N.D. Ill. 2019) 414 F. Supp. 3d 1137, 1141-1142; *see also Batoh v. McNeil-PPC, Inc.* (D. Conn. 2016) 167 F. Supp. 3d 296, 316-17 n.15, 321 n.19; *Reckis v. Johnson & Johnson* (Mass. 2015) 471 Mass. 272, 28 N.E.3d 445, 456. Those holdings are further bolstered by multiple decisions from the United States Supreme Court holding that savings clauses in express preemption statutes such as section 379r do not foreclose "the ordinary working of conflict pre-emption principles" and do not operate to save claims from implied/conflict preemption. *See Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 869-70 (2000) (express preemption clause and saving clause in the National

Traffic and Motor Vehicle Safety Act, "does not foreclose . . . any possibility of implied pre-emption," and "[n]othing in the language of the saving clause suggests an intent to save state-law tort actions that conflict with federal regulations."); *Williamson v. Mazda Motor of Am., Inc.* (2011) 562 U.S. 323, 329-30 (holding similarly); *Sprietsma v. Mercury Marine* (2002) 537 U.S. 51, 64-65 (holding that express preemption and saving clause in the Federal Boat Safety Act did not "bar the ordinary working of conflict pre-emption principles . . . that find implied pre-emption where it is impossible for a private party to comply with both state and federal requirements.").[11]

V. CONCLUSION

Because federal law preempts Plaintiff's claim, Generic Defendants respectfully request that their respective Demurrers to CEH's SAC be sustained, in their entirety, without leave to amend.

DATED: February 19, 2021

STEPTOE & JOHNSON LLP

By: _____
Dennis Raglin
Attorneys for Defendant
PERRIGO COMPANY

DATED: February 19, 2021

LEWIS BRISBOIS BISGAARD & SMITH LLP

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

[11] Federal Circuit Courts, including the Ninth Circuit Court of Appeals, have held similarly. *See National Fed. of the Blind v. United Airlines, Inc.* (9th Cir. 2016) 813 F. 3d 718, 731-32 (express preemption provisions of the Federal Aviation Act did not "foreclose the application of ordinarily implied preemption principles"); *Marentette v. Abbott Labs., Inc.* (2d Cir. 2018) 886 F.3d 112, 120 (express preemption provisions in the Organic Foods Production Act did not bar finding of conflict preemption).

DATED: February 19, 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

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 **February 19, 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.

☐ **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 **February 19, 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

Mark N. Todzo, Esq. mtodzo@lexlawgroup.com Joseph Mann, Esq. jmann@lexlawgroup.com **LEXINGTON LAW GROUP** 503 Divisadero Street San Francisco, CA 94117 Tel: 415.913.7800 Fax: 415.759.4112	Attorneys for Plaintiff CENTER FOR ENVIRONMENTAL HEALTH
Jeffrey Margulies, Esq. jeff.margulies@nortonrosefulbright.com Lauren Shoor, Esq. lauren.shoor@nortonrosefulbright.com Andrew Guo, Esq. andy.guo@nortonrosefulbright.com **NORTON ROSE FULBRIGHT US LLP** 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Tel: 213 892 9225 Fax: 213.892.9494	Attorneys for Defendant TARGET CORPORATION
Paul Desrochers, Esq. paul.desrochers@lewisbrisbois.com **LEWIS BRISBOIS BISGAARD & SMITH LLP** 333 Bush Street, Suite 100 San Francisco, CA 94104 Tel: 415.438.6615 Fax: 415.434.0882	Attorneys for Defendant GRANULES USA, INC.
Cheryl Chang, Esq. chang@blankrome.com Erika Schulz, Esq. eschulz@blankrome.com **BLANKROME LLP** 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Tel: 424.239.3400 Fax: 424.239.3434	Attorneys for Defendant APOTEX CORP.

Brian Ledger, Esq. bledger@gordonrees.com **GORDON REESE SCULLY MANSUKHANI LLP** 101 W. Broadway, Suite 1600 San Diego, CA 92102-8271 Tel: 619.696.6700 Fax: 619.696.7124	Attorneys for Defendants DR. REDDY'S LABORATORIES, INC. DR. REDDY'S LABORATORIES LOUISIANA, LLP
George Gigounas, Esq. george.gigounas@dlapiper.com Greg Sperla, Esq. greg.sperla@dlapiper.com **DLA PIPER** 400 Capitol Mall, Suite 2400 Sacramento, CA 95814-4428 Tel: 916.930.3200 Fax: 916.930.3201	Attorneys for Defendants SANOFI-AVENTIS U.S. LLC CHATTEM INC.
Will Wagner, Esq. wagnerw@gtlaw.com **GREENBERG TRAURIG, LLP** 1201 K Street, Suite 1100 Sacramento, CA 95814 Tel: 916.442.1111 Fax: 916.448.1709 Trenton H. Norris trent.norris@arnoldporter Vanessa C. Adriance vanessa.adriance@arnoldporter.com **ARNOLD & PORTER** Three Embarcadero Center, 10th Floor San Francisco, CA 94111-4075 Tel: (415) 471-3303 Fax: (415) 471-3400	Attorneys for Defendant 7-ELEVEN, INC.

Exhibit 27

Dennis Raglin (SBN 179261)
draglin@steptoe.com
Danielle Vallone (SBN 302497)
dvallone@steptoe.com
STEPTOE & JOHNSON LLP
633 West Fifth Street, Suite 1900
Los Angeles, California 90071
Telephone: 213 439 9400
Facsimile: 213 439 9599

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; and DOES 1 to 20, inclusive,

Defendants.

Case No. RG20054985

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

DECLARATION OF DENNIS E. RAGLIN IN SUPPORT OF GENERIC DEFENDANTS' JOINT REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF GENERIC DEFENDANTS' DEMURRERS TO PLAINTIFF'S SECOND AMENDED COMPLAINT

[*Filed concurrently with Notices of Demurrers and Demurrers, Joint Memorandum of Points and Authorities, Joint Request for Judicial Notice and [Proposed] Order*]

RESERVATION NO.: R-2242700

Hearing Date	**April 30, 2021**
Hearing Time	**10:00 a.m.**
Location	**Dept. 21**
Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

DECLARATION OF DENNIS E. RAGLIN

I, Dennis E. Raglin, declare:

1. I am a lawyer duly authorized to practice before the courts of California. I make this declaration in support of the Request for Judicial Notice brought by the Generic Defendants. I have personal knowledge of the facts contained herein and if called could testify truthfully to them

2. On February 16, 2021, I accessed from the FDA's website the document entitled, "Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations." The address of the webpage is https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm. I searched the term "ranitidine" from that page and was taken to a page listing various companies identified as applicants authorized to market ranitidine products, and which includes each of the moving Defendants. I printed out copies of both webpages. True and correct copies are attached as Exhibit D to the Request for Judicial Notice.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct. Executed this 19th day of February, 2021 at Los Angeles, California.

Dennis E. Raglin

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 **February 19, 2021,** I served the following listed document(s), by method indicated below, on the parties in this **action: DECLARATION OF DENNIS E. RAGLIN IN SUPPORT OF GENERIC DEFENDANTS' JOINT REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF GENERIC DEFENDANTS' DEMURRERS 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.

☐ **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 **February 19, 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

Mark N. Todzo, Esq. mtodzo@lexlawgroup.com Joseph Mann, Esq. jmann@lexlawgroup.com **LEXINGTON LAW GROUP** 503 Divisadero Street San Francisco, CA 94117 Tel: 415.913.7800 Fax: 415.759.4112	Attorneys for Plaintiff CENTER FOR ENVIRONMENTAL HEALTH
Jeffrey Margulies, Esq. Jeff.margulies@nortonrosefulbright.com Lauren Shoor, Esq. lauren.shoor@nortonrosefulbright.com Andrew Guo, Esq. andy.guo@nortonrosefulbright.com **NORTON ROSE FULBRIGHT US LLP** 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Tel: 213 892 9225 Fax: 213.892.9494	Attorneys for Defendant TARGET CORPORATION
Paul Desrochers, Esq. Paul.desrochers@lewisbrisbois.com **LEWIS BRISBOIS BISGAARD & SMITH LLP** 333 Bush Street, Suite 100 San Francisco, CA 94104 Tel: 415.438.6615 Fax: 415.434.0882	Attorneys for Defendant GRANULES USA, INC.
Cheryl Chang, Esq. chang@blankrome.com Erika Schulz, Esq. eschulz@blankrome.com **BLANKROME LLP** 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Tel: 424.239.3400 Fax: 424.239.3434	Attorneys for Defendant APOTEX CORP.

Brian Ledger, Esq. bledger@gordonrees.com **GORDON REESE SCULLY MANSUKHANI LLP** 101 W. Broadway, Suite 1600 San Diego, CA 92102-8271 Tel: 619.696.6700 Fax: 619.696.7124	Attorneys for Defendants DR. REDDY'S LABORATORIES, INC. DR. REDDY'S LABORATORIES LOUISIANA, LLP
George Gigounas, Esq. George.gigounas@dlapiper.com Greg Sperla, Esq. Greg.sperla@dlapiper.com **DLA PIPER** 400 Capitol Mall, Suite 2400 Sacramento, CA 95814-4428 Tel: 916.930.3200 Fax: 916.930.3201	Attorneys for Defendants SANOFI-AVENTIS U.S. LLC CHATTEM INC.
Will Wagner, Esq. wagnerw@gtlaw.com **GREENBERG TRAURIG, LLP** 1201 K Street, Suite 1100 Sacramento, CA 95814 Tel: 916.442.1111 Fax: 916.448.1709 Trenton H. Norris trent.norris@arnoldporter Vanessa C. Adriance vanessa.adriance@arnoldporter.com **ARNOLD & PORTER** Three Embarcadero Center, 10th Floor San Francisco, CA 94111-4075 Tel: (415) 471-3303 Fac: (415) 471-3400	Attorneys for Defendant 7-ELEVEN, INC.

Exhibit 28

Dennis Raglin (SBN 179261)
draglin@steptoe.com
Danielle Vallone (SBN 302497)
dvallone@steptoe.com
STEPTOE & JOHNSON LLP
633 West Fifth Street, Suite 1900
Los Angeles, California 90071
Telephone: 213 439 9400
Facsimile: 213 439 9599

Attorneys for Defendant
PERRIGO COMPANY

[ADDITIONAL MOVING COUNSEL LISTED ON FOLLOWING PAGE]

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; and DOES 1 to 20, inclusive,

Defendants.

Case No. RG 20054985

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

GENERIC DEFENDANTS' JOINT REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF DEMURRERS TO PLAINTIFF'S SECOND AMENDED COMPLAINT

[*Filed concurrently with Notices of Demurrers, Demurrers, Joint Memorandum of Points and Authorities, Declaration of Dennis Raglin and [Proposed] Order*]

RESERVATION NO.: R-2242700

Hearing Date	**April 30, 2021**
Hearing Time	**10:00 a.m.**
Location	**Dept. 21**
Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

Paul Desrochers, Esq.
paul.desrochers@lewisbrisbois.com
LEWIS BRISBOIS BISGAARD & SMITH LLP
333 Bush Street, Suite 100
San Francisco, CA 94104
Tel: 415.438.6615
Fax: 415.434.0882

Attorneys for Defendant
GRANULES USA, INC.

Brian Ledger, Esq.
bledger@gordonrees.com
GORDON REES SCULLY MANSUKHANI LLP
101 W. Broadway, Suite 1600
San Diego, CA 92102-8271
Tel: 619.696.6700
Fax: 619.696.7124

Attorneys for Defendants
DR. REDDY'S LABORATORIES, INC. and DR. REDDY'S LABORATORIES LOUISIANA, LLP

Pursuant to California Evidence Code §§ 452 and 453, and on such other grounds as the Court may consider, Defendants herein bring this joint Request for Judicial Notice and submit that the exhibits accompanying this Request support Defendants' respective demurrers to the Second Amended Complaint brought by Plaintiff Center for Environmental Health. The Defendants bringing this Request are Perrigo Company, Granules USA, Inc., Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories Louisiana, LLC.

The Defendants respectfully request the Court grant their request and take notice of the documents described below pursuant to Evid. Code § 452(c) and as set forth below for each exhibit submitted. Alternatively, Defendants make this Request pursuant to Evid. Code § 452(h) and/or § 453. The documents for which judicial notice is sought:

1. August 30, 2002 and February 5, 2016 letters from FDA to L. Perrigo Company approving, respectively, its 2002 Abbreviated New Drug Applications ("ANDA"), and its 2016 amendment for ANDA No. 76-195, and a May 11, 2011 letter from FDA to Perrigo Research & Development Company approving its ANDA No. 091429.[1] The FDA approval letters were made pursuant to 21 U.S.C. 355, permitting the Perrigo entities to sell its generic versions of the drug ranitidine after the FDA determined they were equivalent to Zantac, the brand-name product containing ranitidine. Pursuant to Evid. Code §452(c), the Court may take judicial notice of "[o]fficial acts of the legislative, executive, and judicial departments of the United States and of any state of the United States." These letters are a formal FDA decision and therefore an act of a department of the executive branch. Courts may take judicial notice of matters of public record outside the pleadings whose accuracy cannot reasonably be questioned. *See MGIC Indemn. Corp. v. Weisman* (9th Cir. 1986) 803 F.2d 500, 504; *Seely v. Cumberland Packing Corp.* (2010) No. 10–CV–02019–LHK; 2010 WL 5300923, at *7 n.5. A true and correct copy of the letters are attached hereto as **Exhibit A.**

2. An August 20, 2018 letter from FDA approving Granules India Ltd.'s[2] ANDA 210243 pursuant to 21 U.S.C. 355, permitting it to sell its generic versions of the drug ranitidine

[1] Perrigo Company is a corporate parent of Perrigo Research & Development Company and L. Perrigo Company.
[2] Granules India, Ltd. sold ranitidine in the United States through Defendant Granules USA, Inc.

after the FDA determined they were equivalent to Zantac, the brand-name product containing ranitidine. Pursuant to Evid. Code §452(c), the Court may take judicial notice of "[o]fficial acts of the legislative, executive, and judicial departments of the United States and of any state of the United States." The letter is a formal FDA decision and therefore an act of a department of the executive branch. Courts may take judicial notice of matters of public record outside the pleadings whose accuracy cannot reasonably be questioned. *See MGIC Indemn. Corp. v. Weisman* (9th Cir. 1986) 803 F.2d 500, 504; *Seely v. Cumberland Packing Corp.* (2010) No. 10–CV–02019–LHK; 2010 WL 5300923, at *7 n.5. A true and correct copy of the letter is attached hereto as **Exhibit B.**

3. March 28, 2000 and August 31, 2007 letters from FDA approving Defendant Dr. Reddy's Laboratories, Inc.'s ANDAs 075294 and 078192 pursuant to 21 U.S.C. 355, permitting it to sell its generic versions of the drug ranitidine after the FDA determined they were equivalent to Zantac, the brand-name product containing ranitidine. Pursuant to Evid. Code §452(c), the Court may take judicial notice of "[o]fficial acts of the legislative, executive, and judicial departments of the United States and of any state of the United States." The letters are formal FDA decisions and therefore acts of a department of the executive branch. Courts may take judicial notice of matters of public record outside the pleadings whose accuracy cannot reasonably be questioned. *See MGIC Indemn. Corp. v. Weisman* (9th Cir. 1986) 803 F.2d 500, 504; *Seely v. Cumberland Packing Corp.* (2010) No. 10–CV–02019–LHK; 2010 WL 5300923, at *7 n.5. A true and correct copy of the letters are attached hereto as **Exhibit C.**

4. A copy of a document available on FDA's website titled "Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations" (hereinafter "Orange Book") listing both all drugs approved by the FDA and the companies, including the moving Defendants, authorized to manufacture and sell each listed drug by way of an approved New Drug, or Abbreviated New Drug, Application. Pursuant to Evid. Code §452 (c), the Court may take judicial notice of "[o]fficial acts of the legislative, executive, and judicial departments of the United States and of any state of the United States." An authorization by FDA is a formal act by a department of the executive branch. Courts may take judicial notice of matters of public records

outside the pleadings whose accuracy cannot reasonably be questioned. *See MGIC Indemn. Corp. v. Weisman* (9th Cir. 1986) 803 F.2d 500, 504; *Seely v. Cumberland Packing Corp.* No. 10–CV–02019–LHK; 2010 WL 5300923, at *7 n.5. A true and correct copy of the downloaded document is attached as **Exhibit D.**

5. Should notice be denied under Evid. Code § 452(c), Defendants alternatively request notice be granted pursuant to either Evid. Code § 452(h) or § 453. First, Evid. Code § 452(h) provides that the Court may take judicial notice of "[f]acts and propositions that are not reasonably subject to dispute and are capable of immediate and accurate determination by resort to courses of reasonable accuracy." Defendants ANDAs confirm their status as generic drug manufacturers. Plaintiff's lawyer does not dispute this fact, and confirms Plaintiff will not oppose the Court granting the Request and accepting the attached exhibits. Defendants' status as generic manufacturers can be promptly verified through the FDA Orange Book or by contacting the FDA's Office of Generic Drugs. Second, Evid. Code §453 provides that a request for judicial notice shall be granted if the requesting party "[g]ives each adverse party sufficient notice of the request..." and "Furnishes the Court with sufficient information to enable it to take judicial notice of the matter." Defendants have submitted evidence to the Court confirming their generic status and Plaintiff's lawyer has previously reviewed the FDA letters attached as exhibits and confirms Plaintiff will not oppose the Court taking judicial notice and as set forth in the exhibits.

DATED: February 19, 2021

STEPTOE & JOHNSON LLP

By: _____
Dennis Raglin
Attorneys for Defendant,
PERRIGO COMPANY

DATED: February 19, 2021

LEWIS BRISBOIS BISGAARD & SMITH LLP

By: _____

Paul Desrochers
Attorneys for Defendant
GRANULES USA, INC.

DATED: February 19, 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

EXHIBIT A

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 076195/S-023

PRIOR APPROVAL SUPPLEMENT
APPROVAL

RECEIVED
FEB 16 2016
By

Perrigo Company
515 Eastern Avenue
Allegan, MI 49010
Attention: Mary Short
Senior Manager, Global Regulatory Affairs

Dear Madam:

Please refer to your supplemental Abbreviated New Drug Application (sANDA) dated April 30, 2015, received April 30, 2015, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding your Abbreviated New Drug Application (ANDA) for Ranitidine Tablets USP, 75 mg.

We acknowledge receipt of your amendments dated May 26, and December 23, 2015.

The supplemental ANDA, submitted as "Prior Approval Supplement," provides for:

- Replacement formulation of Ranitidine Tablets USP, 75 mg that is dose proportionally similar to the formula currently marketed for Ranitidine Tablets USP, 150 mg.
- Updated labeling and biowaver request.
- Notification of inspection requirement for a new foreign testing site, Perrigo Laboratories India Private Limited, located in Maharashtra, India.

We have completed our review of this sANDA, as amended, and it is approved.

We remind you that you must comply with the requirements for the approved ANDA described in 21 CFR 314.80-81.

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your sANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage

forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

The material submitted is being retained in our files.

Sincerely yours,

William P. Rickman -S

Digitally signed by William P. Rickman -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300043242, cn=William P. Rickman -S
Date: 2016.02.05 10:55:19 -05'00'

For Carol A. Holquist, RPh
Acting Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

ANDA 76-195

AUG 30 2002

L. Perrigo Company
Attention: Brian R. Schuster
515 Eastern Avenue
Allegan, MI 49010

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated June 21, 2001, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Ranitidine Tablets USP, 75 mg (base).

Reference is also made to your amendments dated July 31, and August 30, 2002 and to your correspondence dated September 19, and October 29, 2001, addressing patent issues associated with this drug product.

The listed drug product (RLD) referenced in your application, Zantac-75 Tablets of Warner Lambert Consumer Healthcare, is subject to periods of patent protection which expire on December 4, 2002, (U.S. Patent No. 4,521,431 [the '431 patent]) and November 13, 2008 (U.S. Patent No. 4,880,636 [the '636 patent]), respectively. Your application contains patent certifications to each patent under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, or sale of this drug product will not infringe on either patent. Section 505(j)(4)(B)(iii) of the Act provides that approval of an ANDA shall be made effective immediately, unless an action is brought against L. Perrigo and Company (Perrigo) for infringement of one or more of the patents that are the subject of the certifications. This action must be brought against Perrigo prior to the expiration of forty-five days from the dates the notices you provided to the NDA/patent holders under paragraph (2)(B)(i) were received. You have notified the agency that Perrigo has complied with the requirements of Section 505(j)(2)(B) of the Act and that no action for patent infringement was brought against Perrigo within the statutory forty-five day period.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted Over-The-Counter (OTC) labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Ranitidine Tablets USP, 75 mg (base), to be bioequivalent to the listed drug (Zantac-75 Tablets of Warner Lambert Consumer Healthcare). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

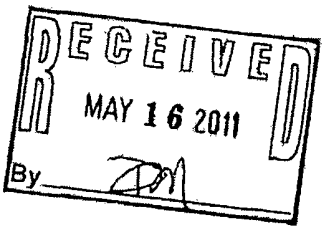
Sincerely yours,

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 091429



Perrigo R&D Company
Attention: Virginia G. Lutke
Manager, Regulatory Affairs - ANDA
515 Eastern Avenue
Allegan, MI 49010

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated April 9, 2009, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Ranitidine Tablets USP, 150 mg (OTC) (Regular and Cool Mint).

Reference is also made to your amendments dated March 25, 2010; and April 11, 2011.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for over-the-counter (OTC) use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Ranitidine Tablets USP, 150 mg (OTC) (Regular and Cool Mint) to be bioequivalent to the reference listed drug, Zantac-150 Tablets, of Boehringer Ingelheim. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Reference ID: 2945065

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at: http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/U CM072392.pdf

The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

(See appended electronic signature page)

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

Reference ID: 2945065

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBERT L WEST
05/11/2011
Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.

Reference ID: 2945065

ANDA 091429

OFFICE OF GENERIC DRUGS

Office of Generic Drugs (HFD–600)
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North VII
7620 Standish Place
Rockville,MD 20855
Fax: 240-276-9327

FAX TRANSMISSION COVER SHEET

APPLICANT: Perrigo R&D Company TEL: (269) 673-8451

ATTN: Virginia G. Lutke FAX: (269) 673-7655

FROM: Frank J. Nice FDA CONTACT PHONE: (240) 276-8555

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated March 9, 2009, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ranitidine Tablets USP , 150 mg (OTC).

We are pleased to inform you that this application is APPROVED!

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 091429

Perrigo R&D Company
Attention: Virginia G. Lutke
Manager, Regulatory Affairs - ANDA
515 Eastern Avenue
Allegan, MI 49010

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated April 9, 2009, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Ranitidine Tablets USP, 150 mg (OTC) (Regular and Cool Mint).

Reference is also made to your amendments dated March 25, 2010; and April 11, 2011.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for over-the-counter (OTC) use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Ranitidine Tablets USP, 150 mg (OTC) (Regular and Cool Mint) to be bioequivalent to the reference listed drug, Zantac-150 Tablets, of Boehringer Ingelheim. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at: http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/U_CM072392.pdf

The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

(See appended electronic signature page)

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBERT L WEST
05/11/2011
Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.

Reference ID: 2945065

EXHIBIT B

U.S. FOOD & DRUG ADMINISTRATION

ANDA 210243

ANDA APPROVAL

Granules Pharmaceuticals Inc.
U.S. Agent for Granules India Limited
3701 Concorde Parkway
Chantilly, VA 20151
Attention: Vamsi Nama

Dear Sir or Madam:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on June 1, 2017, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Ranitidine Tablets USP, 150 mg and 150 mg Cool Mint (OTC).

Reference is also made to the complete response letter issued by this office on March 21, 2018, and to any amendments thereafter.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for over-the-counter (OTC) use as recommended in the submitted labeling. Accordingly the ANDA is **approved**, effective on the date of this letter. The Office of Bioequivalence has determined your Ranitidine Tablets USP, 150 mg and 150 mg Cool Mint (OTC), to be bioequivalent to the reference listed drug (RLD), Maximum Strength Zantac Tablets, 150 mg, of Sanofi-aventis U.S. LLC.

Under section 506A of the FD&C Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Agency should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Agency in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[1] with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the

date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf. The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

{See appended electronic signature page}

For Vincent Sansone, PharmD
Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

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[1] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

Priya Shah

Digitally signed by Priya Shah
Date: 8/20/2018 08:20:08PM
GUID: 5256c7080002b0e78814870319c70608

EXHIBIT C

ANDA 78-192

OFFICE OF GENERIC DRUGS

Food and Drug Administration
HFD-600, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Fax: 301-594-0180

FAX TRANSMISSION COVER SHEET

APPLICANT: Dr. Reddy's Laboratories, Inc. TEL: 908-203-4937

ATTN: Kumara Sekar, Ph.D. FAX: 908-203-4980

FROM: Thomas Hinchliffe for Theresa Liu PROJECT MANAGER: (301) 827-5791

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated March 2, 2006, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ranitidine Hydrochloride Tablets USP, 150 mg (OTC).

We are pleased to inform you that this application is APPROVED!

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 78-192

Dr. Reddy's Laboratories, Inc.
U.S. Agent for: Dr. Reddy's Laboratories Limited
Attention: Kumara Sekar, Ph.D.
Director, Global Regulatory Affairs and Compliance
200 Somerset Corporate Blvd., 7th Floor
Bridgewater, NJ 08807

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated March 2, 2006, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Ranitidine Tablets USP, 150 mg (OTC).

Reference is also made to your amendments dated November 27, 2006; January 2, January 31, February 1, February 19, April 2, May 7, May 30, July 16, July 17, July 30, and August 17, 2007.

We have completed the review of this ANDA and have concluded that adequate information has been provided to demonstrate that the drug is safe and effective for use as recommended in the over-the-counter (OTC) labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Ranitidine Tablets USP, 150 mg (OTC) to be bioequivalent to the reference listed drug, Zantac-150 Tablets, (OTC), of Boehringer Ingelheim Pharmaceuticals, Inc. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Sincerely yours,

(See appended electronic signature page)

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Gary Buehler
8/31/2007 05:35:33 AM

ANDA 75-294

OFFICE OF GENERIC DRUGS

Food and Drug Administration
HFD-600, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Fax: (301-594-0180)

FAX TRANSMISSION COVER SHEET

TO: APPLICANT: Reddy-Cheminor Inc. PHONE: 410-309-3145

ATTN: Jeanne Taborsky FAX: 410-309-3145

FROM: Kassandra Sherrod PROJECT MANAGER (301) 827-5849

Dear Madam:

This facsimile is in reference to your abbreviated new drug application for Ranitidine Tablets USP, 75 mg.

We are pleased to inform you that this application is APPROVED!

X:\new\cgdadmin\macros\faxapp.frm

DEPARTMENT OF HEALTH & HUMAN SERVICES

ANDA 75-294

Food and Drug Administration
Rockville MD 20857

MAR 28 2000

Reddy-Cheminor, Inc.
Attention: Paul V. Campanelli
U.S. Agent for: Cheminor Drugs, Ltd.
66 South Maple Avenue
Ridgewood, NJ 07450

Dear Sir:

This is in reference to your abbreviated new drug application dated December 29, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Ranitidine Tablets USP, 75 mg (OTC).

Reference is also made to your amendments dated April 9, 1998; and January 14, and February 16, 2000.

The listed drug product (RLD) referenced in your application, Zantac-75 Tablets of Glaxo Wellcome Inc., is subject to periods of patent protection which expire on December 4, 2002 (U.S. patent 4,521,431 [the '431 patent] and November 13, 2008 (U.S. patent 4,880,636 [the '636 patent]), respectively. Your application contains patent certifications to each patent under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, or sale of this drug product will not infringe on either patent. Section 505(j)(5)(B)(iii) of the Act provides that approval shall be made effective immediately unless an action is brought for infringement of the patents which are the subject of the certifications before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. You have notified the Agency that Cheminor Drugs Ltd. (Cheminor) has complied with the requirements of Section 505(j)(2)(B) of the Act and that no action for patent infringement was brought against Cheminor within the statutory forty-five day period. It should be noted that the RLD upon which you based your application was also subject to a period of market exclusivity granted under Section 111 of Title I of the Food and Drug Modernization Act of 1997 (FDAMA) that expired on June 19, 1999. In addition, Novopharm Ltd. was granted 180 days of generic drug exclusivity under Section 505(j)(5)(B)(iv) for this drug product which expired on January 14, 2000.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted Over-The-Counter (OTC) labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Ranitidine Tablets, 75 mg to be bioequivalent to the listed drug (Zantac-75 Tablets of Warner Lambert Company). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Sincerely yours,

Gary Buehler
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research

EXHIBIT D

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

On March 23, 2020, FDA removed from the Orange Book the listings for "biological products" that have been approved in applications under section 505 of the FD&C Act because these products are no longer "listed drugs" (see section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009).

Additional information and resources for the Orange Book (https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm)

We've updated our mobile app!
Download Orange Book Express 2.0

Download on the App Store (https://itunes.apple.com/us/app/ob-express-2-0/id1229831803?ls=1&mt=8)

ANDROID APP ON Google play (https://play.google.com/store/apps/details?id=gov.fda.obook)

Find Approved Drugs

Search by Proprietary Name, Active Ingredient or Application Number

Enter at least 3 characters | Search

Search by Applicant (Company)

Search by Dosage Form (for example: *TABLET*)

Search by Route of Administration (for example: *ORAL*)

Find Patent Information

Search by Patent Number

View Newly Added Patents or Delisted Patents

Contact Us

The Orange Book downloadable data files are updated monthly. We make every effort to prevent errors and discrepancies in the Approved Drug Products data files. *If you wish to report an error or discrepancy in drug data*, please send a brief description of the problem to: **orangebook@fda.hhs.gov (mailto:orangebook@fda.hhs.gov)**.

Please send *general questions related to the drug data in these files* to the Center for Drug Evaluation and Research, Division of Drug Information: **druginfo@fda.hhs.gov (mailto:druginfo@fda.hhs.gov)**.

Current through February 2021.
For more information on the Orange Book update frequency, see the **Orange Book FAQs (https://www.fda.gov/Drugs/InformationOnDrugs/ucm114166.htm#updateschedule)**.

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Mkt.Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A211058	CAPSULE	ORAL	EQ 150MG BASE	AB			AUROBINDO PHARMA LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075742	CAPSULE	ORAL	EQ 150MG BASE	AB			DR REDDYS LABORATORIES LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074655	CAPSULE	ORAL	EQ 150MG BASE	AB			SANDOZ INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A211058	CAPSULE	ORAL	EQ 300MG BASE	AB			AUROBINDO PHARMA LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075742	CAPSULE	ORAL	EQ 300MG BASE	AB			DR REDDYS LABORATORIES LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074655	CAPSULE	ORAL	EQ 300MG BASE	AB		RS	SANDOZ INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A079076	INJECTABLE	INJECTION	EQ 25MG BASE/ML	AP			MYLAN LABORATORIES LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074777	INJECTABLE	INJECTION	EQ 25MG BASE/ML	AP			WEST-WARD PHARMACEUTICALS INTERNATIONAL LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077458	INJECTABLE	INJECTION	EQ 25MG BASE/ML	AP			WEST-WARD PHARMACEUTICALS INTERNATIONAL LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A091534	INJECTABLE	INJECTION	EQ 25MG BASE/ML	AP			ZYDUS PHARMACEUTICALS USA INC
RX	RANITIDINE HYDROCHLORIDE	ZANTAC	N019090	INJECTABLE	INJECTION	EQ 25MG BASE/ML	AP	RLD	RS	TELIGENT OU
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A090623	SYRUP	ORAL	EQ 15MG BASE/ML	AA			AUROBINDO PHARMA LTD
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078890	SYRUP	ORAL	EQ 15MG BASE/ML	AA			LANNETT CO INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A091288	SYRUP	ORAL	EQ 15MG BASE/ML	AA			LANNETT CO INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077405	SYRUP	ORAL	EQ 15MG BASE/ML	AA		RS	PHARMACEUTICAL ASSOCIATES INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074680	TABLET	ORAL	EQ 150MG BASE	AB			APOTEX INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A076705	TABLET	ORAL	EQ 150MG BASE	AB			DR REDDYS LABORATORIES INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078542	TABLET	ORAL	EQ 150MG BASE	AB			GLENMARK PHARMACEUTICALS INC USA
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075180	TABLET	ORAL	EQ 150MG BASE	AB			PAR PHARMACEUTICAL INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074467	TABLET	ORAL	EQ 150MG BASE	AB			SANDOZ INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A211289	TABLET	ORAL	EQ 150MG BASE	AB			VKT PHARMA PRIVATE LTD

Mkt.Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074680	TABLET	ORAL	EQ 300MG BASE	AB			APOTEX INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A076705	TABLET	ORAL	EQ 300MG BASE	AB			DR REDDYS LABORATORIES INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078542	TABLET	ORAL	EQ 300MG BASE	AB			GLENMARK PHARMACEUTICALS INC USA
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075180	TABLET	ORAL	EQ 300MG BASE	AB			PAR PHARMACEUTICAL INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074467	TABLET	ORAL	EQ 300MG BASE	AB			SANDOZ INC
RX	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A211289	TABLET	ORAL	EQ 300MG BASE	AB			VKT PHARMA PRIVATE LTD
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A207579	TABLET	ORAL	EQ 75MG BASE				AUROBINDO PHARMA LTD
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075294	TABLET	ORAL	EQ 75MG BASE				DR REDDYS LABORATORIES LTD
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A076195	TABLET	ORAL	EQ 75MG BASE				L PERRIGO CO
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210250	TABLET	ORAL	EQ 75MG BASE				UNIQUE PHARMACEUTICAL LABORATORIES A DIVISION OF J.B. CHEMICALS AND PHARMACEUTICALS LTD
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A207578	TABLET	ORAL	EQ 150MG BASE				AUROBINDO PHARMA LTD
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078192	TABLET	ORAL	EQ 150MG BASE				DR REDDYS LABORATORIES LTD
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A091429	TABLET	ORAL	EQ 150MG BASE				PERRIGO R AND D CO
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A091429	TABLET	ORAL	EQ 150MG BASE				PERRIGO R AND D CO
OTC	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210228	TABLET	ORAL	EQ 150MG BASE				UNIQUE PHARMACEUTICAL LABORATORIES A DIVISION OF J.B. CHEMICALS AND PHARMACEUTICALS LTD
OTC	RANITIDINE HYDROCHLORIDE	ZANTAC 150	N021698	TABLET	ORAL	EQ 150MG BASE		RLD	RS	SANOFI US
OTC	RANITIDINE HYDROCHLORIDE	ZANTAC 150	N021698	TABLET	ORAL	EQ 150MG BASE		RLD		SANOFI US
OTC	RANITIDINE HYDROCHLORIDE	ZANTAC 75	N020520	TABLET	ORAL	EQ 75MG BASE		RLD		SANOFI US
DISCN	RANITIDINE BISMUTH CITRATE	TRITEC	N020559	TABLET	ORAL	400MG				GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A209859	CAPSULE	ORAL	EQ 150MG BASE				AJANTA PHARMA LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A211893	CAPSULE	ORAL	EQ 150MG BASE				APPCO PHARMA LLC

Mkt.Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075564	CAPSULE	ORAL	EQ 150MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210681	CAPSULE	ORAL	EQ 150MG BASE				NOVITIUM PHARMA LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075557	CAPSULE	ORAL	EQ 150MG BASE				TEVA PHARMACEUTICALS USA INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A209859	CAPSULE	ORAL	EQ 300MG BASE				AJANTA PHARMA LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A211893	CAPSULE	ORAL	EQ 300MG BASE				APPCO PHARMA LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075564	CAPSULE	ORAL	EQ 300MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210681	CAPSULE	ORAL	EQ 300MG BASE				NOVITIUM PHARMA LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075557	CAPSULE	ORAL	EQ 300MG BASE				TEVA PHARMACEUTICALS USA INC
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 150	N020095	CAPSULE	ORAL	EQ 150MG BASE **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**		RLD		GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 300	N020095	CAPSULE	ORAL	EQ 300MG BASE **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**		RLD		GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 150	N020251	GRANULE, EFFERVESCENT	ORAL	EQ 150MG BASE/PACKET				GLAXO GROUP LTD ENGLAND DBA GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074764	INJECTABLE	INJECTION	EQ 25MG BASE/ML				BEDFORD LABORATORIES DIV BEN VENUE LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC IN PLASTIC CONTAINER	N019593	INJECTABLE	INJECTION	EQ 1MG BASE/ML				TELIGENT OU
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC IN PLASTIC CONTAINER	N019593	INJECTABLE	INJECTION	EQ 50MG BASE/100ML				TELIGENT OU
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A076124	SYRUP	ORAL	EQ 15MG BASE/ML				ACTAVIS MID ATLANTIC LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A091078	SYRUP	ORAL	EQ 15MG BASE/ML				AKORN OPERATING CO LLC

Mkt.Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078312	SYRUP	ORAL	EQ 15MG BASE/ML				AMNEAL PHARMACEUTICALS
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A090054	SYRUP	ORAL	EQ 15MG BASE/ML				ANDA REPOSITORY LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077602	SYRUP	ORAL	EQ 15MG BASE/ML				APOTEX INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078684	SYRUP	ORAL	EQ 15MG BASE/ML				NOSTRUM LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A091091	SYRUP	ORAL	EQ 15MG BASE/ML				NOSTRUM LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078448	SYRUP	ORAL	EQ 15MG BASE/ML				RANBAXY INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077476	SYRUP	ORAL	EQ 15MG BASE/ML				TARO PHARMACEUTICALS USA INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A090102	SYRUP	ORAL	EQ 15MG BASE/ML				TORRENT PHARMA INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A079211	SYRUP	ORAL	EQ 15MG BASE/ML				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A079212	SYRUP	ORAL	EQ 15MG BASE/ML				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC	N019675	SYRUP	ORAL	EQ 15MG BASE/ML		RLD		GLAXO GROUP LTD ENGLAND DBA GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075212	TABLET	ORAL	EQ 75MG BASE				ANI PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075296	TABLET	ORAL	EQ 75MG BASE				ANI PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075167	TABLET	ORAL	EQ 75MG BASE				APOTEX INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075094	TABLET	ORAL	EQ 75MG BASE				CONTRACT PHARMACAL CORP
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075497	TABLET	ORAL	EQ 75MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075254	TABLET	ORAL	EQ 75MG BASE				RANBAXY PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075519	TABLET	ORAL	EQ 75MG BASE				SANDOZ INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A201745	TABLET	ORAL	EQ 75MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A209160	TABLET	ORAL	EQ 75MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075132	TABLET	ORAL	EQ 75MG BASE				SUN PHARMACEUTICAL INDUSTRIES LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A076760	TABLET	ORAL	EQ 75MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078884	TABLET	ORAL	EQ 75MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077824	TABLET	ORAL	EQ 150MG BASE				AMNEAL PHARMACEUTICALS NY LLC

Mkt.Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074488	TABLET	ORAL	EQ 150MG BASE				ANI PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077426	TABLET	ORAL	EQ 150MG BASE				ANI PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A200172	TABLET	ORAL	EQ 150MG BASE				APOTEX INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074662	TABLET	ORAL	EQ 150MG BASE				BOEHRINGER INGELHEIM CORP
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210243	TABLET	ORAL	EQ 150MG BASE				GRANULES INDIA LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210243	TABLET	ORAL	EQ 150MG BASE				GRANULES INDIA LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075165	TABLET	ORAL	EQ 150MG BASE				HERITAGE PHARMA LABS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074023	TABLET	ORAL	EQ 150MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074552	TABLET	ORAL	EQ 150MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A203694	TABLET	ORAL	EQ 150MG BASE				NOSTRUM LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075000	TABLET	ORAL	EQ 150MG BASE				RANBAXY PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A200536	TABLET	ORAL	EQ 150MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A205512	TABLET	ORAL	EQ 150MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A209161	TABLET	ORAL	EQ 150MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210010	TABLET	ORAL	EQ 150MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075439	TABLET	ORAL	EQ 150MG BASE				SUN PHARMACEUTICAL INDUSTRIES LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074864	TABLET	ORAL	EQ 150MG BASE				WATSON LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075208	TABLET	ORAL	EQ 150MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078653	TABLET	ORAL	EQ 150MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078701	TABLET	ORAL	EQ 150MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077824	TABLET	ORAL	EQ 300MG BASE				AMNEAL PHARMACEUTICALS NY LLC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074488	TABLET	ORAL	EQ 300MG BASE				ANI PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A077426	TABLET	ORAL	EQ 300MG BASE				ANI PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074662	TABLET	ORAL	EQ 300MG BASE				BOEHRINGER INGELHEIM CORP

Mkt.Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075165	TABLET	ORAL	EQ 300MG BASE				HERITAGE PHARMA LABS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074023	TABLET	ORAL	EQ 300MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074552	TABLET	ORAL	EQ 300MG BASE				MYLAN PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A203694	TABLET	ORAL	EQ 300MG BASE				NOSTRUM LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075000	TABLET	ORAL	EQ 300MG BASE				RANBAXY PHARMACEUTICALS INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A205512	TABLET	ORAL	EQ 300MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A210010	TABLET	ORAL	EQ 300MG BASE				STRIDES PHARMA GLOBAL PTE LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075439	TABLET	ORAL	EQ 300MG BASE				SUN PHARMACEUTICAL INDUSTRIES LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A074864	TABLET	ORAL	EQ 300MG BASE				WATSON LABORATORIES INC
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A075208	TABLET	ORAL	EQ 300MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	RANITIDINE HYDROCHLORIDE	A078701	TABLET	ORAL	EQ 300MG BASE				WOCKHARDT LTD
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 150	N018703	TABLET	ORAL	EQ 150MG BASE **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**		RLD		GLAXO GROUP LTD ENGLAND DBA GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 300	N018703	TABLET	ORAL	EQ 300MG BASE **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**		RLD		GLAXO GROUP LTD ENGLAND DBA GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 150	N020251	TABLET, EFFERVESCENT	ORAL	EQ 150MG BASE				GLAXO GROUP LTD ENGLAND DBA GLAXOSMITHKLINE
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 25	N020251	TABLET, EFFERVESCENT	ORAL	EQ 25MG BASE				GLAXO GROUP LTD ENGLAND DBA GLAXOSMITHKLINE

Mkt Status	Active Ingredient	Proprietary Name	Appl. No.	Dosage Form	Route	Strength	TE Code	RLD	RS	Applicant Holder
DISCN	RANITIDINE HYDROCHLORIDE	ZANTAC 75	N020745	TABLET, EFFERVESCENT	ORAL	EQ 75MG BASE; *Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons*		RLD		SANOFI US

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 **February 19, 2021**, I served the following listed document(s), by method indicated below, on the parties in this action: **GENERIC DEFENDANTS' JOINT REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF DEMURRERS 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.

☐ **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 **February 19, 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

Mark N. Todzo, Esq. mtodzo@lexlawgroup.com Joseph Mann, Esq. jmann@lexlawgroup.com **LEXINGTON LAW GROUP** 503 Divisadero Street San Francisco, CA 94117 Tel: 415.913.7800 Fax: 415.759.4112	Attorneys for Plaintiff CENTER FOR ENVIRONMENTAL HEALTH
Jeffrey Margulies, Esq. Jeff.margulies@nortonrosefulbright.com Lauren Shoor, Esq. lauren.shoor@nortonrosefulbright.com Andrew Guo, Esq. andy.guo@nortonrosefulbright.com **NORTON ROSE FULBRIGHT US LLP** 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Tel: 213 892 9225 Fax: 213.892.9494	Attorneys for Defendant TARGET CORPORATION
Paul Desrochers, Esq. paul.desrochers@lewisbrisbois.com **LEWIS BRISBOIS BISGAARD & SMITH LLP** 333 Bush Street, Suite 100 San Francisco, CA 94104 Tel: 415.438.6615 Fax: 415.434.0882	Attorneys for Defendant GRANULES USA, INC.
Cheryl Chang, Esq. chang@blankrome.com Erika Schulz, Esq. eschulz@blankrome.com **BLANKROME LLP** 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Tel: 424.239.3400 Fax: 424.239.3434	Attorneys for Defendant APOTEX CORP.

Brian Ledger, Esq. bledger@gordonrees.com **GORDON REESE SCULLY MANSUKHANI LLP** 101 W. Broadway, Suite 1600 San Diego, CA 92102-8271 Tel: 619.696.6700 Fax: 619.696.7124	Attorneys for Defendants DR. REDDY'S LABORATORIES, INC. DR. REDDY'S LABORATORIES LOUISIANA, LLP
George Gigounas, Esq. george.gigounas@dlapiper.com Greg Sperla, Esq. greg.sperla@dlapiper.com **DLA PIPER** 400 Capitol Mall, Suite 2400 Sacramento, CA 95814-4428 Tel: 916.930.3200 Fax: 916.930.3201	Attorneys for Defendants SANOFI-AVENTIS U.S. LLC CHATTEM INC.
Will Wagner, Esq. wagnerw@gtlaw.com **GREENBERG TRAURIG, LLP** 1201 K Street, Suite 1100 Sacramento, CA 95814 Tel: 916.442.1111 Fax: 916.448.1709 Trenton H. Norris trent.norris@arnoldporter Vanessa C. Adriance vanessa.adriance@arnoldporter.com **ARNOLD & PORTER** Three Embarcadero Center, 10th Floor San Francisco, CA 94111-4075 Tel: (415) 471-3303 Fax: (415) 471-3400	Attorneys for Defendant 7-ELEVEN, INC.

Exhibit 29

Paul A. Desrochers (SBN 214855)
paul.desrochers@lewisbrisbois.com
LEWIS BRISBOIS BISGAARD & SMITH LLP
333 Bush Street, Suite 1100
San Francisco, California 94104-2872
Telephone: 415.362.2580
Facsimile: 415.434.0882

Attorneys for Defendant
GRANULES USA, INC.

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, et. al.,

Defendants.

Case No. RG20054985

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

DEFENDANT GRANULES USA, INC.'S NOTICE OF DEMURRER AND DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT

[*Filed concurrently with Joint Memorandum of Points and Authorities; Joint Request for Judicial Notice; Declaration of Counsel; and Proposed Order*]

RESERVATION NO.:R-2242703

Hearing Date	**April 30, 2021**
Hearing Time	**10:00 a.m.**
Location	**Dept. 21**
Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

NOTICE OF DEMURRER

TO THE COURT, ALL PARTIES AND THEIR ATTORNEY(S) OF RECORD:

PLEASE TAKE NOTICE that on **April 30, 2021**, at 10:00 a.m., or as soon thereafter as counsel may be heard in Department 21 of the above-entitled Court located at 1221 Oak Street, Oakland, CA 94612, defendant Granules USA, Inc. ("GUSA") will and hereby does demur ("Demurrer") generally and specially to plaintiff Center for Environmental Health's ("CEH") second amended complaint ("SAC"). GUSA demurs under California Code of Civil Procedure Sections 430.10(e) and 430.30, on the grounds that the SAC fails to allege sufficient facts to constitute any cause of action against it.

Under California Code of Civil Procedure Section 430.41, counsel for GUSA met and conferred with counsel for CEH via telephone on January 28, 2021, before filing this Demurrer. The parties were not able to resolve the objections that GUSA raises in this Demurrer. *See* Declaration of Megan E. Grossman, Esq.

GUSA bases its Demurrer upon this Notice, the attached Demurrer, the concurrently filed Generic Defendants' Joint Memorandum of Points and Authorities, the concurrently filed Request for Judicial Notice and exhibits, the Declaration of Megan E. Grossman, Esq., the pleadings, files and records in this action, and such additional matters as GUSA may present at or before the hearing on this Demurrer.

DATED: February 19, 2021

LEWIS BRISBOIS BISGAARD & SMITH LLP

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

DEMURRER

Defendant Granules USA, Inc. ("GUSA") demurs to plaintiff Center for Environmental Health's ("CEH") second amended complaint ("SAC") on the following grounds:

GENERAL DEMURRER

GUSA demurs to the sole cause of action asserted in the SAC, violation of Health & Safety Code § 25249.6 *et seq.* ("Proposition 65"), on the ground that it does not state facts sufficient to support a cause of action against GUSA. (Code Civ. Proc. § 430.10(e) and 430.30.)

Demurrer to CEH's First Cause of Action

CEH's sole cause of action, alleging violation of Proposition 65, fails because it does not state sufficient facts to constitute a cause of action against GUSA, because CEH's claim that GUSA failed to include a Proposition 65 warning with its over-the-counter drug ranitidine in violation of this section is preempted by federal law. (Code Civ. Proc. §§ 430.10(e) and 430.30.)

WHEREFORE, GUSA prays that this demurrer be granted without leave to amend, that CEH take nothing by its SAC, and that GUSA be awarded judgment for its costs and all other proper relief.

DATED: February 19, 2021

LEWIS BRISBOIS BISGAARD & SMITH LLP

By: _____
Paul A. Desrochers
Attorneys for Defendant
GRANULES USA, 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: Steptoe & Johnson LLP, 633 West Fifth Street, Suite 1900, Los Angeles, California 90071.

On **February 19, 2021**, I served the following listed document(s), by method indicated below, on the parties in this action: **DEFENDANT GRANULES USA, INC.'S NOTICE OF DEMURRER AND 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.

☐ **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**
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☒ **BY EMAIL**
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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 **February 19, 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

Mark N. Todzo, Esq. mtodzo@lexlawgroup.com Joseph Mann, Esq. jmann@lexlawgroup.com **LEXINGTON LAW GROUP** 503 Divisadero Street San Francisco, CA 94117 Tel: 415.913.7800 Fax: 415.759.4112	Attorneys for Plaintiff CENTER FOR ENVIRONMENTAL HEALTH
Jeffrey Margulies, Esq. Jeff.margulies@nortonrosefulbright.com Lauren Shoor, Esq. lauren.shoor@nortonrosefulbright.com Andrew Guo, Esq. andy.guo@nortonrosefulbright.com **NORTON ROSE FULBRIGHT US LLP** 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Tel: 213 892 9225 Fax: 213.892.9494	Attorneys for Defendant TARGET CORPORATION
Paul Desrochers, Esq. Paul.desrochers@lewisbrisbois.com **LEWIS BRISBOIS BISGAARD & SMITH LLP** 333 Bush Street, Suite 100 San Francisco, CA 94104 Tel: 415.438.6615 Fax: 415.434.0882	Attorneys for Defendant GRANULES USA, INC.
Cheryl Chang, Esq. chang@blankrome.com Erika Schulz, Esq. eschulz@blankrome.com **BLANKROME LLP** 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Tel: 424.239.3400 Fax: 424.239.3434	Attorneys for Defendant APOTEX CORP.

Brian Ledger, Esq. bledger@gordonrees.com **GORDON REESE SCULLY MANSUKHANI LLP** 101 W. Broadway, Suite 1600 San Diego, CA 92102-8271 Tel: 619.696.6700 Fax: 619.696.7124	Attorneys for Defendants DR. REDDY'S LABORATORIES, INC. DR. REDDY'S LABORATORIES LOUISIANA, LLP
George Gigounas, Esq. George.gigounas@dlapiper.com Greg Sperla, Esq. Greg.sperla@dlapiper.com **DLA PIPER** 400 Capitol Mall, Suite 2400 Sacramento, CA 95814-4428 Tel: 916.930.3200 Fax: 916.930.3201	Attorneys for Defendants SANOFI-AVENTIS U.S. LLC CHATTEM INC.
Will Wagner, Esq. wagnerw@gtlaw.com **GREENBERG TRAURIG, LLP** 1201 K Street, Suite 1100 Sacramento, CA 95814 Tel: 916.442.1111 Fax: 916.448.1709 Trenton H. Norris trent.norris@arnoldporter Vanessa C. Adriance vanessa.adriance@arnoldporter.com **ARNOLD & PORTER** Three Embarcadero Center, 10th Floor San Francisco, CA 94111-4075 Tel: (415) 471-3303 Fax: (415) 471-3400	Attorneys for Defendant 7-ELEVEN, INC.

Exhibit 30

23415954

CIV-140

ATTORNEY OR PARTY WITHOUT ATTORNEY: STATE BAR NO: 214855 NAME: Paul A. Desrochers, Esquire FIRM NAME: LEWIS BRISBOIS BISGAARD & SMITH, LLP STREET ADDRESS: 333 Bush Street, Suite 1100 CITY: San Francisco STATE: CA ZIP CODE: 94101 TELEPHONE NO.: 415-362-2580 FAX NO.: 415-434-0882 E-MAIL ADDRESS: *motion to strike, or motion for judgment on the pleadings.* ATTORNEY FOR (*Name*): GRANULES USA, INC.	*FOR COURT USE ONLY* **FILED** ALAMEDA COUNTY MAR 01 2021 CLERK OF THE SUPERIOR COURT By
SUPERIOR COURT OF CALIFORNIA, COUNTY OF ALAMEDA STREET ADDRESS: 1221 Oak Street MAILING ADDRESS: CITY AND ZIP CODE: Oakland, CA 94612 BRANCH NAME: Department 21	
Plaintiff/Petitioner: Center for Environmental Health DECLARATION OF DEMURRING OR MOVING PARTY Granules USA, Inc. et al	
DECLARATION OF DEMURRING OR MOVING PARTY REGARDING MEET AND CONFER	CASE NUMBER: RG-20-054985 [RESERVATION NO. R-2242703]

To the party filing a demurrer, motion to strike, or motion for judgment on the pleadings: This form must be filed with the demurrer, motion to strike, or motion for judgment on the pleadings.

1. (*Name of party making declaration*): GRANULES USA, INC. was served with

☐ a complaint ☒ an amended complaint ☐ a cross-complaint

☐ an answer ☐ other *(specify):*

in the above-titled action and is filing a ☒ demurrer ☐ motion to strike ☐ motion for judgment on the pleadings

DECLARATION *(Choose either a. or b.)*

2. a. ☒ At least five days before the date a responsive pleading was due to be filed (if I am filing a demurrer or motion to strike) or at least five days before filing a motion for judgment on the pleadings (if I am filing a motion for judgment on the pleadings), I met and conferred with the party who filed the pleading ☒ by telephone ☐ in person and we did not reach an agreement resolving the matters raised by the demurrer, motion to strike, or motion for judgment on the pleadings.

b. ☐ The party who filed the pleading subject to demurrer, motion to strike, or motion for judgment on the pleadings failed to respond to my request to meet and confer or otherwise failed to meet and confer in good faith.

To provide additional information, please use form MC-031, Attached Declaration.

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

Date: 2/18/2021

Megan Grossman, Esq.
(NAME OF PARTY OR ATTORNEY FOR PARTY)

Megan E Grossman
(SIGNATURE OF PARTY OR ATTORNEY FOR PARTY)

FAXED

Form Approved for Optional Use
Judicial Council of California
CIV-140 [Rev. January 1, 2019]

DECLARATION OF DEMURRING OR MOVING PARTY REGARDING MEET AND CONFER

Code of Civil Procedure, §§ 430.41, 435.5, 439
www.courts.ca.gov

MAR -1 2021

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 **February 19, 2021** I served the following listed document(s), by method indicated below, on the parties in this action: **DECLARATION OF DEMURRING OR MOVING PARTY REGARDING MEET AND CONFER**

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.

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(to individual persons)
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☐ **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 **February 19, 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

Mark N. Todzo, Esq. mtodzo@lexlawgroup.com Joseph Mann, Esq. jmann@lexlawgroup.com **LEXINGTON LAW GROUP** 503 Divisadero Street San Francisco, CA 94117 Tel: 415.913.7800 Fax: 415.759.4112	Attorneys for Plaintiff CENTER FOR ENVIRONMENTAL HEALTH
Jeffrey Margulies, Esq. Jeff.margulies@nortonrosefulbright.com Lauren Shoor, Esq. lauren.shoor@nortonrosefulbright.com Andrew Guo, Esq. andy.guo@nortonrosefulbright.com **NORTON ROSE FULBRIGHT US LLP** 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Tel: 213 892 9225 Fax: 213.892.9494	Attorneys for Defendant TARGET CORPORATION
Paul Desrochers, Esq. Paul.desrochers@lewisbrisbois.com **LEWIS BRISBOIS BISGAARD & SMITH LLP** 333 Bush Street, Suite 100 San Francisco, CA 94104 Tel: 415.438.6615 Fax: 415.434.0882	Attorneys for Defendant GRANULES USA, INC.
Cheryl Chang, Esq. chang@blankrome.com Erika Schulz, Esq. eschulz@blankrome.com **BLANKROME LLP** 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Tel: 424.239.3400 Fax: 424.239.3434	Attorneys for Defendant APOTEX CORP.

Brian Ledger, Esq. bledger@gordonrees.com **GORDON REESE SCULLY MANSUKHANI LLP** 101 W. Broadway, Suite 1600 San Diego, CA 92102-8271 Tel: 619.696.6700 Fax: 619.696.7124	Attorneys for Defendants DR. REDDY'S LABORATORIES, INC. DR. REDDY'S LABORATORIES LOUISIANA, LLP
George Gigounas, Esq. George.gigounas@dlapiper.com Greg Sperla, Esq. Greg.sperla@dlapiper.com **DLA PIPER** 400 Capitol Mall, Suite 2400 Sacramento, CA 95814-4428 Tel: 916.930.3200 Fax: 916.930.3201	Attorneys for Defendants SANOFI-AVENTIS U.S. LLC CHATTEM INC.
Will Wagner, Esq. wagnerw@gtlaw.com **GREENBERG TRAURIG, LLP** 1201 K Street, Suite 1100 Sacramento, CA 95814 Tel: 916.442.1111 Fax: 916.448.1709 Trenton H. Norris trent.norris@arnoldporter Vanessa C. Adriance vanessa.adriance@arnoldporter.com **ARNOLD & PORTER** Three Embarcadero Center, 10th Floor San Francisco, CA 94111-4075 Tel: (415) 471-3303 Fax: (415) 471-3400	Attorneys for Defendant 7-ELEVEN, INC.

Exhibit 31

Paul A. Desrochers (SBN 214855)
paul.desrochers@lewisbrisbois.com
LEWIS BRISBOIS BISGAARD & SMITH LLP
333 Bush Street, Suite 1100
San Francisco, California 94104-2872
Telephone: 415.362.2580
Facsimile: 415.434.0882

Attorneys for Defendant
GRANULES USA, INC.

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, et. al.,

Defendants.

Case No. RG20054985

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

[PROPOSED] ORDER SUSTAINING DEFENDANT GRANULES USA, INC.'S DEMURRER TO SECOND AMENDED COMPLAINT WITHOUT LEAVE TO AMEND

[*Filed concurrently with Notice of Demurrer, Joint Memorandum of Points and Authorities; Joint Request for Judicial Notice and Declaration of Counsel*]

RESERVATION NO.: R-2242703

Hearing Date	**April 30, 2021**
Hearing Time	**10:00 a.m.**
Location	**Dept. 21**
Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

The Court, having considered the Demurrer of Defendant Granules USA, Inc. ("Granules"), the papers filed in response thereto, all other argument and the record in this case, and for good cause shown:

1. SUSTAINS the Demurrer;

2. Finds Plaintiff's claim against Granules, reflected in the First Cause of Action alleging a violation of Health & Safety Code Section 25249.6, *et seq*, fails to state facts sufficient to constitute a case of actions pursuant to Code of Civil Procedure Sections 430.10(e) and 430.30;

3. Orders the Second Amended Complaint DISMISSED WITH PREJUDICE from this action; and

4. Orders judgment to be entered in favor of Granules.

IT IS SO ORDERED.

DATED: _____

Hon. Winifred Y. Smith
County of Alameda Superior Court

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 **February 19, 2021**, I served the following listed document(s), by method indicated below, on the parties in this action: **[PROPOSED] ORDER SUSTAINING DEFENDANT GRANULES USA, INC.'S DEMURRER TO SECOND AMENDED COMPLAINT WITHOUT LEAVE TO AMEND**

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**
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(via electronic filing service provider)
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☒ **BY EMAIL**
(to individual persons)
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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 **February 19, 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

Mark N. Todzo, Esq. mtodzo@lexlawgroup.com Joseph Mann, Esq. jmann@lexlawgroup.com **LEXINGTON LAW GROUP** 503 Divisadero Street San Francisco, CA 94117 Tel: 415.913.7800 Fax: 415.759.4112	Attorneys for Plaintiff CENTER FOR ENVIRONMENTAL HEALTH
Jeffrey Margulies, Esq. Jeff.margulies@nortonrosefulbright.com Lauren Shoor, Esq. lauren.shoor@nortonrosefulbright.com Andrew Guo, Esq. andy.guo@nortonrosefulbright.com **NORTON ROSE FULBRIGHT US LLP** 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Tel: 213 892 9225 Fax: 213.892.9494	Attorneys for Defendant TARGET CORPORATION
Paul Desrochers, Esq. Paul.desrochers@lewisbrisbois.com **LEWIS BRISBOIS BISGAARD & SMITH LLP** 333 Bush Street, Suite 100 San Francisco, CA 94104 Tel: 415.438.6615 Fax: 415.434.0882	Attorneys for Defendant GRANULES USA, INC.
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Exhibit 32

Dennis Raglin (SBN 179261)
draglin@steptoe.com
Danielle Vallone (SBN 302497)
dvallone@steptoe.com
STEPTOE & JOHNSON LLP
633 West Fifth Street, Suite 1900
Los Angeles, California 90071
Telephone: 213 439 9400
Facsimile: 213 439 9599

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, *et. al.*,

Defendants.

Case No. RG 20054985

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

NOTICE OF DEFENDANT PERRIGO COMPANY'S DEMURRER AND DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT

[*Filed concurrently with Joint Memorandum of Points and Authorities; Joint Request for Judicial Notice; Declaration of Dennis Raglin; and [Proposed] Order*]

RESERVATION NO.: R-2242700

Hearing Date	**April 30, 2021**
Hearing Time	**10:00 a.m.**
Location	**Dept. 21**
Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

TO THE COURT, ALL PARTIES AND THEIR ATTORNEYS OF RECORD:

PLEASE TAKE NOTICE that on **April 30, 2021**, at 10:00 a.m., or as soon as the matter can be heard, in Department 21 of the Alameda County Superior Court, located at 1221 Oak Street, Oakland, California, Defendant Perrigo Company ("Perrigo") will demur to Plaintiffs' Second Amended Complaint pursuant to California Code of Civil Procedure, Sections 430.10(e) and 430.30, on the grounds that it fails to state a cause of action against Perrigo.

Perrigo's Demurrer will be based on this Notice of Demurrer and Demurrer, the accompanying Joint Memorandum of Points and Authorities by the Generic Defendants, the Generic Defendants' Joint Request for Judicial Notice, and the Declaration of Dennis Raglin, as well as such other evidence the Court may consider.

DATED: February 19, 2021

STEPTOE & JOHNSON LLP

By: _____

Dennis Raglin
Attorneys for Defendant,
PERRIGO COMPANY

GENERAL DEMURRER

The Second Amended Complaint against Perrigo fails to state facts sufficient to constitute a case of actions pursuant to Code of Civil Procedure Sections 430.10(e) and 430.30.

Demurrer to Plaintiffs' First Cause of Action for Injunctive Relief and Civil Penalties

1. Plaintiff's First Cause of Action alleging a violation of Health & Safety Code Section 25249.6, *et seq*, does not contain facts sufficient to state a cause of action against Perrigo because Plaintiff's claim that Perrigo failed to provide a Proposition 65 warning with its over-the-counter drug ranitidine in violation of this section is preempted by federal law. (California Code of Civil Procedure Sections 430.10(e), 430.)

WHEREFORE, Perrigo prays that this demurrer be sustained without leave to amend, that Plaintiff take nothing by its Second Amended Complaint, and that Perrigo be awarded judgment for its costs and all other proper relief.

DATED: February 19, 2021

STEPTOE & JOHNSON LLP

By: _____
Dennis Raglin
Attorneys for Defendant,
PERRIGO COMPANY

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 **February 19, 2021**, I served the following listed document(s), by method indicated below, on the parties in this action: **NOTICE OF DEFENDANT PERRIGO COMPANY'S DEMURRER AND DEMURRER TO PLAINTIFF'S SECOND AMENDED COMPLAINT**

SERVICE LIST ATTACHED

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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 **February 19, 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

Mark N. Todzo, Esq. mtodzo@lexlawgroup.com Joseph Mann, Esq. jmann@lexlawgroup.com **LEXINGTON LAW GROUP** 503 Divisadero Street San Francisco, CA 94117 Tel: 415.913.7800 Fax: 415.759.4112	Attorneys for Plaintiff CENTER FOR ENVIRONMENTAL HEALTH
Jeffrey Margulies, Esq. Jeff.margulies@nortonrosefulbright.com Lauren Shoor, Esq. lauren.shoor@nortonrosefulbright.com Andrew Guo, Esq. andy.guo@nortonrosefulbright.com **NORTON ROSE FULBRIGHT US LLP** 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Tel: 213 892 9225 Fax: 213.892.9494	Attorneys for Defendant TARGET CORPORATION
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Will Wagner, Esq. wagnerw@gtlaw.com **GREENBERG TRAURIG, LLP** 1201 K Street, Suite 1100 Sacramento, CA 95814 Tel: 916.442.1111 Fax: 916.448.1709 Trenton H. Norris trent.norris@arnoldporter Vanessa C. Adriance vanessa.adriance@arnoldporter.com **ARNOLD & PORTER** Three Embarcadero Center, 10th Floor San Francisco, CA 94111-4075 Tel: (415) 471-3303 Fax: (415) 471-3400	Attorneys for Defendant 7-ELEVEN, INC.

Exhibit 33

23415964

CIV-140

ATTORNEY OR PARTY WITHOUT ATTORNEY: STATE BAR NO: 179261	FOR COURT USE ONLY
NAME: Dennis Raglin FIRM NAME: Steptoe & Johnson LLP STREET ADDRESS: 633 W 5th Street, Suite 1900 CITY: Los Angeles STATE: CA ZIP CODE: 90017 TELEPHONE NO.: 415-439-9433 FAX NO.: E-MAIL ADDRESS: draglin@steptoe.com ATTORNEY FOR (Name): Defendant PERRIGO COMPANY	FILED ALAMEDA COUNTY MAR 01 2021 CLERK OF THE SUPERIOR COURT By
SUPERIOR COURT OF CALIFORNIA, COUNTY OF STREET ADDRESS: 1221 Oak Street MAILING ADDRESS: CITY AND ZIP CODE: Oakland, CA 94612 BRANCH NAME: County Administration Building	
Plaintiff/Petitioner: Center for Environmental Health Defendant/Respondent: Perrigo Company, etal.	
DECLARATION OF DEMURRING OR MOVING PARTY REGARDING MEET AND CONFER	CASE NUMBER: RG20054985 [RESERVATION NO. R-2242700]

To the party filing a demurrer, motion to strike, or motion for judgment on the pleadings: This form must be filed with the demurrer, motion to strike, or motion for judgment on the pleadings.

1. (*Name of party making declaration*): Defendant Perrigo Company was served with

☐ a complaint ☒ an amended complaint ☐ a cross-complaint

☐ an answer ☐ other (*specify*):

in the above-titled action and is filing a ☒ demurrer ☐ motion to strike ☐ motion for judgment on the pleadings

DECLARATION (*Choose either a. or b.*)

2. a. ☒ At least five days before the date a responsive pleading was due to be filed (if I am filing a demurrer or motion to strike) or at least five days before filing a motion for judgment on the pleadings (if I am filing a motion for judgment on the pleadings), I met and conferred with the party who filed the pleading ☒ by telephone ☐ in person and we did not reach an agreement resolving the matters raised by the demurrer, motion to strike, or motion for judgment on the pleadings.

b. ☐ The party who filed the pleading subject to demurrer, motion to strike, or motion for judgment on the pleadings failed to respond to my request to meet and confer or otherwise failed to meet and confer in good faith.

To provide additional information, please use form MC-031, Attached Declaration.

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

Date: February 17, 2021

Dennis E. Raglin
(NAME OF PARTY OR ATTORNEY FOR PARTY)

(SIGNATURE OF PARTY OR ATTORNEY FOR PARTY)

FAXED

Form Approved for Optional Use
Judicial Council of California
CIV-140 [Rev. January 1, 2019]

DECLARATION OF DEMURRING OR MOVING PARTY REGARDING MEET AND CONFER

Code of Civil Procedure, §§ 430.41, 435.5, 439
www.courts.ca.gov

MAR - 1 2021

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 **February 19, 2021** I served the following listed document(s), by method indicated below, on the parties in this action: **DEFENDANT PERRIGO COMPANY'S DECLARATION OF DEMURRING OR MOVING PARTY REGARDING MEET AND CONFER**

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.

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(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 **February 19, 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

Mark N. Todzo, Esq. mtodzo@lexlawgroup.com Joseph Mann, Esq. jmann@lexlawgroup.com **LEXINGTON LAW GROUP** 503 Divisadero Street San Francisco, CA 94117 Tel: 415.913.7800 Fax: 415.759.4112	Attorneys for Plaintiff CENTER FOR ENVIRONMENTAL HEALTH
Jeffrey Margulies, Esq. Jeff.margulies@nortonrosefulbright.com Lauren Shoor, Esq. lauren.shoor@nortonrosefulbright.com Andrew Guo, Esq. andy.guo@nortonrosefulbright.com **NORTON ROSE FULBRIGHT US LLP** 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Tel: 213 892 9225 Fax: 213.892.9494	Attorneys for Defendant TARGET CORPORATION
Paul Desrochers, Esq. Paul.desrochers@lewisbrisbois.com **LEWIS BRISBOIS BISGAARD & SMITH LLP** 333 Bush Street, Suite 100 San Francisco, CA 94104 Tel: 415.438.6615 Fax: 415.434.0882	Attorneys for Defendant GRANULES USA, INC.
Cheryl Chang, Esq. chang@blankrome.com Erika Schulz, Esq. eschulz@blankrome.com **BLANKROME LLP** 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Tel: 424.239.3400 Fax: 424.239.3434	Attorneys for Defendant APOTEX CORP.

Brian Ledger, Esq. bledger@gordonrees.com **GORDON REESE SCULLY MANSUKHANI LLP** 101 W. Broadway, Suite 1600 San Diego, CA 92102-8271 Tel: 619.696.6700 Fax: 619.696.7124	Attorneys for Defendants DR. REDDY'S LABORATORIES, INC. DR. REDDY'S LABORATORIES LOUISIANA, LLP
George Gigounas, Esq. George.gigounas@dlapiper.com Greg Sperla, Esq. Greg.sperla@dlapiper.com **DLA PIPER** 400 Capitol Mall, Suite 2400 Sacramento, CA 95814-4428 Tel: 916.930.3200 Fax: 916.930.3201	Attorneys for Defendants SANOFI-AVENTIS U.S. LLC CHATTEM INC.
Will Wagner, Esq. wagnerw@gtlaw.com **GREENBERG TRAURIG, LLP** 1201 K Street, Suite 1100 Sacramento, CA 95814 Tel: 916.442.1111 Fax: 916.448.1709 Trenton H. Norris trent.norris@arnoldporter Vanessa C. Adriance vanessa.adriance@arnoldporter.com **ARNOLD & PORTER** Three Embarcadero Center, 10th Floor San Francisco, CA 94111-4075 Tel: (415) 471-3303 Fax: (415) 471-3400	Attorneys for Defendant 7-ELEVEN, INC.

Exhibit 34

Dennis Raglin (SBN 179261)
draglin@steptoe.com
Danielle Vallone (SBN 302497)
dvallone@steptoe.com
STEPTOE & JOHNSON LLP
633 West Fifth Street, Suite 1900
Los Angeles, California 90071
Telephone: 213 439 9400
Facsimile: 213 439 9599

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, *et. al.*,

Defendants.

Case No. RG 20054985

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

[PROPOSED] ORDER SUSTAINING DEFENDANT PERRIGO COMPANY'S DEMURRER TO SECOND AMENDED COMPLAINT WITHOUT LEAVE TO AMEND

[Filed concurrently with Notice of Demurrer and Demurrer; Joint Memorandum of Points and Authorities; Joint Request for Judicial Notice and Declaration of Dennis Raglin]

RESERVATION NO.: R-2242700

Hearing Date	**April 30, 2021**
Hearing Time	**10:00 a.m.**
Location	**Dept. 21**
Complaint Filed:	February 19, 2020
SAC Filed:	January 4, 2021
Trial Date:	None Set

The Court, having considered the Demurrer of Defendant Perrigo Company ("Perrigo"), the papers filed in response thereto, all other argument and the record in this case, and for good cause shown:

1. SUSTAINS the Demurrer;

2. Finds Plaintiff's claim against Perrigo, reflected in the First Cause of Action alleging a violation of Health & Safety Code Section 25249.6, *et seq*, fails to state facts sufficient to constitute a case of actions pursuant to Code of Civil Procedure Sections 430.10(e) and 430.30;

3. Orders the Second Amended Complaint DISMISSED WITH PREJUDICE from this action; and

4. Orders judgment to be entered in favor of Perrigo.

IT IS SO ORDERED.

DATED:

Hon. Winifred Y. Smith
County of Alameda Superior Court

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 **February 19, 2021** I served the following listed document(s), by method indicated below, on the parties in this action: **[PROPOSED] ORDER SUSTAINING DEFENDANT PERRIGO COMPANY'S DEMURRER TO SECOND AMENDED COMPLAINT WITHOUT LEAVE TO AMEND**

SERVICE LIST ATTACHED

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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 **February 19, 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

Mark N. Todzo, Esq. mtodzo@lexlawgroup.com Joseph Mann, Esq. jmann@lexlawgroup.com **LEXINGTON LAW GROUP** 503 Divisadero Street San Francisco, CA 94117 Tel: 415.913.7800 Fax: 415.759.4112	Attorneys for Plaintiff CENTER FOR ENVIRONMENTAL HEALTH
Jeffrey Margulies, Esq. Jeff.margulies@nortonrosefulbright.com Lauren Shoor, Esq. lauren.shoor@nortonrosefulbright.com Andrew Guo, Esq. andy.guo@nortonrosefulbright.com **NORTON ROSE FULBRIGHT US LLP** 555 South Flower Street Forty-First Floor Los Angeles, California 90071 Tel: 213 892 9225 Fax: 213.892.9494	Attorneys for Defendant TARGET CORPORATION
Paul Desrochers, Esq. Paul.desrochers@lewisbrisbois.com **LEWIS BRISBOIS BISGAARD & SMITH LLP** 333 Bush Street, Suite 100 San Francisco, CA 94104 Tel: 415.438.6615 Fax: 415.434.0882	Attorneys for Defendant GRANULES USA, INC.
Cheryl Chang, Esq. chang@blankrome.com Erika Schulz, Esq. eschulz@blankrome.com **BLANKROME LLP** 2029 Century Park East, 6th Fl. Los Angeles, CA 90067 Tel: 424.239.3400 Fax: 424.239.3434	Attorneys for Defendant APOTEX CORP.

Brian Ledger, Esq. bledger@gordonrees.com **GORDON REESE SCULLY MANSUKHANI LLP** 101 W. Broadway, Suite 1600 San Diego, CA 92102-8271 Tel: 619.696.6700 Fax: 619.696.7124	Attorneys for Defendants DR. REDDY'S LABORATORIES, INC. DR. REDDY'S LABORATORIES LOUISIANA, LLP
George Gigounas, Esq. George.gigounas@dlapiper.com Greg Sperla, Esq. Greg.sperla@dlapiper.com **DLA PIPER** 400 Capitol Mall, Suite 2400 Sacramento, CA 95814-4428 Tel: 916.930.3200 Fax: 916.930.3201	Attorneys for Defendants SANOFI-AVENTIS U.S. LLC CHATTEM INC.
Will Wagner, Esq. wagnerw@gtlaw.com **GREENBERG TRAURIG, LLP** 1201 K Street, Suite 1100 Sacramento, CA 95814 Tel: 916.442.1111 Fax: 916.448.1709 Trenton H. Norris trent.norris@arnoldporter Vanessa C. Adriance vanessa.adriance@arnoldporter.com **ARNOLD & PORTER** Three Embarcadero Center, 10th Floor San Francisco, CA 94111-4075 Tel: (415) 471-3303 Fax: (415) 471-3400	Attorneys for Defendant 7-ELEVEN, INC.