UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

IN RE MIRENA IUD PRODUCTS LIABILITY LITIGATION	)	
	)	
	)	**No.: 13 MD 2434 (CS)**
***This Document Relates to*:**	)	
	)	
***Jennifer Danley v. Bayer*, 13-cv-06586-CS**	)	
***Christie Hayes v. Bayer*, 14-cv-00288-CS**	)	
	)	

PLAINTIFFS' MEMORANDUM OF LAW IN SUPPORT OF THEIR MOTION FOR SUMMARY JUDGMENT ON DEFENDANT'S AFFIRMATIVE DEFENSE OF PREEMPTION

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Plaintiffs have filed this Motion for Summary Judgment on the Affirmative Defense of Preemption to narrow the issues for trial in all Mirena cases. The preemption defense asserted by Defendants (collectively, "Bayer" or "Defendant")[1] cannot be supported under the applicable facts and law, and should be stricken.

I. INTRODUCTION

Plaintiffs have brought failure-to-warn claims pursuant to state law because Bayer's warnings are inadequate regarding the risks that Mirena can migrate and perforate the uterus after it is inserted. Bayer has pled that federal law prohibits such state law failure-to-warn claims through the doctrine of federal preemption.[2] Defendant's preemption affirmative defense invokes conflict preemption based on impossibility, which exists only when "compliance with both federal and state regulations is a physical impossibility." *Arizona v. United States*, 567 U.S. ___, 132 S. Ct. 2492, 2500-01 (2012) (quoting *Florida Lime & Avocado Growers, Inc. v. Paul*, 373

[1] For convenience, the Bayer Defendants will be referred to in the singular throughout this memorandum, and references to "Bayer" or "Defendant" will include reference to Berlex and other related entities.

[2] *See* Ex. 1 (Bayer's Answer to First Amended Complaint, p. 21, ¶ 139 and p. 27, ¶ 169, filed November 2, 2015 in *Bryttany Wright v. Bayer Healthcare Pharmaceuticals Inc., et al.*, Docket No. BER-L-4690-13 (N.J. Superior Court, Bergen County). (All references to "Ex. __" are to exhibits annexed to the accompanying Declaration of Diogenes P. Kekatos, dated November 17, 2015.)

Bayer has not yet filed Answers in this MDL, but both the courts and all counsel have engaged in informal coordination between the Mirena MDL and New Jersey Multi-County Mirena litigations from their inception. Bayer's preemption defenses will presumably be the same in both courts. Nonetheless, if Bayer does not assert preemption as an affirmative defense in the MDL, this motion will be withdrawn. Similarly, if Bayer raises a preemption defense inconsistent with its defenses in the cognate New Jersey litigation, or if the Court simply prefers to defer Plaintiffs' preemption-based summary judgment motion in this MDL until Bayer has formally answered the Initial Disposition Pool Plaintiffs' complaints, this motion will be withdrawn and refiled at such time as the Court directs.

U.S. 132, 142-43 (1963)).

To succeed with a federal preemption defense in a pharmaceutical failure-to-warn case, the manufacturer must prove by "clear evidence"[3] that if it had added the type of warning sought by plaintiffs, the U.S. Food and Drug Administration ("FDA") would have rejected the warning and made the manufacturer remove it. *Wyeth v. Levine*, 555 U.S. 555, 571 (2009); *see also Pliva, Inc. v. Mensing*, 564 U.S. ___,131 S. Ct. 2567, 2581 n.8 (2011) ("Wyeth could have attempted to show by 'clear evidence' that the FDA would have rescinded any change in the label and thereby demonstrate that it would in fact have been impossible to do under federal law what state law required.").

Bayer's warnings for Mirena have never addressed the risks of migration and perforation as clearly and strongly as the warnings used by other IUD manufacturers, and despite others having warned about the risks of secondary perforation, Bayer has never done so.[4] Bayer has been quick to respond that its conduct is justified because FDA has edited some of its proposed Mirena warnings, but Bayer has never questioned FDA about those edits; has never pointed FDA staff to the FDA-approved language used by other IUD manufacturers that justifies stronger warnings for Mirena; and has never engaged FDA in discussions about strengthening its migration and perforation warnings for Mirena.

There is no "clear evidence" that FDA would have rejected stronger warnings for Mirena regarding migration and perforation. To the contrary, the existence of stronger FDA-approved

[3] The Supreme Court has used the term "clear evidence" to mean "clear and convincing." *E.g.*, *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. ___, 131 S. Ct. 2238, 2243 (2011).

[4] Secondary perforation has been used by the parties as shorthand for a uterine perforation that occurs after insertion of Mirena and is unrelated to any injury occurring at the time of insertion. As discussed further below in Part II(H), Bayer's regulatory experts have both admitted that Bayer has *never attempted to include a secondary perforation warning* in its Mirena label.

warnings used by other manufacturers for comparable IUDs provides clear evidence that Bayer could easily have strengthened its Mirena warnings, simply by asking FDA to review the warnings it had approved for others and requesting similar warnings for Mirena. Because it would not have been "impossible" for Bayer to comply with both its state and federal warning obligations, the "impossibility preemption" argument must fail. Plaintiffs are entitled to summary judgment striking Bayer's preemption affirmative defense.

II. STATEMENT OF FACTS

The following summary is drawn from Plaintiffs' Local Civil Rule 56.1(a) Statement of Undisputed Material Facts ("SUMF"), filed contemporaneously with this motion.

A. General Overview of Mirena

Mirena is an intrauterine device ("IUD") used primarily for birth control, though it can also be prescribed for heavy menstrual bleeding. It is sometimes referred to as a "hormonal IUD" or an "intrauterine system" ("IUS") because it incorporates a birth control hormone, levonorgesterel, which is slowly released in the uterus. When Mirena is properly inserted and remains correctly positioned in the uterus, it can provide effective birth control protection for up to five years. Mirena is manufactured by Bayer and has been sold in the United States since it was approved by the FDA in December 2000. More than two million women in the United States use Mirena. SUMF ¶¶ 1-4.

B. The ParaGard and Progestasert IUDs are Comparable to Mirena

At the time of Mirena's approval, there were only two other IUDs approved by the FDA and sold in the United States:

> **IUDs currently approved in the U.S. are the ParaGard T 380A IUD**, a copper-containing IUD providing 10 years of contraception, **and the Progestasert**, a progesterone-containing IUD providing 1 year of contraception.

Ex. 4 (FDA Medical Review for Mirena, NDA 21-225, p. 11) (emphasis added); SUMF ¶ 5. Although ParaGard and Progestasert are not identical to Mirena, FDA understood that both of those IUDs were comparable to Mirena, and recommended that their warnings – whether for migration, perforation, or other risks – be included on the Mirena label:

> **Recommended warnings include the warnings that are currently on the USA labels for the other two USA-approved IUDs….**

Ex. 4 (FDA Medical Review for Mirena, NDA 21-225, p. 6) (emphasis added); SUMF ¶ 6.

[redacted]

At the time of Mirena's approval in 2000, the ParaGard label had an FDA-approved warning for migration: **"There are reports of IUD migration after insertion."** Ex. 10 (1997 ParaGard label) (emphasis added); SUMF ¶ 8. A modification of the ParaGard migration warning was approved by FDA in 2005. The warning was changed to: "Spontaneous migration has also been reported." Ex. 11 (2005 ParaGard label); SUMF ¶ 8. ParaGard's spontaneous migration warning remains unchanged today. Ex. 12 (2013 ParaGard label); SUMF ¶ 8.

When Mirena was approved, the Progestasert label carried FDA-approved language in the Patient Information section, informing women that **"Partial or total perforation of the uterus may occur *at the time of or after* PROGESTASERT system insertion."** Ex. 13 (1987 Progestasert label) (emphasis added); SUMF, ¶ 9. The FDA had approved Progestasert in 1976 and it was discontinued in the U.S. market in 2001. SUMF ¶ 9.

C. Original Perforation Warnings for Mirena (2000)

The relevant part of the perforation warning that Bayer originally proposed for Mirena

read as follows:

[redacted] This language was based on the then-current ParaGard label. [redacted] Ex. 10 (1997 ParaGard label); SUMF ¶ 11. Although Bayer's proposed language was ambiguous, the use of the terms "most often during insertion" at least *suggested* that while perforation occurred most frequently during insertion, it could also occur *after* insertion. FDA left that language in place, but proposed striking the sentence referring to "reports of IUD migration after insertion." Ex. 15; SUMF ¶ 10. That sentence was a verbatim quote of the FDA-approved language from the ParaGard label. *See* Section II(B), *supra*.

Bayer did not engage the FDA in a dialogue about the perforation warnings. It did not question the agency about its proposal to strike the migration language; nor did Bayer point out that the FDA-approved warnings for ParaGard – which the FDA had explicitly recommended be included in the Mirena label – contained language identical to the sentence FDA proposed striking from the Mirena label. SUMF ¶¶ 12-14. Bayer also neglected to mention that the Patient Information section of the FDA-approved label for the other comparable IUD, Progestasert, stated that partial or total perforations could occur "at the time of *or after*" insertion. SUMF ¶ 15.

D. Revised Perforation Warnings for Mirena (2008)

In 2008, Bayer proposed the following language as part of the "Perforation" section of the Mirena label:

[redacted] SUMF ¶ 16. This time, FDA proposed striking the "rarely, most often" language. The FDA's suggested edit was accompanied by a comment stating in part: "We recommend against using nonspecific terms." *Id.* Again, Bayer did not engage in discussions with FDA about the perforation warnings. It did not question the agency about its proposed edits or direct the FDA's attention to the labels for either ParaGard or Progestasert. SUMF ¶ 17.

E. Perforation Warnings for Bayer's "Skyla" IUD (2013)

In January 2013, Bayer received FDA approval for Skyla, a slightly smaller version of the Mirena IUD. Skyla is said to provide contraceptive protection for up to three years. The "Perforation" section of the original Skyla label contained the following language:

> Perforation (total or partial, including penetration/embedment of Skyla in the uterine wall or cervix) *may occur most often during insertion*, although the perforation may not be detected until sometime later.

Ex. 21 (Skyla label, Jan. 2013) (emphasis added); SUMF ¶ 18. This perforation language remains unchanged in the Skyla label today. *Id.*

F. Revised Perforation Warnings for Mirena (2014)

After Skyla's approval, the language referenced immediately above was substituted for the language then being used in the "Perforation" section of Mirena's label. The FDA approved this language in May 2014, and it was identical to that used for Skyla, save the substitution of "Mirena" in place of "Skyla":

> Perforation (total or partial, including penetration/embedment of Mirena in the uterine wall or cervix) *may occur most often during insertion*, although the perforation may not be detected until sometime later.

Ex. 23 (Mirena label, May 2014) (emphasis added); SUMF ¶ 19. The perforation language approved in May 2014 remains unchanged in Mirena's label today. Ex. 2.

G. Bayer's Knowledge of the Risk of Secondary Perforation

Bayer has long been aware of the risk of secondary perforation and the potential mechanism for causing it. This dates back at least to 2000, when Mirena entered the U.S. market. In [redacted] Another email sent over a decade ago was even more explicit:

[redacted]

Id. at 7. [redacted]

[redacted]

[redacted] Of course, this suggested label change was shelved by Bayer, and was never implemented or even proposed to FDA. To this day, the risk of spontaneous perforation has never been communicated to the millions of women who use Mirena, or to the physicians who prescribe it.

H. Bayer Has Never Tried to Warn of the Risk of Secondary Perforation

Despite Bayer's knowledge of the risk of secondary perforation, [redacted] Accordingly, there are no statements of record from the FDA as to how it may respond or what its reasoning

may be when Bayer puts the subject of warnings for secondary perforation before it. That has been true since Mirena was approved in 2000, and it remains true today.

III. ARGUMENT

BAYER'S PREEMPTION DEFENSE FAILS AS A MATTER OF LAW

A. Standard for Summary Judgment

Summary judgment is appropriate if the movant establishes there is no genuine dispute as to any material fact and the moving party is entitled to judgment as a matter of law. Fed. R. Civ. P. 56(a). A genuine issue of material fact exists only whe n the evidence is such that a reasonable fact finder could return a verdict for the nonmoving party. *Magan v. Lufthansa German Airlines*, 339 F.3d 158, 161 (2d Cir. 2003). Although the evidence is viewed in the light most favorable to the non-moving party, once the moving party has satisfied its burden, it is entitled to summary judgment if the non-moving party fails to present "specific facts showing that there is a genuine issue for trial." *Celotex Corp. v. Catrett*, 477 U.S. 317, 324 (1986). "Conclusory allegations, conjecture, and speculation … are insufficient to create a genuine issue of fact." *Kerzer v. Kingly Mfg.*, 156 F.3d 396, 400 (2d Cir. 1998) (citation omitted).

In the context of a plaintiff's motion for summary judgment on the affirmative defense of federal preemption, "defendants' speculation regarding how the FDA would have viewed [a proposed warning] does not constitute clear evidence that the FDA would have rejected the particular warning at issue[.]" *Koho v. Forest Labs., Inc.*, 17 F. Supp. 3d 1109, 1119 (W.D. Wash. 2014). It is not enough for the manufacturer to offer "theoretical assumptions" or "possibilities" about what the FDA may have done in response to a proposed label change. *Id.*, citing *Dorsett v. Sandoz, Inc.*, 699 F. Supp. 2d 1142, 1159 (C.D. Cal. 2010).

B. Federal Regulation of Drug Labeling

All prescription drugs sold in the United States must have labeling that provides adequate information about the risks of using the drug, for the benefit of prescribers and patients.[5] Federal law bars the sale of a drug, and deems it misbranded, if its labeling lacks "adequate warnings against use . . . where its use may be dangerous to health." 21 U.S.C. § 352(f). Adequate drug labeling must include information concerning, *inter alia*, a drug's approved indications and usage, dosage and administration, contraindications, warnings and precautions, and adverse reactions. 21 C.F.R. § 201.57(c)(2)-(7).

Knowledge about a drug's risks and benefits grows over time, especially after its marketing has begun. It is "a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times. It 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." *Levine*, 555 U.S. at 570-71; *see also id.* at 579 (drug manufacturers "bear primary responsibility for their drug labeling at all times").

Although the FDA has the final authority to approve or disapprove drug labeling, FDA regulations permit a manufacturer to "add or strengthen a contraindication, warning, precaution, or adverse reaction" for its drug's labeling without awaiting prior approval from the agency. 21 C.F.R. § 314.70(c)(6)(iii)(A). The manufacturer does so by filing a Changes Being Effected ("CBE") supplement with the FDA, notifying the agency of the labeling change at the same time the manufacturer puts the new labeling into service. *Id.* A drug's labeling "must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of

[5] Mirena was approved as a drug, not a device, under section 505(b) of the Food, Drug and Cosmetic Act ("FDCA"), because it emits levonorgestrel, a synthetic progestogen.

a causal association with a drug; a causal relationship need not have been definitely established." 21 C.F.R. § 201.57(c)(6)(i).

C. State Law Failure-to-Warn Litigation Does Not Conflict with Federal Regulation of Prescription Drugs

The FDCA, codified at 21 U.S.C. § 301 *et seq*., reflects the judgment of Congress and the traditional view of the FDA that state law failure-to-warn claims do not conflict with federal regulation of the drug industry but, rather, complement such regulation. *Levine*, 555 U.S. at 579. For decades, patients injured by prescription drugs successfully brought state law failure-to-warn claims against drug companies, with little or no suggestion that federal law preempted those claims. In the early 2000s, however, the FDA did a temporary about-face, arguing that "FDA approval of labeling . . . preempts conflicting or contrary State law." *Id*. at 575 (quoting preamble of FDA regulation at 71 Fed. Reg. 3922, 3934 (2006)). The thrust of the FDA's argument at that time was that its approval of a drug's label reflected a careful balancing of risks and benefits, and that state law should not be allowed to question the adequacy of an FDA-approved label. The Supreme Court squarely rejected this argument in *Levine*.

The Court made clear in *Levine* that while federal law controls the FDA's approval of drugs for marketing purposes, FDA approval "does not represent a finding that the drug, as labeled, can never be deemed unsafe by later federal action, or … the application of state law." *Levine*, 555 U.S. at 592 (Thomas, J., concurring). It is well understood that drug labels evolve because "risk information accumulates over time and . . . the same data may take on a different meaning in light of subsequent developments." *Id*. at 569.

D. Plaintiffs Are Entitled to Summary Judgment on Bayer's Affirmative Defense of Federal Preemption

There is no genuine dispute of material fact regarding the absence of "clear evidence"

that FDA would have prevented Bayer from adding clearer and stronger migration and perforation warnings to the Mirena label, or that the FDA would have prevented Bayer from adding a warning about secondary perforation. Because Bayer cannot make the required "clear evidence" showing, Plaintiffs are entitled to judgment as a matter of law on the preemption defense. *See, e.g., Koho*, 17 F. Supp. 3d at 1119; *Bennett v. Forest Labs.*, 2015 WL 1418444, at *5 (M.D. Fla. Mar. 27, 2015) (collecting cases where "preemption is not a viable defense").

Bayer has asserted two separate affirmative defenses regarding preemption. Each will be separately addressed below.

1. PLAINTIFFS ARE ENTITLED TO JUDGMENT ON BAYER'S ARGUMENT THAT THE FDA'S THOROUGHLY DISCREDITED 2006 LABELING "PREAMBLE" HAS PREEMPTIVE EFFECT

In an unusual twist, Bayer has tried to revive the "preamble" argument. This was a short-lived preemption defense raised by drug manufacturers from 2006 until 2009, when the Supreme Court firmly rejected it in the *Levine* case. The defense is meritless and – until now – has not appeared since *Levine*. Bayer contends:

> Plaintiff's claims are preempted, in whole or in part, by reason of the FDA's preamble to the *Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products*, 71 Fed. Reg. 3922 (Jan. 24, 2006).

Ex. 1 (Bayer's Answer in the *Wright* case, Separate Defense Fifty-Five, p. 27, ¶ 169). This is exactly what Wyeth contended in *Levine*. The Supreme Court summarized Wyeth's "preamble" argument as follows:

> Wyeth … maintains that, because the FDCA requires the FDA to determine that a drug is safe and effective under the conditions set forth in its labeling, the agency must be presumed to have performed a precise balancing of risks and benefits and to have established a specific labeling standard that leaves no room for different state-law judgments. In advancing this argument, **Wyeth relies not on any statement by Congress, but instead on the preamble to a 2006 FDA regulation governing the content and format of prescription drug labels.** See Brief for Petitioner 8, 11, 42, 45, and 50 **(citing 71 Fed. Reg. 3922 (2006)). In**

> **that preamble, the FDA declared that the FDCA establishes "both a 'floor' and a 'ceiling,' " so that "FDA approval of labeling ... preempts conflicting or contrary State law."** *Id.*, at 3934-3935. It further stated that certain state-law actions, such as those involving failure-to-warn claims, "threaten FDA's statutorily prescribed role as the expert Federal agency responsible for evaluating and regulating drugs." *Id.*, at 3935.

Levine, 555 U.S. at 575-76 (emphasis added).

The Supreme Court addressed Wyeth's argument by first noting that while "agency regulation with the force of law can pre-empt conflicting state requirements," *id*. at 576, the preamble did *not* have the force of law but, rather, was "an agency's mere assertion that state law is an obstacle to achieving its statutory objectives." *Id*. The Court continued:

> **Further, the preamble is at odds with what evidence we have of Congress' purposes, and it reverses the FDA's own longstanding position without providing a reasoned explanation, including any discussion of how state law has interfered with the FDA's regulation of drug labeling during decades of coexistence. . . .** For instance, in 1998, the FDA stated that it did "not believe that the evolution of state tort law [would] cause the development of standards that would be at odds with the agency's regulations." It further noted that, in establishing "minimal standards" for drug labels, it did not intend "to preclude the states from imposing additional labeling requirements."

Levine, 555 U.S. at 577-78 (internal citations and footnote omitted; emphasis added). The Supreme Court held that **"the FDA's 2006 preamble *does not merit deference*,"** *id*. at 577 (emphasis added), and noted:

> Wyeth has not persuaded us that failure-to-warn claims like Levine's obstruct the federal regulation of drug labeling. Congress has repeatedly declined to pre-empt state law, and the **FDA's recently adopted position that state tort suits interfere with its statutory mandate is entitled to no weight.**

Id. at 581 (emphasis added); *accord N.Y. SMSA Ltd. P'ship v. Town of Clarkstown*, 603 F. Supp. 2d 715, 717 (S.D.N.Y. 2009) (quoting *Levine*, three weeks after the decision, for the proposition that the subject FDA preamble "does not merit deference"), *aff'd*, 612 F.3d 97 (2d Cir. 2010).

The "preamble" defense asserted by Bayer was thoroughly analyzed and completely rejected by the U.S. Supreme Court over five years ago in *Levine*, and the effect of that decision

was immediately recognized by the courts in this district. Bayer's "preamble" defense is dead and should not have been raised here at all, but having been raised, it must again be rejected.

2. PLAINTIFFS ARE ENTITLED TO JUDGMENT ON BAYER'S ARGUMENT THAT THEIR CLAIMS ARE PREEMPTED UNDER THE SUPREMACY CLAUSE

In addition to its "preamble" argument, Bayer asserted in more general terms that all of Plaintiffs' claims are preempted under the Supremacy Clause:

> Plaintiff's claims are preempted, in whole or in part, by federal law pursuant to the Supremacy Clause of the United States Constitution by reason of the federal government's regulation of the manufacturing, testing, marketing, sale and labeling of prescription drugs.

Ex. 1 (Bayer's Answer in the *Wright* case, Separate Defense Twenty-Five, p. 21, ¶ 139). This argument also fails under the facts of this case and the rules laid down in *Levine*.

a. Bayer Cannot Show by "Clear Evidence" that the FDA Would Have Rejected Warnings for Mirena Regarding Migration

There is no genuine dispute that the FDA has approved warnings regarding migration for comparable IUDs, and that Mirena's label does not have a migration warning. An FDA-approved migration warning has been part of the ParaGard IUD's label for approximately 20 years. *See* Section II(B), *supra*. The FDA specifically recommended that Mirena's label include the ParaGard warnings, and Bayer's experts admit that these IUDs have similar perforation risks. *Id*. A migration warning should have been incorporated in Mirena's label because common sense alone suggests that there are women who would choose to monitor their IUD more carefully if they knew that spontaneous migration was a risk, while others would avoid the uncertainty associated with that risk by choosing not to use Mirena at all.

Bayer may argue that claims regarding migration are preempted because it included a migration warning 15 years ago in its original proposed label for Mirena, and the FDA requested

the removal of that language. *See* Section II(C), *supra*.[6] Bayer simply accepted FDA's proposed edit, and did not direct FDA's attention to the FDA-approved ParaGard warning about migration, or even bother to discuss the matter with FDA. That does not provide "clear evidence" that it would have been impossible for Bayer to add the migration warning. It simply shows that Bayer made virtually no effort to bring its Mirena warnings up to industry standards. As demonstrated in *Levine*, a manufacturer's *lack of serious effort to warn* does not preempt a state law failure-to-warn claim.

A review of the *Levine* facts is instructive. In *Levine*, the plaintiff was injured by an "IV-push injection" of Phenergan in 2000, and plaintiff "alleged that the labeling was defective because it failed to instruct clinicians to use the IV-drip method of intravenous administration instead of the higher risk IV-push method." *Levine*, 555 U.S. at 560. As the Supreme Court recounted, Wyeth had long been conferring with the FDA about the labeling for IV-push injection. After adverse events involving IV-push injection were reported to Wyeth in 1967, "it notified the FDA and worked with the agency to change Phenergan's label." *Id.* at 569. Thereafter, "Wyeth and the FDA intermittently corresponded about Phenergan's label." *Id.* at 561. As the Court described:

> The most notable activity occurred in 1987, when the FDA suggested different warnings about the risk of arterial exposure, and in 1988, when Wyeth submitted revised labeling incorporating the proposed changes. The FDA did not respond. Instead, in 1996, it requested from Wyeth the labeling then in use and, without addressing Wyeth's 1988 submission, instructed it to "[r]etain verbiage in current label" regarding intra-arterial injection.

Id. at 561-62. Despite Wyeth's reporting to the FDA of adverse events and Wyeth's conferring

[6] Bayer has previously indicated that it may raise this defense. *E.g.*, Bayer's Preliminary Position Statement, dated May 10, 2013 (ECF No. 80), at p. 4 (claiming that "FDA carefully considered and edited the warning language").

with the FDA with regard to IV-push injection warnings, the Supreme Court nonetheless rejected "Wyeth's contention that the FDA would have prevented it from adding a stronger warning about the IV-push method of intravenous administration." *Id.* at 572.

In the instant case, there is no question that Bayer's effort to warn about migration falls far short of the efforts Wyeth made to provide an adequate warning in *Levine*. Bayer has done *nothing* to secure a migration warning since its original proposed language was edited by FDA over 15 years ago. It is undisputed that Bayer has since received many adverse event reports for Mirena that reference "migration" after insertion:

[redacted] The same type of adverse event reports were what led to the FDA-approved warning for ParaGard regarding the risk of spontaneous migration. There is no meaningful likelihood that FDA would reject a similar migration warning for Mirena if Bayer directed FDA's attention to the ParaGard label. All of the parties to this dispute agree that ParaGard is a comparable product for this purpose, and ParaGard *already has an FDA-approved migration warning*.[7]

Under these facts, Bayer cannot show by "clear evidence" or otherwise that FDA would have rejected a migration warning for Mirena. Plaintiffs' migration claims are not preempted.

[7] If, as Bayer appears to contend, migration warnings were actually *inappropriate* for IUDs, FDA would have been required to bring an enforcement action against the maker of ParaGard to force the removal of its migration warning. That has not happened, and in light of the continuing stream of adverse event reports of IUD migration, there is no basis to think it ever will.

b. Bayer Cannot Show by "Clear Evidence" that the FDA Would Have Rejected Clearer and Stronger Warnings for Mirena Regarding Perforation

There is also no genuine dispute that FDA has approved clearer and stronger warnings regarding perforation for comparable IUDs, and that Mirena's label does not have such warnings. The Progestasert IUD label made it clear that perforation could occur "at the time of ***or after***" insertion. Ex. 13 (1987 Progestasert label; emphasis added); SUMF ¶ 9. Until Mirena's label was revised in 2008, it at least warned that perforation occurred "most often" at insertion. *See* Sections II(C)-(D), *supra*. The FDA proposed the removal of that language – again with no protest or discussion by Bayer – when Bayer attempted to limit the warning by adding the qualifier "rarely" to it in 2008. *Id*. The "most often" language was added back to Mirena's label again in 2014, but there is no "clear evidence" that FDA would have rejected that language in the 2008-14 time-frame if Bayer had requested it. Bayer never engaged in label negotiations with FDA, and there is no record of any intent by FDA to categorically prohibit the "most often" language. *Id*. Any speculation by Bayer to the contrary "does not constitute clear evidence that the FDA would have rejected the particular warning at issue[.]" *Koho*, 17 F. Supp. 3d at 1119.

Accordingly, as with the migration warning discussed immediately above, Bayer made no meaningful effort to provide an adequate warning regarding perforation. Bayer cannot produce "clear evidence," as required by *Levine*, that the FDA would have rejected an appropriate perforation warning for Mirena. Plaintiffs' perforation claims are not preempted.

c. Bayer Cannot Show by "Clear Evidence" that the FDA Would Have Rejected a Warning for Mirena Regarding Secondary Perforation

Finally, there is no genuine dispute that the FDA has approved secondary perforation

warnings for comparable IUDs. These warnings inform physicians and patients that partial or total uterine perforations can occur *after* insertion of the IUD, with no suggestion that such perforations are related in any way to injury occurring at insertion:

> Partial or total perforation of the uterus may occur ***at the time of or after*** PROGESTASERT system insertion.

Ex. 13 (1987 Progestasert label) (emphasis added). There is no evidence that Bayer has ever requested such a secondary perforation warning from FDA, and there is no "clear evidence" that FDA would reject that warning if requested – particularly in light of the *FDA-approved* warning used in the Progestasert label.

The lack of "clear evidence" that FDA would reject a secondary perforation warning is particularly compelling here because Bayer has known about the risk of secondary perforation for many years (*see* Section II(G), *supra*), yet has not presented any analysis of that risk to the FDA. In *Levine*, Wyeth had, in fact, taken the issue to the FDA on multiple occasions, but the Supreme Court still rejected its suggestion that the agency's refusal to act constituted clear evidence of FDA's intent to prohibit a stronger warning. *See* Section III(D)(2)(c), *supra*. In this case, there is no sign that Bayer ever "supplied the FDA with an evaluation or analysis" regarding the risk at issue, as required by *Levine*. 555 U.S. at 572-73; *see also McCarrell v. Hoffman-La Roche, Inc.*, 2009 WL 614484 (N.J. Super Ct. App. Div. Mar. 12, 2009) (unpublished) (to prevail on preemption defense in failure-to-warn case under *Levine*, drug manufacturer must "establish whether it advocated [for a] stronger warning"). It is undisputed that Bayer did not "advocate" at all. It simply accepted FDA's edits and swept the issue under the rug. That negates any preemption defense.

The lesson of *Levine* is clear: a manufacturer that has not made a serious effort to warn cannot look to the *absence* of a warning on its label and declare the plaintiffs' failure-to-warn

claims "preempted." As Mirena's manufacturer, Bayer has "responsibility for the content of its label at all times." *Levine*, 555 U.S. at 570-71. Bayer has failed to maintain Mirena's warnings even in accordance with the industry standards of its competitors. There is no basis – and certainly no "clear evidence" – for an assertion that FDA would have prohibited Bayer from doing so. Plaintiffs' secondary perforation claim is therefore not preempted.

IV. CONCLUSION

For the reasons set forth above, there is no genuine dispute of material fact concerning Bayer's inability to show "clear evidence" that the FDA would have rejected appropriate warnings for Mirena regarding migration and perforation. Such warnings were already on the FDA-approved labels of comparable IUDs. Bayer's failure to confer with FDA about those warnings, and its failure to advocate for such warnings on the Mirena label, bar any "preemption" defense. Accordingly, the Court should grant summary judgment in Plaintiffs' favor on the affirmative defense of federal preemption.

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Respectfully submitted,

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