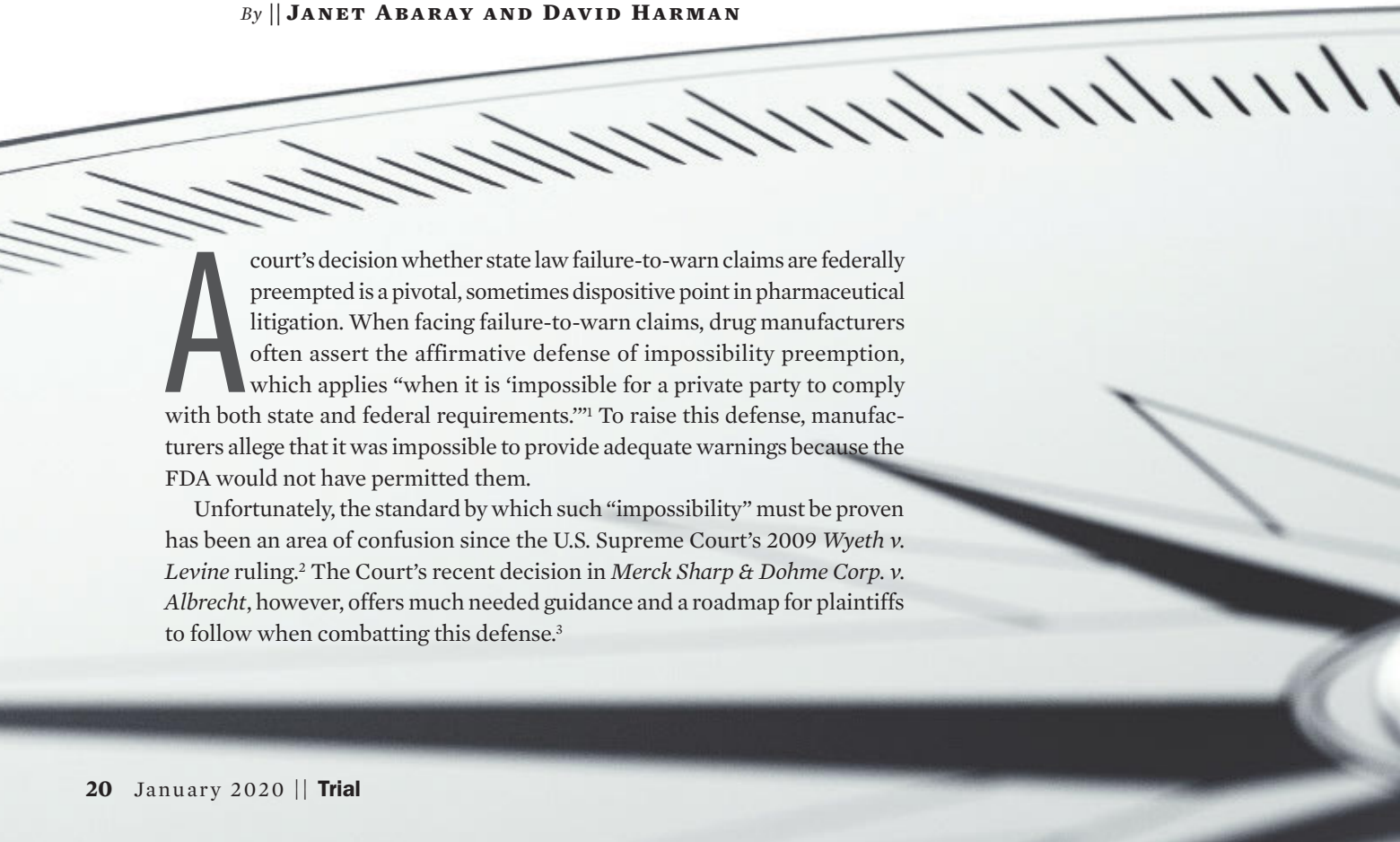
NAVIGATING PREEMPTION AFTER MERCK

By || Janet Abaray and David Harman



A court's decision whether state law failure-to-warn claims are federally preempted is a pivotal, sometimes dispositive point in pharmaceutical litigation. When facing failure-to-warn claims, drug manufacturers often assert the affirmative defense of impossibility preemption, which applies "when it is 'impossible for a private party to comply with both state and federal requirements.'"[1] To raise this defense, manufacturers allege that it was impossible to provide adequate warnings because the FDA would not have permitted them.

Unfortunately, the standard by which such "impossibility" must be proven has been an area of confusion since the U.S. Supreme Court's 2009 *Wyeth v. Levine* ruling.[2] The Court's recent decision in *Merck Sharp & Dohme Corp. v. Albrecht*, however, offers much needed guidance and a roadmap for plaintiffs to follow when combatting this defense.[3]

A 2019 SCOTUS decision provides new direction and clarity on the difficult standard drugmakers must meet to prove impossibility preemption. Learn how to use targeted discovery and motions to overcome this defense.

Merck requires a court to look at what the FDA—the agency, not its employees—decided. What the FDA could have done, might have done, or considered doing is irrelevant.

In *Wyeth*, the Supreme Court held that state law failure-to-warn claims that are related to injuries caused by FDA-approved drugs are preempted when there is "clear evidence that the FDA would not have approved a change" to a drug's label.[4] Although the Court also noted that impossibility preemption "is a demanding defense,"[5] drug manufacturers have cited *Wyeth*'s clear evidence language to file preemption motions based on speculation about what the FDA *would have* done if the manufacturer had requested a label change, thereby asking courts to analyze hypothetical situations, not actual events. For close to 10 years, courts have debated whether evidence of informal communications with FDA employees or nonbinding agency decisions could constitute clear evidence that the FDA would have rejected changes to drug labels had the drug manufacturer requested them.

In *Merck*, the Supreme Court firmly moved the preemption inquiry from hypotheticals to reality, reiterating that the mere "possibility of impossibility [is] not enough."[6] Clear evidence, the Court held, 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."[7] In other words, the manufacturer must have submitted a label change, and the FDA must have rejected it. The Court also determined that whether a drug manufacturer has met its burden to prove clear evidence of impossibility is a question of law for a judge, not a jury.[8]

Merck refocuses the required rationale for impossibility preemption: Only actual requirements imposed by federal law make it impossible for the manufacturer to comply with a state law duty to warn. As the Supreme Court made clear, only binding FDA actions, such as a formal denial of a labeling change, have the force and effect of a federal requirement.[9] Lesser steps such as conversations with FDA employees, email exchanges, or internal FDA analyses of scientific data do not establish a federal requirement that can give rise to impossibility preemption.

This standard is consistent with the U.S. Constitution's supremacy clause and also recognizes the practical difficulties of collecting and interpreting non-final documentation on proposed label changes. Documents that contain interim intra-agency analyses, discussions, and communications generally are protected by the "deliberative process" privilege and are not discoverable.[10] And even if certain provisional FDA analyses are obtained through Freedom of Information Act requests or are reflected in emails and notes that the drug company produces in discovery, these informal statements are not binding on the FDA.[11]

By limiting the preemption analysis to formal FDA decisions that carry the force of law, *Merck* requires a court to look at what the FDA—the agency, not its employees—decided. What the FDA could have done, might have done, or considered doing is irrelevant. *Merck*'s clear evidence analysis prohibits a drug manufacturer from proving preemption based on conjecture. Unless the federal government issued a final decision with the force of law prohibiting the defendant from making the requested label change, the impossibility preemption defense should fail.

Defeating Preemption Motions

After *Merck*, plaintiffs can overcome an impossibility preemption motion when a drug manufacturer fails to prove any of the following:

- The drug manufacturer asked the FDA to change the label to include the warning required by state law.

- The manufacturer fully informed the FDA of the justifications for the warning.
- The FDA rejected the proposed change to the label that would have included the warning.

In pharmaceutical cases, plaintiff attorneys should anticipate that preemption will be an issue and use targeted discovery to develop the evidence necessary to attack these elements.

Did the defendant prove it submitted a label change? Under *Merck*, a drug manufacturer's failure to formally submit a proposed label change to the FDA containing the warning required under state law should end the impossibility preemption inquiry in most circumstances.[12] Begin discovery with interrogatories asking whether the defendant submitted a label change through "changes being effected" (CBE)[13] or "prior approval" supplements (PAS).[14] If the defendant answers "no," then preemption is out of the question because without those submissions, the formal FDA review process triggering final decisions with the force of law does not begin.

A recent state trial court ruling illustrates this point. In *Commonwealth v. Bayer Corp.*, the manufacturer failed to request a label change but argued that the plaintiff's claims were nonetheless preempted.[15] As purported proof of clear evidence of impossibility, the manufacturer cited FDA reviews of studies and independent actions concerning the drug at issue. In line with *Merck*, the court rejected these arguments, finding that the manufacturer mischaracterized the clear evidence standard and attempted to shift the burden to the FDA. The court noted that the "onus is on drug manufacturers to inform the FDA of proposed label changes in order to establish clear evidence of impossibility preemption."[16] Because the record lacked any indication that the manufacturer took action to inform the FDA or request a label change, the court ruled that the plaintiff's claims were not preempted.

Did the defendant prove the FDA rejected the proposed change? To establish clear evidence of impossibility, a drug manufacturer must prove that the FDA rejected a proposed label change with the force of law, thereby creating a conflict between the manufacturer's state and federal law duties.[17] If discovery reveals that the defendant submitted a CBE or PAS, send an interrogatory asking whether the FDA issued a formal decision rejecting the proposed label change. If the drug manufacturer answers "no," then consider filing a motion for judgment as a matter of law.

If the drug manufacturer responds that the FDA formally rejected the proposed label change, request all documents and communications with the FDA that support this contention. Often, the defendant will provide only informal emails or internal memoranda of calls in which an FDA employee allegedly questioned or criticized the evidence the manufacturer provided to support the label change request.

Before *Merck*, drug manufacturers cited such informal communications as key exhibits in their preemption motions, claiming that this provided the necessary clear evidence of impossibility.[18] After *Merck*, however, this tactic should be wholly ineffective because such informal, hearsay communications do not carry the force of law and are insufficient to establish that the FDA formally rejected the proposed change.[19]

Although *Merck* did not list all of the agency actions that carry the force of law, it provided useful examples and noted that federal law "permits the FDA to communicate its disapproval of a warning by means of notice-and-comment rulemaking setting forth labeling standards; by formally rejecting a warning label that would have been adequate under state law; or with other agency action carrying the force of law."[20] As succinctly noted in Justice Clarence Thomas's concurrence in *Merck*, "neither agency musings nor hypothetical future rejections constitute pre-emptive 'Laws' under the Supremacy Clause."[21]

When opposing a preemption motion or filing an offensive motion, highlight the difference between the formal means of agency communication set forth in *Merck* and the hearsay proffered by the manufacturer. Without the FDA's formal and final rejection of a proposed label change, clear evidence of impossibility does not exist, and the affirmative defense of preemption cannot be established.

Did the defendant prove it fully informed the FDA of the justifications? Even if a drug manufacturer submitted a request to change its label and the FDA appears to have formally rejected that change, the manufacturer cannot establish impossibility preemption without proof that the drug manufacturer fully informed the FDA of the justifications for the proposed warning required by state law.[22] If the manufacturer establishes that the FDA denied the proposed label change, request discovery of all communications between the defendant and the agency pertaining to the risk at issue, and specifically request the drug manufacturer's CBE or PAS submissions asking for the label change.

During discovery, you and your experts will identify all the studies and articles that you believe support a label change. When the drug manufacturer produces its CBE or PAS submissions, look for studies and articles that the defendant omitted, mischaracterized, or failed to analyze. Next, examine the manufacturer's CBE or PAS statements to the FDA justifying the proposed label change. Did the manufacturer, for example, undermine the basis for adding a warning by questioning the reliability of the studies justifying the proposed

warning or saying it was submitting the new warning only out of an abundance of caution? If evidence exists that the manufacturer excluded, misrepresented, or downplayed the justifications for the warnings, argue to the court that the manufacturer has not proven clear evidence of impossibility because it failed to demonstrate it fully informed the FDA of the justifications for the warning.[23]

When challenging the adequacy of a drug manufacturer's submission to the FDA, be prepared for two potential responses. First, the defendant likely will argue that critiques of its submissions to the FDA are prohibited by *Buckman Co. v. Plaintiffs' Legal Committee*, the Supreme Court decision that preempts causes of action premised on fraud on the FDA.[24] *Merck*, however, renders this position completely erroneous because the Court explicitly stated that "in litigation between a drug consumer and a drug manufacturer . . . the litigants may dispute whether the drug manufacturer submitted all material information to the FDA."[25] Accordingly, *Buckman* should not be an obstacle to challenging a drug manufacturer's deficient submissions to the FDA.

Second, the drug manufacturer may advocate for the court to invite the FDA to submit an amicus brief on whether the alleged deficiencies in its submissions made a difference in the FDA's final labeling decision.[26] Such a request essentially asks the court and the FDA to speculate about what the agency would have done in a counterfactual world in which the drug manufacturer fully informed the FDA. Based on *Merck*, such speculation has no place in a preemption analysis.

Explain to the court that *Merck* focuses the preemption inquiry on what happened, not hypotheticals. If the drug manufacturer failed to do what was possible—in other words, to fully inform the FDA of the justifications for the label change—then it cannot meet its burden of proof to establish preemption.

When a trial judge rules that failure-to-warn claims are not preempted, consider filing a motion in limine to exclude from trial any evidence pertaining to the FDA.

Citizen Petitions and Independent Risk Assessments

Before *Merck*, drug manufacturers occasionally argued that FDA decisions not to change warning labels following citizen petitions or FDA independent risk assessments formed sufficient clear evidence of impossibility. *Merck* should dismantle this argument in most cases.

Merck did not define clear evidence of impossibility as evidence that the FDA rejected a label change after being fully informed *by any source* of the justifications for the proposed warning. Rather, *Merck* stated that clear evidence of impossibility exists when the *drug manufacturer* fully informs the FDA of the justifications for the label change.[27] As such, the ruling reaffirms the manufacturer's obligation to maintain an adequate label.[28] Requiring the drug manufacturer to be the source of full information justifying the label change also recognizes the deference the FDA rightfully gives to a manufacturer as the expert on the safety of its drug.

In keeping with *Merck*'s definition of clear evidence, an FDA decision that responds to a citizen petition or an independent risk assessment without input from the drug manufacturer on the full risk information and its justifications for the new label should be insufficient to establish preemption.[29] If you suspect a manufacturer may attempt to base its impossibility preemption defense on an FDA response to a citizen petition or independent risk assessment, send discovery requests specifically asking whether the FDA consulted with the drug manufacturer prior to the agency's decision and whether the manufacturer fully informed the FDA of the justifications for the proposed label change. Absent proof that the

drug manufacturer was consulted and fully informed the FDA, clear evidence should not be found.

After Defeating Preemption

When a trial judge has ruled that your failure-to-warn claim is not preempted, that judge has ruled as a matter of law that the FDA did not make it impossible for the manufacturer to provide an adequate warning. Consider filing a motion in limine to exclude from trial any evidence pertaining to the FDA.

In the motion, explain that because the FDA did not preclude the drug manufacturer from providing an adequate warning, any communications the manufacturer had with the FDA are marginally relevant at best. Indeed, any testimony and evidence about such communications regarding the drug's risks could confuse liability issues or waste substantial time. If you succeed on the motion, you may be able to streamline the trial and avoid hours of potentially prejudicial and expensive testimony from regulatory experts.

Merck's definition of clear evidence of impossibility firmly grounds the preemption analysis in real-world events, not hypotheticals. By using *Merck* as a roadmap for framing discovery and arguments in motion practice, plaintiff attorneys can hold drug manufacturers to their burden of proof and defeat unfounded preemption arguments. T


Janet Abaray *and* **David Harman** *are shareholders of Burg Simpson Eldredge Hersh & Jardine in Cincinnati and can be reached at jabaray@burgsimpson.com and dharman@burgsimpson.com.*

Notes

1. *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1672 (quoting *Mut. Pharm. Co. v. Bartlett*, 570 U.S. 472, 480 (2013)); *see Brown v. Earthboard Sports USA, Inc.*, 481 F.3d 901, 912 (6th Cir. 2007) (noting that "[f]ederal preemption is an affirmative defense upon which the defendants bear the burden of proof" (quoting *Fifth Third Bank v. CSX Corp.*, 415 F.3d 741, 745 (7th Cir. 2005))).
2. 555 U.S. 555 (2009).
3. *Merck*, 139 S. Ct. 1668.
4. *Wyeth*, 555 U.S. at 571.
5. *Id.* at 573, *quoted with approval in Merck*, 139 S. Ct. at 1678.
6. *Merck*, 139 S. Ct. at 1678 (quoting *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 625 n.8 (2011)).
7. *Id.* at 1672.
8. *Id.* at 1676, 1679.
9. *See id.* at 1679; *see also id.* at 1683 (Thomas, J., concurring).
10. *See, e.g., Schell v. U.S. Dep't of Health & Human Servs.*, 843 F.2d 933, 939 (6th Cir. 1988).
11. *See* 21 C.F.R. §10.85(k) (2014) ("A statement or advice given by an FDA employee orally, or given in writing but not under this section or §10.90, is an informal communication that represents the best judgment of that employee at that time but does not constitute an advisory opinion, does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed.").
12. The only exception supported by *Merck* is the rare situation in which the FDA learns of new safety information and asks the drug manufacturer for information and comment regarding the risk. *See infra* p. 24–25 discussing citizen petitions and independent risk assessments*; see also Merck*, 139 S. Ct. at 1679 (citing 21 U.S.C. §355(o)(4)(A) (2018)).
13. *See* 21 C.F.R. §314.70(c)(6)(iii)(A) (2016) (providing that a drug manufacturer can change its label to "add or strengthen a contraindication, warning, precaution, or adverse reaction" prior to receiving FDA approval).
14. *See* 21 C.F.R. §314.70(b). When submitting a prior approval supplement, a drug manufacturer asks the FDA to review proposed label changes prior to implementing those changes.
15. *See* Order, *Commonwealth v. Bayer Corp.*, No. 07-CI-00148 (Ky. Cir. Ct. Franklin Cnty. Sept. 10, 2019) (order denying motion for summary judgment, denying *Daubert* motions, and holding in abeyance motion to dismiss supplemental complaint).
16. *Id.* (citing *Wyeth*, 555 U.S. at 570–71.)
17. *See Merck*, 139 S. Ct. at 1679 ("The Supremacy Clause grants 'supreme' status only to the 'the [sic] *Laws* of the United States.'" (quoting U.S. Const. art. VI, cl. 2).
18. *See, e.g., Rheinfrank v. Abbott Labs., Inc.*, 119 F. Supp. 3d 749 (S.D. Ohio 2015).
19. Such informal communications often consist of inadmissible hearsay that should not be considered by the court. *See, e.g., Patterson v. Cent. Mills, Inc.*, 64 F. App'x 457, 462 (6th Cir. 2003) ("The public records exception . . . extends only to opinions of the agency or public office *itself*, not to those of its individual members contained within the records."); *Smith v. Isuzu Motors Ltd.*, 137 F.3d 859, 862 (5th Cir. 1998) (finding that memo from regulatory agency staffer did not qualify as a public record).
20. *Merck*, 139 S. Ct. at 1679 (internal citations omitted).
21. *Id.* at 1682 (Thomas, J., concurring).
22. *Id.* at 1672; *see also In re Actos (Pioglitazone) Prods. Liab. Litig.*, 2014 WL 4286927, at *20–23 (W.D. La. Aug. 28, 2014) (finding that clear evidence was lacking because there was evidence that the drug manufacturer withheld information from the FDA).
23. *See Merck*, 139 S. Ct. at 1682; *see also In re Actos,* 2014 WL 4286927, at *20–23 (finding that clear evidence was lacking because there was evidence that the drug manufacturer engaged in a concerted effort to resist a label change and withheld information from the FDA about a particular risk); *Aaron v. Wyeth*, 2010 WL 653984, at *6 (W.D. Pa. Feb. 19, 2010) (finding that FDA rejection of proposed label changes was not clear evidence when the manufacturer did not press its position and instead acquiesced to the FDA's decision not to strengthen the label).
24. 531 U.S. 341 (2001).
25. *Merck*, 139 S. Ct. at 1680.
26. GSK's Memorandum Regarding Preemption, *In re Zofran (Ondansetron) Prods. Liab. Litig.*, No. 1:15-md-2657 (D. Mass. July 1, 2019), https://tinyurl.com/y2o2o5rh.
27. *Merck*, 139 S. Ct. at 1672.
28. *Wyeth*, 555 U.S. at 570–71 (explaining that manufacturers are responsible for the content of their drugs' labels at all times and are "charged both with crafting an adequate label and with ensuring that [their] warnings remain adequate as long as [their drugs are] on the market").
29. *But see Cerveny v. Aventis, Inc.*, 2019 WL 3763441, at *n.9 (10th Cir. Aug. 9, 2019) (distinguishing *Merck* and finding that the FDA's "unequivocal" response to a citizen petition was sufficient to justify preemption without commenting on whether the drug manufacturer had been consulted by the FDA or had provided the FDA with any analysis of the risk at issue in the petition).