UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

IN RE: Acetaminophen – ASD-ADHD Products Liability Litigation	:	22md3043 (DLC) 22mc3043 (DLC) 22cv9011 (DLC) 22cv9012 (DLC)
This Document Relates To: Hatfield et al. v. Wal-Mart Stores, Inc., 22cv9011 Roberts et al. v. Wal-Mart Stores, Inc., 22cv9012	:	OPINION AND ORDER

APPEARANCES:

For plaintiffs:
Keller Postman LLC
Ashley C. Keller
Ashley Barriere
150 N. Riverside Plaza, Suite 4100
Chicago, IL 60606

Holwell Shuster & Goldberg LLP
Richard J. Holwell
Daniel Martin Sullivan
425 Lexington Avenue
New York, NY 10017

For defendant:
King & Spalding
Donald Frederick Zimmer, Jr.
Ethan Price Davis
50 California Street, Suite 3300
San Francisco, CA 94111
-and-
Livia M. Kiser
110 N Wacker Drive, Suite 3800
Chicago, IL 60606
-and-
Kristen Renee Fournier
1185 Avenue of the Americas
New York, NY 10036
-and-
Jeffrey S. Bucholtz

1700 Pennsylvania Ave., NW
Washington, DC 20006

Quattlebaum, Grooms, Tull & Burrow, PLLC
Thomas G. Williams
111 Center Street, Suite 1900
Little Rock, AR 72201

In two separate actions, plaintiffs Robin Hatfield and Lisa Roberts (collectively, "Plaintiffs"), individually and on behalf of their minor children, have sued Wal-Mart Stores, Inc. ("Walmart"), alleging that their children have autism spectrum disorder ("ASD") and attention-deficit/hyperactivity disorder ("ADHD") because Hatfield and Roberts took Equate, Walmart's brand of over-the-counter ("OTC") acetaminophen, while pregnant. The Plaintiffs allege that Walmart violated state law when it failed to warn of the risks of prenatal exposure to acetaminophen. Walmart has moved to dismiss on the ground that the state law claims are preempted. For the following reasons, the motions to dismiss are denied.

Background

The following facts are drawn from the two complaints and the documents integral to them, including Equate's label. The facts are taken as true for the purposes of these motions.

The facts underlying both complaints are similar. Hatfield took Equate in or around October 2011 when she was pregnant with her child two to three times a week during her third trimester to treat back pain. Roberts took Equate in early 2008 when she

was pregnant with her child two to four times over the course of her pregnancy to treat headaches. Both women believed it was safe to take Equate during their pregnancies and would not have taken the drug if they had been warned that it could cause ASD or ADHD in their children. Hatfield's child was diagnosed with ASD when he was about two years old. Roberts's child was diagnosed with ASD and ADHD when he was five years old.

Acetaminophen has long been marketed as the only safe OTC pain reliever for pregnant women. At the time Hatfield and Roberts took Equate, the label contained one warning related to pregnancy. The label stated: "If pregnant or breast-feeding, ask a health professional before use." There was no specific warning about the risks of ASD or ADHD.

The Plaintiffs filed their complaints on June 7, 2022 in the U.S. District Court for the Western District of Arkansas, alleging, among other state-law claims, that Walmart failed to warn them about the risks of prenatal exposure to acetaminophen. The complaints in each action asserted diversity jurisdiction pursuant to 28 U.S.C. § 1332. Walmart has its principal place of business in Arkansas.[1] Walmart moved to dismiss both

[1] Hatfield and her child are and have been during the relevant time period residents of Tennessee. Roberts and her child are and have been during the relevant time period residents of Nevada.

complaints on September 6. On October 5, the Judicial Panel on Multidistrict Litigation consolidated these two actions with other actions asserting claims that prenatal exposure to acetaminophen causes ASD and ADHD in children and transferred the cases to this Court under 28 U.S.C. § 1407. Pursuant to an October 18 Order, the Plaintiffs filed an opposition to both motions on October 28, and Walmart replied on November 11. Accordingly, the motions are fully submitted.

Discussion

Walmart asserts that federal law preempts the Plaintiffs' state law claims.[2] Those state law claims may arise under the law of Arkansas or the states in which the Plaintiffs reside.

A multidistrict litigation transferee court "applies the substantive state law, including choice-of-law rules, of the jurisdiction in which the action was filed." Desiano v. Warner-Lambert & Co., 467 F.3d 85, 91 (2d Cir. 2006) (citation omitted). Under Arkansas law, courts consider the doctrine of lex loci delicti and five additional factors "to soften the formulaic application" of that doctrine in tort cases. Schubert v. Target Stores, Inc., 201 S.W.3d 917, 922 (Ark. 2005). Lex

[2] The Plaintiffs assert other claims in addition to strict liability under a duty to warn. Because the Plaintiffs and the defendant only address the duty to warn in their motion papers and appear to agree that all of Plaintiffs' claims hinge upon the defendants breach of a state law duty to warn, only state law duties to warn are addressed in this Opinion.

loci delicti counsels that "the law of the place where the wrong took place is the proper choice of law." Ganey v. Kawasaki Motors Corp., USA, 234 S.W.3d 838, 846 (Ark. 2006), overruled on other grounds by Lawson v. Simmons Sporting Goods, 569 S.W.3d 865 (Ark. 2019). The five additional factors to be applied are: "(1) predictability of results, (2) maintenance of interstate and international order, (3) simplification of the judicial task, (4) advancement of the forum's governmental interests, and (5) application of the better rule of law." Schubert, 201 S.W.3d at 921.

For Hatfield's claims, the choice of law is between Tennessee and Arkansas. For Roberts's claims, the choice of law is between Nevada and Arkansas. No party has argued that the choice of law inquiry will affect the preemption question. The state law duties under Arkansas, Tennessee, and Nevada law are nearly identical. In Tennessee, "[d]rug manufacturers have a duty to exercise ordinary and reasonable care not to expose the public to an unreasonable risk of harm from the use of their products." Pittman v. Upjohn Co., 890 S.W.2d 425, 428 (Tenn. 1994) (citation omitted). The Tennessee Products Liability Act of 1978, Tenn. Code. Ann. §§ 29-28-101 to -108 (West 2022), governs failure to warn claims. See Tenn. Code. Ann. § 29-28-102(6) (West 2022). Under Nevada law, "the lack of a warning functions as the relevant [product] defect." Motor Coach

Indus., Inc. v. Khiabani by and through Rigaud, 493 P.3d 1007, 1011 (Nev. 2021) (citation omitted). In Arkansas, an inadequate warning is also a type of product defect. West v. Searle & Co., 806 S.W.2d 608, 610 (Ark. 1991). Accordingly, it is unnecessary for the purpose of this motion to weigh the five factors and resolve the choice of law inquiry.

At the heart of both complaints is the assertion that Walmart had a duty under state law to warn of the risks of prenatal exposure to acetaminophen. Walmart asserts that this state law duty is preempted by regulations promulgated by the Food and Drug Administration ("FDA") that govern how OTC drugs are manufactured and marketed to consumers. Before discussing the jurisprudence on preemption, it is helpful to review the FDA regulatory scheme for new drugs and OTC drugs generally and the federal regulation of acetaminophen.

I. FDA Regulatory Scheme for New Drugs and OTC Drugs

"The federal government regulates the manufacture, labeling, and sale of pharmaceuticals pursuant to the" Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301-399g ("FDCA"). Gibbons v. Bristol-Meyers Squibb Co., 919 F.3d 699, 707 (2d Cir. 2019). No drug can enter interstate commerce "unless [the] FDA determines that it is generally recognized as safe and effective ("GRAS/E") for the particular use described in its product labeling." Nat. Res. Def. Council, Inc. v. U.S. FDA, 710 F.3d

71, 75 (2d Cir. 2013) (addressing new drug regulation). How the FDA determines whether a drug is GRAS/E depends on the applicable regulatory scheme. Once a drug is deemed GRAS/E, it is a "central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times." Wyeth v. Levine, 555 U.S. 555, 570-71 (2009).

"In the 1930's, Congress became increasingly concerned about unsafe drugs and fraudulent marketing, and it enacted the" FDCA. Id. at 566. "The FDCA's most substantial innovation was its provision for premarket approval of new drugs." Id. A new drug is defined as:

> any drug . . . the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof . . . .

21 U.S.C. § 321(p)(1). "[A] manufacturer seeking federal approval to market a new drug must prove that it is safe and effective and that the proposed label is accurate and adequate." PLIVA, Inc. v. Mensing, 564 U.S. 604, 612 (2011). Manufacturers may obtain federal approval by submitting a new drug application ("NDA"). Wyeth, 555 U.S. at 566. "The FDA's premarket approval of a new drug application includes the approval of the exact text in the proposed label." Id. at 568. Drugs approved

through the NDA process are commonly referred to as brand-name drugs.

After an NDA is approved, the FDA permits a brand-name drug manufacturer to "make certain changes to its label before receiving the agency's approval" through the changes being effected ("CBE") regulation. Id. These changes include those that "add or strengthen a contraindication, warning, precaution, or adverse reaction [or that] add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product." Id. (citing 21 C.F.R. § 314.70(c)(6)(iii)(A), (C)). Overall, then, a brand-name drug manufacturer "is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market."[3] Id. at 571.

In 1972, the FDA developed a separate regulatory process, known as the monograph system, for the approval of classes of OTC drug products and their active ingredients. As the Second Circuit has explained:

[3] In 1984, the FDA created a process by which generic drugs can gain FDA approval "simply by showing equivalence to a reference listed drug that has already been approved by the FDA." Mensing, 564 U.S. at 612; see also FTC v. Shkreli, 581 F. Supp. 3d 579, 594 (S.D.N.Y. 2022). Generic drugs labels must "be the same at all times as the corresponding brand-name drug labels." Mensing, 564 U.S. at 618. Therefore, unlike brand-name drugs, generic drugs cannot unilaterally change their labels without violating the FDA. Id. at 614.

> Commenced in 1972, the OTC Drug Review established FDA's "monograph" system for regulating over-the-counter drugs. While FDA must generally approve drugs as GRAS/E individually, the monograph system allows manufacturers to bypass individualized review. Under this system, FDA issues a detailed regulation -- a "monograph" -- for each therapeutic class of OTC drug products. Like a recipe, each monograph sets out the FDA-approved active ingredients for a given therapeutic class of OTC drugs and provides the conditions under which each active ingredient is GRAS/E.

NRDC, 710 F.3d at 75 (citation omitted).

The monograph system establishes conditions under which certain classes of drugs will be considered GRAS/E and not misbranded.[4] See 21 C.F.R. § 330.1. Critically, if the drug meets the required conditions and is therefore GRAS/E, it is not a "new drug" that requires premarket approval. Conversely, any drug covered by the monograph system that does not conform to the conditions "is liable to regulatory action." Id.; see also Over-the-Counter Drug Monograph System -- Past, Present, and Future; Public Hearing, 79 Fed. Reg. 10168, 10169 (Feb. 24, 2014) (hereinafter "OTC Drug Monograph System Public Hearing").

Thus, for certain categories of drugs, the monograph system replaces the individualized NDA approval process with a

[4] The regulations provide that

> [a]n over-the-counter (OTC) drug listed in this subchapter is generally recognized as safe and effective and is not misbranded if it meets each of the conditions contained in this part and each of the conditions contained in any applicable monograph.

21 C.F.R. § 330.1.

rulemaking process. From 1972 to 2020, the monograph system involved four regulatory steps: (1) an advisory review panel was established to evaluate the safety and effectiveness of the OTC drug; (2) the advisory review panel submitted its report to the FDA Commissioner; (3) the FDA published a tentative final monograph ("TFM"); and (4) after receiving comments on the TFM, the FDA published a final monograph. 21 C.F.R. § 330.10. The monographs, then, set out the conditions with which manufacturers had to comply in order to bypass the NDA process.

The monograph system was reformed as a part of the Coronavirus Aid, Relief, and Economic Security Act, Pub. L. 116-136, 134 Stat. 281 (2020) ("CARES Act"). See Final Administrative Orders for Over-the-Counter Monographs; Availability, 86 Fed. Reg. 52474, 52474-75 (Sept. 21, 2021). The rulemaking process governing monographs "was replaced with an administrative order process." Id. at 52475. The CARES Act also made existing TFMs final orders if they met certain conditions. See 21 U.S.C. § 355h. Lastly, the CARES Act created a process by which drug manufacturers can request that the FDA issue administrative orders stating that a drug is GRAS/E or that a change to a condition of use of a drug is GRAS/E. Id. § 355h(b)(5)(B).

II. FDA Regulation of Acetaminophen

Acetaminophen is regulated under the monograph system. Therefore, drug labels for acetaminophen must comply with the relevant monograph and OTC drug labeling requirements. 21 C.F.R. § 330.1. This section of the Opinion will discuss the monographs and the OTC drug labeling requirements separately, with a focus on the regulations that speak to pregnancy.

A. Monographs Governing Acetaminophen

In 1988, the FDA published a TFM that regulated internal analgesic, antipyretic, and antirheumatic ("IAAA") drug products. See Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use; Tentative Final Monograph, 53 Fed. Reg. 46204 (Nov. 16, 1988) (hereinafter "IAAA TFM"). As a TFM, the document's legal status was that of a proposed rule. Id. at 46204. It invited written comments, objections, or requests for a hearing. Id.

The IAAA TFM defines analgesics as drugs "used to alleviate pain and reduce fever." Id. at 46255. Among the analgesics described in the IAAA TFM were acetaminophen and aspirin. Id. Since 1988, the FDA has proposed amendments to the IAAA TFM and finalized certain sections,[5] but until the passage of the CARES

[5] For example, the FDA finalized a monograph relating to the professional labeling of IAAA products containing aspirin in 1998. See 21 C.F.R. pt. 343.

Act, many of the sections relating to acetaminophen remained tentative.

The IAAA TFM states that a drug product containing acetaminophen as the active ingredient is "generally recognized as safe and effective and is not misbranded if it meets each of the conditions in" the TFM and 21 C.F.R. § 330.1. Id. at 46255. One of the conditions is that "the labeling of the product contains the following statements under the heading 'Warnings.'" Id. at 46256. For IAAA drug products that contain acetaminophen as the active ingredient, the IAAA TFM does not include a warning specific to pregnancy. The IAAA TFM does, however, include pregnancy warnings for other active ingredients, such as aspirin. Id.

In 2009, the FDA finalized a monograph governing certain organ-specific warnings for labels of OTC drug products containing IAAA active ingredients. See Organ-Specific Warnings; Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use; Final Monograph, 74 Fed. Reg. 19385 (Apr. 29, 2009); 21 C.F.R. § 201.326. None of the warnings for acetaminophen under this regulation deal with pregnancy. See id. § 201.326(a).

The IAAA TFM became a final order effective March 27, 2020 under the CARES Act. The FDA published the IAAA TFM, as amended in the years since 1988, as a final administrative order on

October 14, 2022. U.S. Food and Drug Administration, Over-the-Counter (OTC) Monograph M013: Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use (Oct. 14, 2022). Because the IAAA TFM as published in 1988 was the applicable regulation for acetaminophen products at the times relevant in this action, this Opinion will reference the 1988 publication along with other applicable regulations rather than the recently published final order.

B. OTC Drug Labeling Requirements

Drugs regulated under the monograph system are required to comply with the FDA's regulations for drug labeling, including those regulating OTC drug labels. 21 CFR § 330.1(c)(1) (incorporating 21 C.F.R. § 201.66); id. § 201.66. Section 201.66 states that OTC drug labels "shall contain" certain content, including warnings. Id. § 201.66(c).

When the FDA finalized § 201.66 in 1999, it explained that several manufacturers had asked the FDA to "allow voluntary warnings to appear under the appropriate headings to further protect consumers from possible misuse of the product." Over-the-Counter Human Drugs; Labeling Requirements, 64 Fed. Reg. 13254, 13271 (Mar. 17, 1999). In response, the FDA encouraged

> manufacturers to discuss with the agency the addition of voluntary warnings to OTC drug products. As a general matter, FDA agrees that consumers may be confused if an appropriate warning were placed outside of the Drug Facts area. Thus, the agency expects such

> warnings to appear under the "Warnings" heading, preceded by an appropriate subheading.

Id. (emphasis supplied).

C. Pregnancy Warning for Acetaminophen

The regulations of OTC drug labels include the requirement that all OTC drug products intended for systemic absorption contain a pregnancy and breast-feeding warning ("Pregnancy Warning" or "§ 201.63"). 21 C.F.R. § 201.63. A brief history of the Pregnancy Warning provides context to this regulation.

In 1982, the FDA finalized a regulation adding a "pregnancy-nursing warning" to OTC drugs that were "intended for systemic absorption." Pregnant or Nursing Women; Delegations of Authority and Organization; Amendment of Labeling Requirements for Over-the-Counter Human Drugs, 47 Fed. Reg. 54750, 54757 (Dec. 3, 1982) (hereinafter "1982 Pregnancy Warning Regulation"). The warning read: "As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product." Id. at 54758. This regulation was incorporated into the regulations for drugs manufactured and sold under the monograph system. Id.; 21 C.F.R. § 330.2.

In 1999, the Pregnancy Warning was amended to its current form as a part of a final rule that added many additional

requirements for OTC drug labels.[6] Over-the-Counter Human Drugs; Labeling Requirements, 64 Fed. Reg. at 13286. The regulation states:

> The labeling for all over-the-counter (OTC) drug products that are intended for systemic absorption, unless specifically exempted, shall contain a general warning under the heading "Warning" (or "Warnings" if it appears with additional warning statements) as follows: "If pregnant or breast-feeding, ask a health professional before use." [first four words of this statement in bold type] In addition to the written warning, a symbol that conveys the intent of the warning may be used in labeling.

21 C.F.R. § 201.63(a). The Pregnancy Warning is mandatory unless an NDA or final monograph states otherwise, id. § 201.63(b), or the FDA grants a manufacturer an exemption. Id. § 201.63(d).

III. Preemption Standard

With the framework for the federal regulation of acetaminophen described, the preemption question can be addressed. "The Supremacy Clause establishes that federal law 'shall be the supreme Law of the Land . . . any Thing in the Constitution or Laws of any State to the Contrary notwithstanding.'" Mensing, 564 U.S. at 617 (quoting U.S. Const., art. VI, cl. 2). One type of preemption is conflict preemption, and it is on that doctrine that Walmart relies. See

[6] The express incorporation of the Pregnancy Warning to OTC drug labels is governed by § 210.66(c)(5)(ix).

N.Y. SMSA Ltd. P'ship v. Town of Clarkstown, 612 F.3d 97, 104 (2d Cir. 2010) (explaining the three types of preemption).

"Where federal and state law conflict -- that is, where it is impossible for a party to follow both federal and state law -- state law must give way." Gibbons, 919 F.3d. at 708. As the Supreme Court has observed, "[i]mpossibility pre-emption is a demanding defense." Wyeth, 555 U.S at 573. Walmart "must show that the conflict between the federal and state laws is so direct and positive that the two cannot be reconciled or consistently stand together." N.Y. Pet Welfare Ass'n, Inc. v. City of New York, 850 F.3d 79, 87 (2d Cir. 2017) (citation omitted).

Neither the Supreme Court nor any circuit court has addressed preemption in the context of drugs regulated under the monograph system. Three Supreme Court decisions involving preemption and FDA regulation of prescription drugs through the NDA process nevertheless provide helpful guidance. In Wyeth, the Court found that the FDA does not preempt state law failure to warn claims against manufacturers of brand-name drugs marketed pursuant to NDAs. 555 U.S. at 581. The Court reasoned that because a brand-name manufacturer can "unilaterally strengthen" warnings on its label, it is not impossible for a manufacturer to comply with both state and federal law. Id. at 573. Next, in Mensing, the Court held that the FDA does preempt

state law failure to warn claims brought against generic drug manufacturers. 564 U.S. at 609. The Court emphasized that generic drug manufacturers are required by FDA regulations to have the same label as the brand-name drug, so they cannot unilaterally change their labels without violating FDA regulations. See id. at 612-13. Lastly, in Mutual Pharmaceutical Co., Inc. v. Bartlett, the Court expanded Mensing and held that the FDA also preempts state law design-defect claims made against generic drug manufacturers. See 570 U.S. 472, 476 (2013). Thus, if a defendant could have unilaterally strengthened warnings on its label without prior approval from the FDA, a state law failure to warn claim is not preempted. Gibbons, 919 F.3d at 708.

IV. Application

Applying the principles underlying Wyeth, Mensing, and Bartlett, the Plaintiffs' failure to warn claims are not preempted. The dispositive question here is: could the manufacturer have unilaterally changed the label on Equate without violating the IAAA TFM, the regulations governing the Pregnancy Warning, and other applicable regulations? The answer is yes.

It is a foundational principle for OTC drugs, as it is for brand-name drugs issued through an NDA, that a manufacturer is responsible for the adequacy of the warnings on its drug label.

The regulation of acetaminophen generally and the Pregnancy Warning regulation in particular do not alter that responsibility. The language of the IAAA TFM required the manufacturer of acetaminophen to meet the conditions in the TFM and other applicable regulations. See IAAA TFM, 53 Fed. Reg. at 46255. Critically, the IAAA TFM does not include any language to suggest that the requirements in the monograph are exclusive of any other warnings that a manufacturer may add to the label. Nor does the Pregnancy Warning regulation contain language purporting to limit a manufacturer's obligation to ensure that its label is adequate. See 21 C.F.R. § 201.63. In other words, a manufacturer of acetaminophen can meet the conditions in the IAAA TFM and the Pregnancy Warning regulation while also complying with a state law duty to warn.

Walmart acknowledges that there is no preemption of state law duty to warn claims if federal law permitted the manufacturer of acetaminophen unilaterally to add an additional warning on its labels regarding the prenatal use of acetaminophen and ASD and ADHD. Walmart relies principally on eight arguments, five of which rest on its construction of the Pregnancy Warning regulation and the statement accompanying the 1982 final rule creating the Pregnancy Warning ("1982 Statement"), to argue that a manufacturer's hands were tied when it came to adding a warning about the use of acetaminophen

during pregnancy. For ease of reference, the current Pregnancy Warning regulation states, in relevant part:

> (a) The labeling for all over-the-counter (OTC) drug products that are intended for systemic absorption, unless specifically exempted, shall contain a general warning under the heading "Warning" (or "Warnings" if it appears with additional warning statements) as follows: "If pregnant or breast-feeding, ask a health professional before use." [first four words of this statement in bold type] In addition to the written warning, a symbol that conveys the intent of the warning may be used in labeling.
>
> (b) Where a specific warning relating to use during pregnancy or while nursing has been established for a particular drug product in a new drug application (NDA) or for a product covered by an OTC drug final monograph in part 330 of this chapter, the specific warning shall be used in place of the warning in paragraph (a) of this section, unless otherwise stated in the NDA or in the final OTC drug monograph.
>
> . . .
>
> (e) The labeling of orally or rectally administered OTC aspirin and aspirin-containing drug products must bear a warning that immediately follows the general warning identified in paragraph (a) of this section. The warning shall be as follows:
>
> "It is especially important not to use" (select "aspirin" or "carbaspirin calcium," as appropriate) "during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery."

21 C.F.R. § 201.63 (emphasis supplied).[7]

[7] The regulation quoted above was enacted in 1999. When the Pregnancy Warning regulation was first issued in 1982, it included an additional phrase -- "As with any drug" -- at the beginning of the general warning. For context, the Pregnancy Warning as promulgated in 1982 was:

Walmart first argues that the word "shall" in § 201.63 means that manufacturers of acetaminophen must include the Pregnancy Warning on the drug label and cannot add to that warning. "The word 'shall' in a statute indicates a command." N.J. Carpenters Health Fund v. NovaStar Mortg., 28 F.4th 357, 371 (2d Cir. 2022). Walmart is thus correct when it states that every manufacturer of OTC drugs intended for systemic absorption, including manufacturers of drugs containing acetaminophen, were required to include the Pregnancy Warning on their labels. But for the reasons already explained, that requirement did not prevent a manufacturer of acetaminophen from including other warnings on its label, including warnings related to the use of acetaminophen during pregnancy. Cf. Isett

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> (a) The labeling for all over-the-counter (OTC) drugs that are intended for systemic absorption, unless specifically exempted, shall contain a general warning under the heading Warning (or Warnings if it appears with additional warning statements) as follows: "As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product." In addition to the written warning, a symbol that conveys the intent of the warning may be used in labeling.

Pregnant or Nursing Women, 47 Fed. Reg. at 54757-58 (emphasis supplied). Subsection (b) has not been amended since the 1982 promulgation. The warning in subsection (e) regarding aspirin and carbaspirin calcium was added in 1990 and amended in 1999. See Labeling for Oral and Rectal Over-the-Counter Aspirin and Aspirin-Containing Drug Products; Final Rule, 55 Fed. Reg. 27776, 27784 (July 5, 1990); Over-the-Counter Human Drugs; Labeling Requirement, 64 Fed. Reg. at 13286.

v. Aetna Life Ins. Co., 947 F.3d 122, 132 (2d Cir. 2020) (finding no limitation in a regulation when the text did not include one expressly).

In its reply brief, Walmart adds three additional points to its argument that § 201.63 is exclusive and preemptive. First, Walmart asserts that adding a specific warning regarding ASD or ADHD to the label "would run counter" to the regulation's focus on a "general warning". This argument misunderstands the function of the word "general" in the regulation.

As the 1982 Statement explains, the warning was required for all labels for all OTC drugs that are systemically absorbed. It was intended to cover "those drugs for which the available evidence shows neither that the product is unsafe for use by pregnant or nursing women nor that the product is safe for use by these women." 1982 Pregnancy Warning Regulation, 47 Fed. Reg. at 54752. Even though there was "a lack of specific evidence to show that many of these [OTC] drugs cause[d] harm to the fetus or nursing infant," there was a "potential for some OTC drugs to have harmful effects." Id. at 54754. As the FDA explained, it believed that "appropriate general warnings . . . are an important means of educating the public about drug use." Id. It added its expectation that, as "consumers become familiar with the general pregnancy-nursing warning, because of their increased awareness they may more readily understand the

significance of specific warnings that describe demonstrated risks of particular drugs to pregnant and nursing women." Id. The 1982 Statement makes clear that by creating a "general warning," the FDA intended to craft a warning that would be broad enough to apply to numerous OTC drugs and direct pregnant women to "advice that will enable [them] to make an informed choice with respect to an OTC drug, balancing the benefit it would provide against the potential risk." Id. at 54755. The FDA added that "the general warning will usually not be required for products labeled with specific warnings against use by pregnant women, such as specific warnings developed in the course of OTC drug review" and incorporated into a drug's monograph. Id. The warning is therefore "general" because it applies to a wide range of OTC drugs, not because it requires a general warning over any other specific warning that a manufacturer could voluntarily add to a drug's label.

Second, by adding a separate paragraph to the regulation that is addressed to "specific" warnings related to pregnancy, see 21 C.F.R. § 201.63(b), Walmart argues that the FDA was indicating that manufacturers are not free to devise their own additional specific warnings. This argument also fails. Paragraph (b) is addressed to circumstances in which an NDA or monograph has required the use of a specific pregnancy-related warning. It does not address the ability of manufacturers to

supplement the general warning with safety warnings specific to their OTC drug.

Third, Walmart emphasizes that § 201.63 makes it optional for manufacturers to include "a symbol that conveys the intent of the warning" in addition to the prescribed written warning. Id. § 201.63(a). From the fact that the FDA specifically references one optional warning, Walmart contends that no other optional warnings can be added to the label. Read in context, this construction of the regulation also fails. The option to add a symbol responded to manufacturers' concerns that consumers who did not speak English would not be able to comprehend the general warning. 1982 Pregnancy Warning Regulation, 47 Fed. Reg. at 54753. By allowing manufacturers the option to add a symbol, the FDA did not delineate the only circumstance under which consumer safety could be enhanced through improved warnings.

Together, these textual and structural elements of the Pregnancy Warning do not suggest that manufacturers cannot add a more specific warning regarding acetaminophen in addition to the general warning that applies to all OTC drugs that are systemically absorbed. Complying with a state law duty to place a warning about the risks of prenatal exposure of an OTC drug would not require a manufacturer to replace or otherwise modify the general Pregnancy Warning. It is worth repeating that

"[i]mpossibility pre-emption is a demanding defense." Wyeth, 555 U.S at 573. As written, § 201.63 does not conflict with a manufacturer's state law duty to add an additional warning relating to pregnancy to an OTC drug label.

Walmart makes one final argument in reliance on § 201.63, specifically in reliance on the 1982 Statement. Walmart asserts that the FDA "determined" that warnings regarding use of OTC drugs during pregnancy should be limited to avoid conflict with the federal Pregnancy Warning and avoid consumer confusion. Again, the context in which the FDA discussed these issues matters.

When the FDA finalized the regulation in 1982, the agency addressed comments that inquired as to the preemptive effect of the Pregnancy Warning. 1982 Pregnancy Warning Regulation, 47 Fed. Reg. at 54756. At the time, a "substantially similar" pregnancy warning was about to become operational in California. Id. Because the California warning and the federal Pregnancy Warning were so similar, the FDA noted that the issue of preemption was largely "academic." Id. In any event, when the FDA issued a final rule on OTC drug labeling in 1999, the agency addressed the issue of preemption head on. The agency decided against any express prohibition of additions to federally

approved labels.[8] Over-the-Counter Human Drugs; Labeling Requirement, 64 Fed. Reg. at 13272. In explaining its decision, the FDA referred to an amendment to the FDCA embodied in the Food and Drug Administration Modernization Act of 1997, Pub. L. 105-115, 111 Stat. 2296 ("FDAMA"). The FDAMA prohibits state and local governments from establishing requirements for nonprescription drugs, 21 U.S.C. § 379r(a), but includes a carveout for products liability suits. It states, "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) (emphasis supplied); see also Wyeth, 555 U.S. at 575 n.8 (In 1997, Congress "expressly preserved product liability actions."). Thus, the FDA has not "determined" that state law failure to warn claims are preempted.

Turning away from § 201.63 and the 1982 Statement, Walmart next argues that the absence of any federal regulatory path for obtaining FDA approval of additions to labels of drugs approved for sale through monographs is further evidence that

[8] Under a proposed version of § 201.66, the rule would have stated: "No State or local governing entity may establish or continue in effect any law, rule, regulation, or requirement for OTC drug product labeling format or content that is different from, or in addition to, that required by FDA." Over-The-Counter Human Drugs; Proposed Labeling Requirements, 62 Fed. Reg. 9024, 9052 (Feb. 27, 1997).

manufacturers are not allowed to unilaterally change labels. As Walmart points out, the Supreme Court relied on the existence of the CBE regulation for labeling changes by NDA holders when it held that NDA holders could unilaterally strengthen their labels' warnings. See Wyeth, 555 U.S. at 569. This comparison is inapt. Under the NDA process, premarket approval of the new drug includes approval of the exact text of a proposed label. Id. at 568. A regulatory path to change the label -- the CBE regulation -- is therefore necessary. In contrast, drugs sold under the monograph system do not need FDA approval of their labels at any point. 21 C.F.R. § 330.1; OTC Drug Monograph System Public Hearing, 79 Fed. Reg. at 10169. A manufacturer of an OTC drug sold under the monograph system is permitted to change its label so long as it meets the requirements of its monograph and other applicable OTC drug regulations.

In further support of its position that the preemption doctrine forbids manufacturers to alter labels in the way the Plaintiffs may seek through this litigation, Walmart worries that any other conclusion may subject consumers to "a dizzying array of different and potentially conflicting warnings." Walmart's concern is not insignificant as a policy matter, but that concern does not control the conflict preemption analysis. It is worth noting that the state tort system plays an important role in protecting the health and safety of communities.

Because there are so many drugs on the market, the FDA, with its "limited resources," has chosen not to individually approve each label and instead to rely on manufacturers who have "superior access to information about their drugs," to ensure that the drugs are adequately labeled. Wyeth, 555 U.S. at 578-79. Ultimately the extent of our scientific knowledge will dictate whether any label change is necessary or appropriate. And, if it is necessary for the FDA to add to its labeling requirements to avoid consumer confusion, it has the authority and expertise to act.

Indeed, Walmart points a publication by the FDA itself in 2015 to suggest that no labeling change to the Pregnancy Warning is appropriate. At that time, the FDA reviewed studies that reported a connection "between acetaminophen use in pregnancy and ADHD in children" and found "methodological limitations" that made the "weight of the evidence" regarding the connection "inconclusive." See U.S. Food & Drug Administration, FDA Has Reviewed Possible Risks of Pain Medicine Use During Pregnancy (Jan. 9, 2015), https://www.fda.gov/media/90209/download. The FDA noted that it would "continue to monitor and evaluate the use of pain medicines during pregnancy" and would "update the public as new safety information becomes available." Id. Whatever weight should be given to the FDA's 2015 statement, the statement does not alter the preemption analysis. Moreover, the

Plaintiffs rely on more recent studies to support their claim that manufacturers of acetaminophen had a duty to warn of the risk of prenatal exposure to acetaminophen.

Lastly, Walmart argues that the state law claims against it are certainly preempted since manufacturers are responsible under the law for the contents of the labels, not retailers. The complaints allege that Walmart manufactures and labels Equate. On a motion to dismiss, the facts asserted in the complaint are accepted as true. Walmart's argument that it has "no authority to alter a drug's composition, label, or design" does not impact the preemption analysis undertaken here.[9]

Conclusion

Walmart's September 6 motions to dismiss are denied.

Dated: New York, New York
November 14, 2022

DENISE COTE
United States District Judge

[9] In its motions, Walmart also asserts that it does not hold the NDA for Equate. This is inapposite, as there is no NDA that governs acetaminophen in the dosage that Walmart is selling it. The sale of Equate is governed by the monograph system. In its reply, Walmart abandons this argument.