UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

IN RE : ZOFRAN® (ONDANSETRON) PRODUCTS LIABILITY LITIGATION	**MDL No. 1:15-md-2657-FDS** **This document relates to:** ***All Actions***

GSK'S MEMORANDUM REGARDING
MERCK SHARP & DOHME CORP. V. ALBRECHT

In response to the Court's minute order of May 20, 2019, GSK respectfully submits this memorandum regarding how the Court should proceed in light of the Supreme Court's decision in *Merck Sharp & Dohme Corp. v. Albrecht*, which reversed the decision of the Third Circuit and held that preemption questions such as those presented here are for the court, not the jury. GSK respectfully proposes to resolve the preemption defense by way of a renewed summary judgment motion based on the now-existing evidentiary record. The Supreme Court's holding in *Merck* that preemption is a matter of law for the court is a foundational change from this Court's approach in its February 5, 2019 order denying summary judgment on preemption grounds. Plaintiffs acknowledge that the FDA repeatedly rejected their proposed labeling change but claim that the FDA lacked four categories of information. This Court held that the materiality of those four categories was a question for the jury at trial. The Supreme Court has now made clear that this Court, not the jury, must resolve the materiality of such information. In short, because the preemption question in this case "involves the use of legal skills to determine whether agency disapproval fits facts that are not in dispute," *Merck* slip op. at 15-16, preemption is now ripe for resolution by the Court.

Determining whether the FDA was "fully informed . . . of the justifications" for Plaintiffs' desired warning, *id.* at 13, requires the Court to apply FDA regulations to determine whether Plaintiffs' four categories of information are material information that justify a labeling change. That legal inquiry can and should be resolved by way of summary judgment. And because the fundamental question before this Court is one of law, not fact, a bench trial—which this Court has acknowledged would be "lengthy," ECF No. 1325 at 32—is unnecessary and would be an inefficient way to resolve this legal question.

Although GSK believes that the legal question before the Court is not difficult or subject to reasonable debate, if the Court does not grant summary judgment to GSK, it should refer the matter to the FDA under the doctrine of primary jurisdiction. If Plaintiffs truly believe that their four categories of information would have made a difference to the FDA, they could have submitted a citizen petition to the FDA requesting a labeling change based on that information. Surely Plaintiffs should heartily embrace hearing from the FDA on this issue. Their failure to solicit the FDA's views is telling.

ARGUMENT

I. The Court Should Decide the Preemption Question by Way of a Renewed Summary Judgment Motion.

A. As this Court previously acknowledged, "a drug manufacturer may prevail on a preemption defense if (1) the CBE [changes-being effected] process was not available, and therefore it could not make unilateral changes to the label, or (2) it establishes by 'clear evidence' that the FDA would not have approved the changes to the label that plaintiffs contend should have been made." ECF No. 1325 at 28. In *Merck*, the Supreme Court elaborated on the second of these inquiries. The Supreme Court explained that "showing that federal law prohibited the drug manufacturer from adding a warning that would satisfy state law requires the drug manufacturer

to show that it fully informed the FDA of the justifications for the warning required by state law and that FDA, in turn, informed the drug manufacturer that the FDA would not approve changing the drug's label to include that warning." *Merck* slip op. at 13.

As this Court previously acknowledged, Plaintiffs do not dispute Zofran's labeling history, including the FDA's repeated rejections of Plaintiffs' precise desired labeling change. ECF No. 1325 at 15. Accordingly, there is no question that this case satisfies the second prong of the clear evidence test, as elaborated in *Merck*. The parties' dispute concerns the first prong of *Merck*—*i.e.*, Plaintiffs contend that the FDA was not "fully informed" when it rejected those labeling changes. *Merck* slip op. at 13; ECF No. 1325 at 15-16. Plaintiffs have identified four categories of information that they claim the FDA lacked and that would have caused the FDA to mandate a labeling change. The question requiring resolution under *Merck* is whether those categories of information were "material," *Merck* slip op. at 16—that is to say, whether, "in light of the governing statutory and regulatory context," they justify the warning allegedly required by state law. *Id.*; *see also* ECF No. 1325 at 40 ("GSK has to show that the FDA was fully informed as to the relevant science, and that any alleged omission or failure to disclose was not material."); *id*. at 35 ("[T]he term "clear evidence" implies that a materiality standard should apply to claims based on alleged false statements and omissions to the FDA. If, for example, the allegedly omitted information was cumulative, irrelevant, trivial, or inconclusive, its omission surely was of no consequence."). Under *Merck*, that is a question of law for this Court.

The relevant historical facts are undisputed, including what information was in fact before the FDA. GSK does not anticipate that the Court will need to resolve "contested brute" historical facts. *Merck* slip op. at 16. Nor does GSK see on what issue the Court could possibly need to assess the credibility of fact witnesses. Instead, the Court will need to "interpret agency decisions

in light of the governing statutory and regulatory context," and in light of the evidence (including the types of evidence typically submitted in support of a summary judgment motion) relating to Plaintiffs' four categories of information. *Id.* This quintessentially legal analysis that *Merck* demands is well-suited to resolution by way of summary judgment.

In conducting this inquiry, the Court should not consider the opinions of Plaintiffs' regulatory expert Dr. Brian Harvey. Under Federal Rule of Evidence 702, experts may permissibly opine about the scientific significance of certain information, but, as GSK has already argued, they cannot opine on whether the FDA or its regulations would have required a labeling change had it received that information.[1] *See, e.g.*, *Nieves-Villanueva v. Soto-Rivera*, 133 F.3d 92, 99-101 (1st Cir. 1997) (holding that expert testimony regarding whether certain conduct violated the law was unhelpful to the jury and thus inadmissible); *see also Pelletier v. Main Street Textiles, LP*, 470 F.3d 48, 54-55 (1st Cir. 2006) (affirming exclusion of expert testimony regarding applicability of OSHA regulations to the defendant). Here, Dr. Harvey's speculation about the effect of Plaintiffs' four categories of information on the FDA's labeling decisions improperly invades this Court's preemption duty "to interpret agency decisions in light of the governing statutory and regulatory context." *Merck* slip op. at 16.

To provide just one example, Dr. Harvey purports to opine that the FDA would have concluded that the Japanese rat studies provide a sufficient basis to require a labeling change under FDA regulations. *See* GSK's Mot. To Exclude Pls.' Expert Dr. Brian E. Harvey at 7 (filed under seal Jan. 11, 2019). That is the ultimate issue before this Court under *Merck*. Relying on that speculative legal conclusion would be no different than relying on an opinion from a former PTO

[1] GSK has previously explained that Dr. Harvey's opinions are not admissible because, among other grounds, they express legal conclusions. *See* GSK's Reply in Supp. of Mot. To Exclude Pls.' Expert Dr. Brian E. Harvey at 2, 5, 31 (filed under seal Mar. 5, 2019).

official regarding how the PTO would construe a certain patent claim. Of course, courts cannot rely on such opinions to avoid exercising their legal duty to construe patent claims under *Markman*. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 983 (Fed. Cir. 1995) ("[Expert] testimony about construction, however, amounts to no more than legal opinion—it is precisely the process of construction that the court must undertake."), *aff'd*, 517 U.S. 370 (1996); *Vitrionics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1585 (Fed. Cir. 1996) ("[O]pinion testimony on claim construction should be treated with the utmost caution, for it is no better than opinion testimony on the meaning of statutory terms."). Dr. Harvey's proffered testimony is equally improper. *Cf. Merck* slip op. at 16 (comparing the preemption analysis to claim construction under *Markman*).

This is not to say that the Court is precluded from considering the evidentiary record related to the underlying science, including expert testimony on causation. That "scientific" testimony, if otherwise reliable, will be "helpful" to the Court in understanding the scientific significance (or lack thereof) of Plaintiffs' four categories of information. Fed. R. Evid. 702(a); *see Vitrionics*, 90 F.3d at 1585 (distinguishing between appropriate expert "testimony on the technology" and inappropriate expert testimony "on the proper construction of a disputed claim term"). The Court needs to understand the scientific significance of that information in order to determine whether it would have been material to the FDA under FDA regulations. GSK anticipates presenting that evidence to the Court as part of its summary judgment motion.[2] But, as just discussed, *Merck* reaffirms that the Court may not rely on expert opinions regarding what labeling decisions the FDA would have reached when assessing the preemption question before it. Because the question whether the agency was fully informed of all material information justifying a labeling change is now an inquiry delegated exclusively to the Court, the Court must resolve that question by

[2] The causation experts had not yet testified in depositions when GSK first moved for summary judgment on preemption grounds, but have since done so.

reference to the applicable law, not by reference to competing expert opinions on the application of the law.

If the Court disagrees and concludes that it is appropriate for the Court to consider expert testimony regarding whether Plaintiffs' four categories of information would be material to the FDA, and if the Court otherwise denies GSK's motion to exclude Dr. Harvey's unreliable testimony, GSK will present the Court with the competing opinions of its own regulatory expert.

B. GSK proposes to file a renewed motion for summary judgment. To be clear, it is GSK's position that the Court should have granted its prior summary judgment motion on preemption grounds, and GSK expressly reserves all rights with respect to that prior ruling. But GSK believes that filing a renewed motion will aid the Court's preemption decision. This is for two reasons. First, filing a renewed motion will allow the parties to revise their arguments to incorporate the Supreme Court's guidance in *Merck*. Second, the evidentiary record in this case has expanded since GSK last moved for summary judgment on this issue. Notably, Plaintiffs' causation experts (and GSK's experts) have testified regarding the scientific significance—or, more precisely, the lack of scientific significance—of Plaintiffs' four categories of undisclosed information. GSK intends to incorporate the new evidence into a renewed summary judgment motion.

GSK proposes the following timeline for its renewed summary judgment motion. GSK will file its motion within 45 days of this memorandum—*i.e.*, by July 18. Plaintiffs would respond within 45 days—*i.e.*, by September 3. GSK would file a reply within 21 days—*i.e.*, by September 24. The Court could hear attorney argument on a convenient date following the filing of the reply. And to the extent the Court identifies any factual disputes that it cannot resolve on the summary

judgment record, the parties could present evidence at a short hearing limited to the specific disputed facts—a far more efficient procedure than a full-blown bench trial.

GSK acknowledges that this schedule will require postponing the first bellwether trial. That is an inevitable result of the timing of the Supreme Court's decision in *Merck*. Rushing into trial—especially after the Supreme Court has emphasized the legal nature of the preemption inquiry and where that inquiry if resolved in GSK's favor would obviate the need for any trial—will not expedite resolution of these case; it will have the opposite effect. It bears reminder: Plaintiffs are seeking to hold GSK liable for failing to provide a warning that the FDA repeatedly rejected based on the scientific record. To this day, the FDA has not approved the warning that Plaintiffs seek, and Zofran is not contraindicated for use in pregnancy. Given this record and given the significance of the preemption issue for these cases, GSK cannot, and will not, resolve the MDL cases (if at all) until final resolution of the preemption issue, including by the First Circuit and Supreme Court if necessary. The preemption question in this case warrants thorough briefing and careful consideration. The parties and the Court cannot give the issue the attention it requires on an expedited timeline while also preparing for a September trial that will be obviated if the Court grants GSK's renewed summary judgment motion.

II. A Bench Trial Would Not Materially Advance Resolution of the Preemption Question.

For the foregoing reasons, the relevant evidence can be presented to the Court as exhibits to the summary judgment briefing. Because the Court should not accept testimony regarding the application of law to facts from Plaintiffs' regulatory expert, there is no need to conduct a bench trial to hear that testimony. GSK opposes a bench trial and reserves its right in that regard. Of course, if the Court decides to hold a bench trial over GSK's objection, GSK will present evidence

at the bench trial, including the testimony of its regulatory expert if necessary to rebut the improper opinions of Plaintiffs' regulatory expert Dr. Harvey.

A bench trial would only delay resolution of the case-dispositive preemption question. To enable both parties to prepare effectively for a bench trial, the Court would need to order submission of pre-trial briefs setting forth each party's view of the issues in dispute in light of the *Merck* decision. The parties would need sufficient time to prepare for the bench trial following the receipt of the opposing party's brief. The Court would need to carve out time for what it has acknowledged would be "a lengthy bench trial." ECF No. 1325 at 32. And the parties would want the opportunity to submit proposed findings of fact and conclusions of law after the bench trial incorporating the evidentiary record developed at the bench trial. This cumbersome approach is far less effective than resolution on a renewed summary judgment motion, particularly where the relevant historical facts are not in dispute.

III. If the Court Does Not Grant Summary Judgment to GSK, the Court Should Refer the Case to the FDA.

GSK is confident that, after considering the renewed summary judgment record, the Court will hold that Plaintiffs' four categories of undisclosed information are immaterial under FDA regulations and would not have altered the FDA's considered decisions rejecting Plaintiffs' proposed warning, which reflected the FDA's view that the science did not warrant the warning. However, to the extent the Court has any lingering doubt as to that question after considering the summary judgment record, the Court should stay this MDL under the doctrine of primary jurisdiction, refer the matter to the FDA under 21 C.F.R. § 10.25(c), and/or order Plaintiffs to refer the question to the FDA by way of a citizen petition seeking a labeling change based on their four categories of information. *See* ECF No. 1325 at 11 n.2 (describing the regulatory framework by which citizens may request a labeling change).

The doctrine of primary jurisdiction exists to "serve[] as a means of coordinating administrative and judicial machinery and to promote uniformity and take advantage of agencies' special expertise." *Pejepscot Indus. Park, Inc. v. Maine Cent. R. Co.*, 215 F.3d 195, 205 (1st Cir. 2000) (alteration in original) (internal quotation marks omitted). The First Circuit has enumerated three factors to guide courts' decisions regarding whether to invoke the doctrine and refer a question to the appropriate agency:

> (1) whether the agency determination lies at the heart of the task assigned the agency by Congress; (2) whether agency expertise is required to unravel intricate, technical facts; and (3) whether, though perhaps not determinative, the agency determination would materially aid the court.

Id. (alterations omitted) (quoting *Massachusetts v. Blackstone Valley Elec. Co.*, 67 F.3d 981, 992 (1st Cir. 1995)). If referral is warranted under these factors, the court must then balance the considerations favoring referral "against the potential for delay." *Palmer Foundry, Inc. v. Delta-HA, Inc.*, 319 F. Supp. 2d 110, 113 (D. Mass. 2004) (quoting *Am. Auto. Mfrs. Ass'n v. Mass. Dep't of Envtl. Prot.*, 163 F.3d 74, 81 (1st Cir. 1998)).

Courts have clarified that the term "referral" is a "misnomer" in this context. "[F]ew statutes allow a court to demand or request a determination from an agency." *Id.* (alteration and internal quotation marks omitted). Instead, when a court invokes the doctrine, it typically stays its proceedings "to allow one of the parties to file an administrative complaint seeking resolution of a particular issue." *Id.* Here, FDA regulations actually allow a court to request a determination from an agency. *See* 21 C.F.R. § 10.25(c). Therefore, the Court could either refer the question to the FDA itself or order Plaintiffs to file a citizen petition requesting a label change.

Each of the three factors considered by courts in this Circuit favors referral to the agency. Determining whether evidence justifies a labeling change "lies at the heart of the task assigned the agency by Congress." *Pejepscot Indus. Park*, 215 F.3d at 205 (alteration omitted) (quoting

Blackstone Valley, 67 F.3d at 992); *see* 21 U.S.C. § 355(o)(4) (authorizing the FDA to require labeling changes as "new safety information" becomes available).[3] The FDA possesses technical expertise in analyzing the import of new scientific evidence against the backdrop of the existing body of scientific knowledge regarding a drug. And the FDA's determination "would materially aid the court" in its resolution of the preemption inquiry. *Pejepscot Indus. Park*, 215 F.3d at 205 (quoting *Blackstone Valley*, 67 F.3d at 992). If the FDA informs the Court that Plaintiffs' four categories of information are cumulative of existing information and do not warrant a labeling change, GSK is entitled to summary judgment on its preemption defense. If it says the opposite, then FDA was not "fully informed" and GSK's preemption defense would fail. On balance, referral is appropriate. *See also, e.g., Bernhardt v. Pfizer, Inc.*, No. 00-civ-4042-LMM, 2000 WL 1738645 (D.N.J. Nov. 22, 2000) (referring to FDA question whether new information regarding prescription drug's safety and efficacy required notice to physicians and users).

CONCLUSION

For these reasons, GSK respectfully submits that the Court should resolve GSK's preemption defense by way of a renewed summary judgment motion pursuant to the schedule set forth above.

[3] In lieu of deferring the question to the FDA under the primary-jurisdiction doctrine, the Court could also invite the FDA to file an amicus brief in this case setting forth its views on Plaintiffs' four categories of information. *See TCG N.Y., Inc. v. City of White Plains*, 305 F.3d 67, 74 (2d Cir. 2002) ("Amicus briefs from an agency can serve much of the interest in consistency and uniformity of law that underlies the doctrine of primary jurisdiction, while avoiding some of the delay that sometimes results from dismissing on the ground of primary jurisdiction.").

Dated: June 3, 2019

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that the foregoing document, which was filed with the Court through the CM/ECF system, will be sent electronically to all registered participants as identified on the Notice of Electronic Filing ("NEF") and paper copies will be sent via first class mail to those identified as non-registered participants.

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