UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

KELLY S. PFAFF, *et al.*,	:	
	:	**MEMORANDUM DEICSION AND ORDER**
Plaintiffs,	:	
	:	
- against -	:	15-cv-3355 (BMC)
	:	12-md-02331 (BMC)
MERCK & CO., INC., *et ano.*,	:	
	:	
Defendants.	:	
	:	

COGAN, District Judge.

Plaintiffs bring failure-to-warn and breach of warranty claims against Merck & Co., Inc. and Merck Sharp & Dohme Corp. (together, "Merck") for injuries arising from the death of their father and husband, John D. Pfaff. Plaintiffs argue that Pfaff's suicide was a result of Merck's failure to warn him of the hair loss drug Propecia's allegedly "dangerous side effects" including "depression and suicide ideation."

Merck moves for partial summary judgment as to whether two of plaintiffs' arguments are preempted: that it should have (1) added a warning regarding suicidality; and (2) listed depression in the Warnings & Precautions ("W&P") section of Propecia's label. For the reasons that follow, Merck's motion is GRANTED.

BACKGROUND

I. FDA approval of Propecia and its label

In 1997, the Federal Drug Administration ("FDA") granted approval of Merck's drug Propecia.[1] Propecia is a one milligram tablet of finasteride, which treats androgenetic alopecia or, as it is more commonly known, male pattern hair loss. Finasteride is a selective inhibitor of Type II 5α-reductase, an enzyme that (among other things) "converts . . . testosterone into 5α-dihydrotestosterone (DHT)." Propecia was not Merck's only orally administered finasteride product. Merck also marketed Proscar, which contains five times more finasteride than Propecia.[2]

When the FDA approved Propecia for sale, it also was required to greenlight its initial label. Pursuant to the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 301 *et seq.*, the FDA strictly monitors and controls the labels for all FDA-approved drugs. When a new drug is initially approved, the FDA is responsible for approving its label, see 21 U.S.C. § 355; 21 C.F.R. § 314.105(b), and determining about which risks consumers must be warned.

Not all risks necessitate a warning on a drug label. See 21 C.F.R. § 201.57(c) (discussing requirements for the contents of prescription drug labels). This is because "[t]he FDA has recognized that '[e]xaggeration of risk, or inclusion of speculative or hypothetical risks, could discourage appropriate use of a beneficial drug . . . or decrease the usefulness and accessibility of important information by diluting or obscuring it.'" Utts v. Bristol-Myers Squibb Co., 251 F. Supp. 3d 644, 659 (S.D.N.Y. 2017) (quoting Supplemental Applications Proposing Labeling

[1] On December 4, 2020, Merck submitted to the FDA a notice of transfer of ownership of the Propecia and Proscar NDAs from Merck to Organon LLC. As both drugs were owned by Merck during all times relevant to this lawsuit, for the purposes of this decision, this Court will refer to Merck as their owner or sponsor of both.

[2] Proscar is predominantly used to treat benign prostatic hyperplasia in people with enlarged prostates.

Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 2848, 2851 (Jan. 16, 2008)). The FDA thus "seeks to allow 'only information for which there is a scientific basis to be included.'" Id. Accordingly, the earliest version of Propecia's label did not refer to or include any warnings for depression or suicidality.

As new risks will often arise only after FDA approval, manufacturers are required to "disclose to the FDA any adverse health consequences reported" on a continuous basis. Id. at 658. This requirement includes submitting Periodic Safety Update Reports ("PSURs") to the FDA. See 21 C.F.R § 314.80(c)(2).[3] Beginning in 1997, Merck commenced submitting such PSURs, which covered information about adverse drug reactions ("ADRs") and new scientific and medical literature on Propecia, including those involving depression and suicidality.[4]

II. 2010 CBE Supplement

In early 2010, the Swedish Medical Products Agency, a Swedish regulatory agency, asked Merck to "present a cumulative review of depression, including suicide related ADRs" in future PSURs. Merck agreed. In compiling the review, Merck searched the Worldwide Adverse Events ("WAES") database for depression and suicide related events since Propecia's approval up through April 30, 2010. After a review of the data, Merck recognized that it could not exclude a possible causal association between Propecia and "depression-related terms."

This left Merck facing an important decision regarding how to best meet its regulatory obligations. Under FDA regulations, it was required to ensure that its warnings regarding Propecia "remain adequate as long as the drug is on the market." Wyeth v. Levine, 555 U.S.

[3] FDA regulations require that drug manufacturers fully disclose all pertinent safety information, an obligation which applies both at the time of an initial approval, see, e.g., 21 C.F.R. § 314.50, and on an ongoing basis thereafter, see, e.g., 21 C.F.R § 314.81. Between 1997 and 2010, Merck submitted 24 PSURs.

[4] Additionally, in both 2000 and 2006, Merck submitted cumulative reviews to the FDA, which analyzed reports from Propecia patients from the date of market introduction.

555, 571 (2009). However, although it bore the primary "responsibility for the content of its label at all times," FDA regulations also forbid it from unilaterally altering Propecia's label in any respect without the express approval of the FDA. Id.

This rule against unilateral alteration is subject to one exception.[5] Drug manufacturers are permitted by the FDA to make changes to a product label prior to FDA approval in a process known as changes being effected ("CBE"). Using this process, a drug manufacturer may update its labeling of a drug to "add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion" where it has "newly acquired information." 21 C.F.R § 314.70(c)(6)(iii)(A). For the purposes of the CBE process, newly acquired information includes:

> [D]ata, analyses, or other information not previously submitted to the Agency, which may include (but is not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events, or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.

21 C.F.R. § 314.3(b). Where a manufacturer decides to follow the CBE process, the FDA allows it to implement labeling changes simultaneously with the submission of a supplemental application for changes to the FDA for review and approval (the "CBE supplement"). The FDA retains the authority to ultimately reject or otherwise modify the label change. See 21 C.F.R. § 314.70(c)(7).

Accordingly, on July 16, 2010, Merck decided to submit a CBE supplement to the FDA, and more specifically the Division of Dermatology and Dental Products ("DDDP"), requesting that it add "depression" to the Adverse Reaction ("AR") section of Propecia's label. This section

[5] Manufacturers may also file a "Prior Approval Supplement" requesting revisions to the label. See 21 C.F.R. § 314.70(b). Unlike the CBE process, this process necessitates FDA approval before implementation, and is more like the process for initial approval of a label.

of a drug's label lists "undesirable effect[s]" if "there is some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event." 21 C.F.R. § 201.57(c)(7). The AR section contains less serious warnings than those found in the W&P section, which include "clinically significant adverse reactions," where "there is reasonable evidence of a causal association." C.F.R. § 201.57(c)(6)(i).

To assist in the review of Merck's CBE, the DDDP asked the FDA's Division of Pharmacovigilance ("DPV") "to provide an assessment of [Merck's] request to add 'depression' to the Propecia product label." Rather than only relying on Merck's reports, the DVP also conducted its own research, which included analyzing all the reports of depression-related or suicide-related events associated with finasteride that were submitted to the FDA's Adverse Event Reporting System ("AERS") up until September 25, 2020. The DVP also undertook a "[search of] the medical literature (PubMed@FDA) on September 24, 2010 for case reports of depression-related or suicide-related adverse events associated with finasteride."[6]

Ultimately, the DVP concurred with Merck's "assessment to add depression to the Adverse Events, Postmarketing Experience section of the label." Although Merck did not request any other changes, the DPV, acting on its own accord, decided to also recommend adding "suicidal thoughts and behavior" to this same section.

Relying on the DVP's report, the DDDP reached the same conclusion regarding the addition of the depression warning. But the DDDP opposed adding the suicide warning. One reviewer, Dr. Woitach, found that (i) "[t]he number of suicide ideation, attempts and completed

[6] The DVP deemed cases to be suicide-related if they had a "temporal relationship between finasteride" and certain other factors, including "Completed suicide, Depression suicide, Intentional overdose, Intentional self-injury, Multiple drug overdose intentional, Poisoning deliberate, Self-injurious behavior, Self-injurious ideation, Suicidal behavior, Suicidal ideation, [or] Suicide Attempt." The DVP determined that 29 ADRs were suicide-related, with only 15 being tied to Propecia as opposed to Proscar. Of these, 2 were completed suicides, 1 was a suicide attempt, one was an intentional overdose, and the rest consisted of reports of suicidal ideation.

suicide [was] lower than would be expected" in the population; (ii) "[t]he two reported cases of completed suicide contain[ed] limited information," and one of them was "confounded with other potential life stressors"; and (iii) "[t]he relationship between depression potentially associated with Propecia and suicidality [was] difficult to assess," including because "[p]ublications report a difference in the nature of drug-induced depression and major depression." Dr. Woitach further concluded that, "[g]iven the few cases of completed suicide and the lack of temporal relationship with Propecia and suicide (as is seen for depression)" he did "not recommend including risk of suicide in the label at this juncture." A second DDDP reviewer concurred with his conclusion, finding that "adding suicide to the label is [not] warranted."

The FDA formally approved Merck's CBE supplement on March 11, 2011, without requiring additional changes. In informing Merck of the approval, the FDA did not share its underlying reports, or that it had rejected adding a warning regarding suicidality.

III. Post-CBE Supplement developments

After Merck submitted its CBE supplement, it continued to submit PSURs. Between 2010 and 2012, it disclosed 27 additional adverse event reports related to suicidality.

Research on depression and finasteride continued to progress as well. Between July 2010 and March 2012, seven medical and scientific studies were published on the topic.[7] Shortly thereafter, in August 2012, the first study to purportedly link finasteride and suicidality was

[7] Merck only disclosed one of these in a PSUR.

published by the Journal of Clinical Psychiatry.[8] The study was conducted between 2010 and 2011 by Dr. Michael Irwig. [9]

Irwig's study was followed in 2017 by an observational epidemiologic study designed to evaluate suicidality in men taking finasteride, and in particular whether the use of 5α-reductase inhibitors for the treatment of benign prostatic hyperplasia was associated with a risk of suicide, self-harm behavior, or depression.[10] Ultimately, this study found that although "[m]en who used 5αRIs were not at a significantly increased risk of suicide," the "[r]isk of self-harm was significantly increased during the initial 18 months after 5αRI initiation."

After the FDA's approval of Merck's CBE supplement in 2011, Merck did not request further modifications to the Propecia label with respect to depression or suicidality. However, in September 2017, the Post-Finasteride Syndrome Foundation ("PFS") filed a citizen petition with the FDA.[11] See 21 C.F.R. § 10.30. The group requested that the FDA either withdraw marketing approval for Propecia or order new labeling to strengthen or add warnings of "major depressive disorder and suicidal ideation." The primary basis for the petition's argument that suicidality should be added was the 2017 study, which petitioner noted was "the first study to firmly establish a statistically significant association between the use of 5αRIs and depression/suicidality."

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[8] M.S. Irwig, Depressive Symptoms and Suicidal Thoughts Among Former Users of Finasteride with Persistent Sexual Side Effects, 73 J. Clin. Psychiatry 1220 (2012).

[9] Although Merck discussed the study in its October 8, 2012, Proscar PSUR in response to a mandate from the FDA, it did not do so in its 2012 or 2013 PSURs.

[10] Welk B et al., Association of Suicidality and Depression With 5α-Reductase Inhibitors, JAMA Intern Med (2017), Vol. 177(5), pp. 683-691.

[11] PTS is a patient advocacy and research organization. See pfsfoundation.org.

The petition went unanswered for five years until, in 2022, the FDA responded.[12] Regarding the depression warning, the FDA determined that upgrading the warning to the W&P section was "not justified" because "[c]linicians and patients are adequately informed of the potential for major depressive disorder because it is listed within the" AR section. However, the FDA concluded that "based on our analysis contained in part and prompted by your Petition, including postmarketing reports", it was requiring the addition of "suicidal ideation/behavior" to the AR section of the label. The FDA believed the AR section was appropriate because "[b]ased on the mechanism of action of finasteride, there is a possible tie between Propecia and suicide related adverse events" but that it "could not conclude that there was reasonable evidence of a causal association."

IV. Pfaff's history with Propecia

Against this backdrop, the current lawsuit arises from one specific patient's experience with Propecia. Pfaff, the husband and father of plaintiffs Kelly, J.A.P., and C. P., was initially prescribed Propecia by his dermatologist in May 2008 for hair loss. He took the drug almost continuously up until February or March 2012. His last prescription was issued on January 17, 2012, well after the labeling change regarding depression took effect.

In 2009, Pfaff began to exhibit behavioral issues, which plaintiffs contend are tied to his use of Propecia. Over the next two years, he purportedly suffered from a variety of side effects including, among others, a "lack of sex drive, anxiety, depression," and "extreme insomnia, anger, suicide ideation, and social withdrawal." Pfaff ceased taking Propecia in early 2012, but

[12] The FDA's response to the citizen petition was while this motion was *sub judice*.

many of these side effects continued to worsen. He ultimately committed suicide on March 5, 2013.[13]

V. Procedural history

Plaintiffs filed their complaint in 2015 in the Southern District of California, asserting claims stemming from alleged deficiencies in Merck's labeling of Propecia with respect to depression and suicidality. Their claims included both strict liability and negligence for Merck's failure to warn of the "potential side effects of depression and suicide ideation" and breach of warranty claims, also premised on Merck's alleged failure to warn.[14] Plaintiffs argue that, beginning at the latest in May 2008, the Propecia label should have "warned specifically about depression and suicidality risks" in both the AR and W&P sections.

Subsequently, the action was transferred under 28 U.S.C. § 1407(c) to the Eastern District of New York pursuant to an order from the Judicial Panel on Multidistrict Litigation. It was joined to the In Re: Propecia (Finasteride) Products multidistrict litigation, then pending before this Court. In 2019, this Court approved the settlement and distribution of settlement funds in the MDL. Plaintiffs decided not to opt-in to the settlement, and the Court directed plaintiffs to show cause by why this case should not be returned to the Southern District of California. Ultimately, over plaintiffs' objections, this Court found that the case should remain in the Eastern District for all pretrial proceedings.

The parties went on to complete discovery, at the close of which Merck moved for partial summary judgment. This is the motion now before the Court.

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[13] The causes of Pfaff's suicide are disputed. Before Pfaff's suicide, he also took a drug called ciprofloxacin, the label of which indicated that it "may also cause . . . depression, and, rarely, suicidal thoughts or acts." However, these issues are not material for the purposes of the instant motion.

[14] Plaintiffs also bring derivative survivorship and wrongful death claims.

DISCUSSION

I. Applicable law

When determining questions of federal law, MDL transferee courts apply the law of the circuit in which it is located. See Menowitz v. Brown, 991 F.2d 36, 40 (2d Cir. 1993); see also In re Methyl Tertiary Butyl Ether ("MTBE") Prod. Liab. Litig., No. 00-md-1898, 2005 WL 106936, at *5 (S.D.N.Y. Jan. 18, 2005) ("district courts should apply the law of the transferee circuit."). Although the law of the Second Circuit is controlling for all issues of federal law raised in this motion, prudential concerns allow a federal court overseeing an MDL to "consult the law of the transferor circuit, given that the case will ultimately be remanded there for trial." In re Refco, Inc. Sec. Litig., 628 F. Supp. 2d 432, 439 (S.D.N.Y. 2008).

II. Preemption

In their complaint, plaintiffs allege that Merck is liable for its failure to adequately warn Pfaff about the risks of depression and suicidality associated with Propecia. Plaintiffs' claims all arise under California state law.[15] Under California law, drug manufacturers may be strictly, as well as negligently, liable "for injuries caused by their failure to provide adequate warnings of known or reasonably scientifically knowable dangers at the time they manufactured and distributed their product." Marroquin v. Pfizer, Inc., 367 F. Supp. 3d 1152, 1160 (E.D. Cal. 2019). Additionally, "breach of express or implied warranty claims . . . may [] be maintained against a manufacturer of prescription drugs who has [not] properly prepared the product and marketed it with warnings of known or knowable dangers." Hufft v. Horowitz, 4 Cal. App. 4th 8, 24, 5 Cal. Rptr. 2d 377, 387 (1992).

[15] For questions of state law, MDL transferee courts "must apply the state law that would have applied to the individual cases had they not been transferred for consolidation." In re Gen. Motors LLC Ignition Switch Litig., Nos. 14-md-2543 et al., 2017 WL 3382071, at *7 (S.D.N.Y. Aug. 3, 2017) (internal quotation marks omitted)).

Merck asserts that these claims are preempted, as it would have been impossible for it to comply with both these California law requirements and the FDA's regulatory scheme, which by strictly controlling drug labels, confines Merck's ability to act. See Gibbons v. Bristol-Myers Squibb Co., 919 F.3d 699, 707 (2d Cir. 2019) ("drug manufacturers are limited in their ability to unilaterally change the labels on their products"). Under the Supremacy Clause of the United States Constitution, "Congress has the power to preempt state law." Crosby v. Nat'l Foreign Trade Council, 530 U.S. 363, 372 (2000). Federal preemption occurs "when it is 'impossible for a private party to comply with both state and federal requirements.'" Merck Sharp & Dohme Corp. v. Albrecht, 139 S. Ct. 1668, 1672 (2019) (quoting Mutual Pharm. Co. v. Bartlett, 570 U.S. 472, 480 (2013)). The "same ordinary pre-emption principles [apply] whether the relevant federal law is a statute or a regulation." N.Y. Pet Welfare Ass'n, Inc. v. City of New York, 850 F.3d 79, 87 (2d Cir. 2017) (quotation marks omitted). There are three types of preemption: "(1) express preemption, where Congress has expressly preempted local law; (2) field preemption, where Congress has legislated so comprehensively that federal law occupies an entire field of regulation and leaves no room for state law; and (3) conflict preemption, where local law conflicts with federal law such that it is impossible for a party to comply with both[,] or the local law is an obstacle to the achievement of federal objectives." Figueroa v. Foster, 864 F.3d 222, 227-28 (2d Cir. 2017) (quotation marks omitted).

Merck relies on the third form of preemption analysis – conflict preemption – as the basis for its preemption argument. Generally, the party "asserting that federal law preempts state law bears the burden of establishing preemption." In re Methyl Tertiary Butyl Ether (MTBE) Prod. Liab. Litig., 725 F.3d 65, 96 (2d Cir. 2013). This burden is a demanding one and requires a showing that "compliance with federal and state law is an impossibility." Id. at 97 (quotation

marks omitted). This occurs, for example, when state law "penalizes what federal law requires," or when state law claims "directly conflict[ ] with federal law." Id. (quotation marks omitted).

In the instant case, the FDCA and FDA regulations require that the FDA approve a drug's exact initial label and significantly limit manufacturers' ability to update that label. Therefore, where plaintiffs' California state law failure-to-warn and breach of warranty claims directly conflict with this regulatory scheme, they are preempted.

But this is not the end of the inquiry "[b]ecause manufacturers may unilaterally update a drug's label if the change complies with the CBE regulation." Gibbons, 919 F.3d at 708.[16] Therefore, plaintiffs' claims will only be preempted where either: "(1) the CBE process was not available, and therefore [the drug manufacturer] could not make unilateral changes to the label, or (2) [a drug manufacturer] establishes by clear evidence that the FDA would not have approved the changes to the label that the plaintiffs contend should have been made." In re Zofran (Ondansetron) Prod. Liab. Litig., 541 F. Supp. 3d 164, 195 (D. Mass. 2021).

In the first scenario, the CBE process will not be available where a drug manufacturer does not have newly acquired information on which to base a request for a change. The burden falls on plaintiffs to identify such newly acquired information. See Gibbons, 919 F.3d at 708 ("to state a claim for failure-to-warn that is not preempted by the FDCA, a plaintiff must plead a labeling deficiency that [defendants] could have corrected using the CBE regulation.") (quotation marks omitted). Newly acquired information is information that "reveal[s] risks of a different type or greater severity or frequency than previously included in submissions to [the] FDA." 21 C.F.R. § 314.3(b). Importantly, "newly acquired information is not limited to new data, but also

[16] The "newly acquired information" standard was not added to the CBE regulation until 2008. Wyeth, 555 U.S. at 568.

encompasses new analyses of previously submitted data." Wyeth, 555 U.S. at 569 (internal quotation marks omitted). Still, the new analysis, and any new data, must reveal "risks of a different type or of greater severity or frequency" to constitute "newly acquired information." Id. (internal citation and quotation marks omitted).

Where a plaintiff can point to newly acquired information, and the CBE process would otherwise be available, the second scenario applies. Here, "the burden shifts to the party asserting a preemption defense to demonstrate that there is clear evidence that the FDA would not have approved a change to the [prescription drug's] label." Gibbons, 919 F.3d at 708 (quotation marks omitted). The issue of what constitutes "clear evidence" such that the FDA would not have approved the change is a "critical question not as a matter of fact for a jury but as a matter of law for the judge to decide." Albrecht, 139 S. Ct. at 1679. Clear evidence is evidence "that shows the court that the drug manufacturer fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the drug manufacturer that the FDA would not approve a change to the drug's label to include that warning." Id. at 1678. However, it need not be the drug manufacturer that requested the change. See In re Zofran, 541 F. Supp. 3d at 204 ("[p]reemption thus does not depend on whether the defendant manufacturer is the one who asked for the changes, or to which the FDA explicitly communicated its decision); see also In re Incretin-Based Therapies Prods. Liab. Litig., 524 F. Supp. 3d 1007, 1031-32 (S.D. Cal. 2021) (finding preemption based, in part, on the FDA's denial of a citizen petition.

Under this framework, plaintiffs' state law claims based on Merck's failure to upgrade the depression warning to the W&P section are clearly preempted. This is because the FDA has explicitly declined to require such a warning in its letter response to the September 2017 citizen

petition. There, the FDA unequivocally denied the petitioner's "request to add major depressive disorder to the [W&P] section of labeling." See Cerveny v. Aventis, Inc., 783 F. App'x 804, 808 (10th Cir. 2019) (noting, post-Albrecht, that the manufacturer had a "separate avenue [for establishing preemption] – the FDA's unequivocally having rejected [a] citizen petition advocating for the warning that the [plaintiffs] now assert").

The Court agrees with Merck that this is dispositive of the issue. No clearer evidence could be forthcoming that the FDA would not have approved the change in 2011 or anytime thereafter. Therefore, all of plaintiffs' state law claims relying on this alleged failure to warn are preempted.

III. Suicidality

This leaves plaintiffs' claims regarding suicidality. In 2022, the FDA determined that adding a warning for "suicidal ideation/behavior" in the AR section of Propecia's label was warranted, although inclusion of this warning in the W&P section was not. Therefore, for the same reasons as above, plaintiffs' claims regarding adding suicidality to the W&P section of the label are preempted.

Less clear is whether plaintiffs' claim surrounding the lack of a suicidality warning in the AR section is preempted. Considering that the FDA approved this change in 2022, the operative question becomes whether it was possible for Merck to make this change before Pfaff ceased using the drug in March 2012.

Merck's argument here proceeds in two parts. First, it contends that there is clear evidence that the FDA would have rejected a suicidality warning based on the information included in and evaluated during the FDA's review of its 2010 CBE supplement. Second, Merck argues that plaintiffs have also failed to point to any information that emerged thereafter until March 2012 that could be considered newly available information.

Merck's argument rests on certain "[f]reshly unredacted documents obtained through FOIA." They argue that these documents show that, in connection with its 2010 CBE supplement, "the FDA specifically considered . . . whether to add a suicide-related warning" and decided against it. Merck asserts that this rejection is therefore the "clear evidence" needed to determine that plaintiffs' claims on this ground – at least up until that point – were preempted.

As the Supreme Court recently articulated in Albrecht, clear evidence is evidence "that shows the court that the drug manufacturer fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the drug manufacturer that the FDA would not approve a change to the drug's label to include that warning." Albrecht, 139 S. Ct. at 1678.[17] When the FDA approved Merck's CBE supplement back in 2011, the FDA did not also inform the company that it would disapprove adding the unrequested suicidality warning. However, the FDA has since included documents in its response to the 2017 Citizen Petition, which make clear that, in retrospect, it would not have approved a suicidality warning in 2011.

Whether this is enough to constitute "inform[ing] the drug manufacturer" is an open question of law. Albrecht, 139 S. Ct. at 1672. In its most recent decision on the topic, the Supreme Court refused to opine on a precise disapproval method, noting only that it must consist of "agency actions taken pursuant to the FDA's congressionally delegated authority." Id. Courts have construed this to include the FDA's disapproval of a citizen's petition, as this is agency action undertaken pursuant to congressionally delegated authority. See Cerveny, 783 F. App'x at 808.

[17] Plaintiffs point out that Merck never actually requested a suicidality warning in its 2010 CBE supplement. The Court does not see why this matters. See In re Zofran, 541 F. Supp. at 204.

Merck's decision to rely on and incorporate these documents into the citizen petition was clearly lawful agency action. But the facts here are not nearly as neat as in Cerveny. The disapproval at issue occurred many years ago, and was merely illuminated by the citizen petition, rather than being resolved by it. When the FDA approved Merck's supplemental CBE in 2011, Merck was not aware of the impossibility of adding a suicidality warning under federal law. Instead, it simply got lucky when it first uncovered these documents through FOIA, and then again when the FDA later decided to rely on them in its partial rejection of the citizen petition.

Critically, however, courts have not construed impossibility preemption to turn on a private party's mental state regarding impossibility. Instead, it turns on whether, in fact, compliance with both state and federal regimes was legally impossible. See Grand River Enterprises Six Nations, Ltd. v. Boughton, 988 F.3d 114, 126 (2d Cir. 2021). Under this standard, the FDA adequately informed Merck of this decision.

Plaintiffs raise another point. The FDA's 2011 conclusion that the suicidality warning was unnecessary would typically be dispositive of the question of preemption, at least up until that point in time. However, to constitute clear evidence, "drug manufacturer[s]" must have also "fully informed the FDA of the justifications for the warning required by state law." Plaintiffs argue that Merck did not do so. Among the missing information, plaintiffs note that Merck's 2010 cumulative review did not include adverse event reports for Proscar, analyzed just six representative case reports "deemed by [Merck] to be of clinical significance," and did not discuss eight published studies purportedly relevant to depression or suicidality risk.

Plaintiffs' argument is unsupported by the record. First, an examination of the pertinent evidence reveals that the FDA was fully informed of much of this information when it completed its CBE review. Merck separately provided the FDA with adverse event reports relating to

Proscar and, further, the DVP also unequivocally stated that it included this information its analysis, as well as all other adverse event reports related to Propecia.

Additionally, to the extent the eight studies plaintiffs point to are relevant, only two include human subjects, both of which the FDA knew about. See McGrath v. Bayer HealthCare Pharms. Inc., 393 F. Supp. 3d 161, 169-70 (E.D.N.Y. 2019) (discounting the relevance of a "study performed on mice"). Moreover, none of these studies directly discussed or even mention suicidality, a point on which plaintiffs are silent. Therefore, as the FDA either knew of this information, or considered it immaterial, it is clear that the FDA was proceeding on a fully informed basis when it decided not to add the suicidality warning. Plaintiffs' claims up until July 2010 on this basis are preempted.

IV. Post-CBE Supplement claims

Plaintiffs also argue that after the FDA's rejection of a suicidality warning, newly acquired information available to Merck would not have allowed it to request changes.

Under Second Circuit precedent, it is plaintiffs' burden to first point to specific new information following Propecia's approval that would have justified a label change via the CBE regulation. Merck also must have been able to use such information to change the label in time to prevent Pfaff's injuries, as otherwise it would be irrelevant to the failure-to-warn claim. See Mahnke v. Bayer Corp., No. 19-cv-07271, 2020 WL 2048622, at *3 (C.D. Cal. March 10, 2020) ("This newly acquired information must have been available to Bayer after the FDA approved the relevant label on August 19, 2010, but before Plaintiff last used Magnevist on May 1, 2015."). Therefore, any newly acquired information must be from before March 2012, and after Merck submitted its CBE supplement in July 2010.

From this period, plaintiffs point out that Merck disclosed 27 new adverse event reports related to suicidality for both Propecia and Proscar. Additionally, they note that seven medical

and scientific studies were published during this period which could provide a basis for finding a link between finasteride use in men and depression.

None of this constitutes "newly acquired information" that would have permitted Merck to request a labeling change under the CBE process. First, for an adverse event to qualify as "newly acquired information" here, plaintiffs must have demonstrated that there is "some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event." 21 C.F.R. § 201.57(c)(7). Plaintiffs have not done so, only arguing in a wholly conclusory fashion that "[t]hese adverse events . . . indicate an increase in severity and frequency of the risks." Plaintiffs therefore provide nothing more than repetition of the standard that newly acquired information must reveal risks that are occurring at a "greater severity or frequency than previously included in submissions to FDA." 21 C.F.R. § 314.3(b). At the conclusion of discovery, much more is necessary for plaintiffs to meet their burden. Further, "[t]he fact that a user of a drug has suffered an adverse event, standing alone, does not mean that the drug caused that event." Matrixx Initiatives, Inc. v. Siracusano, 563 U.S. 27, 44 (2011); see also Gayle v. Pfizer Inc., 452 F. Supp. 3d 78, 88 (S.D.N.Y. 2020) ("adverse event reports" alone, "without any analysis indicating causality, cannot constitute 'newly acquired information'" sufficient to trigger a revised label).

Second, the seven studies plaintiffs point out also cannot constitute "newly acquired information" because, again, none of them even address suicidality. Plaintiffs assert that these articles provided "a substantial basis for finding a link between finasteride use in men and depression, and including moderate to severe depression, *which increases suicidality*." But this sort of conclusory statement is not enough to find a causal relationship.

To be fair, there are now studies that provide "some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event," 21 C.F.R. § 201.57(c)(7), by tying finasteride's "mechanism of action" to suicidality. This is why the FDA concluded in 2022 that "there was reasonable evidence of a causal association between Propecia and suicidality, the mechanism of action." But these studies were published after Pfaff ceased taking Propecia. See Knight v. Boehringer Ingelheim Pharms., Inc., 984 F.3d 329, 338 (4th Cir. 2021) ("by the date the paper was published, the information in it would not have made any difference to Knight").

Plaintiffs have failed to meet their burden to point to adequate newly acquired information. The CBE process would not have been available to Merck anytime prior to Pfaff's death. Their claims on this basis are also preempted.

CONCLUSION

Merck's motion for partial summary judgment is GRANTED. The parties are directed, within one week of this decision, to provide the Court with a status report concerning the disposition of the remaining claims.

SO ORDERED.

Digitally signed by Brian M. Cogan

U.S.D.J.

Dated: Brooklyn, New York
September 8, 2022