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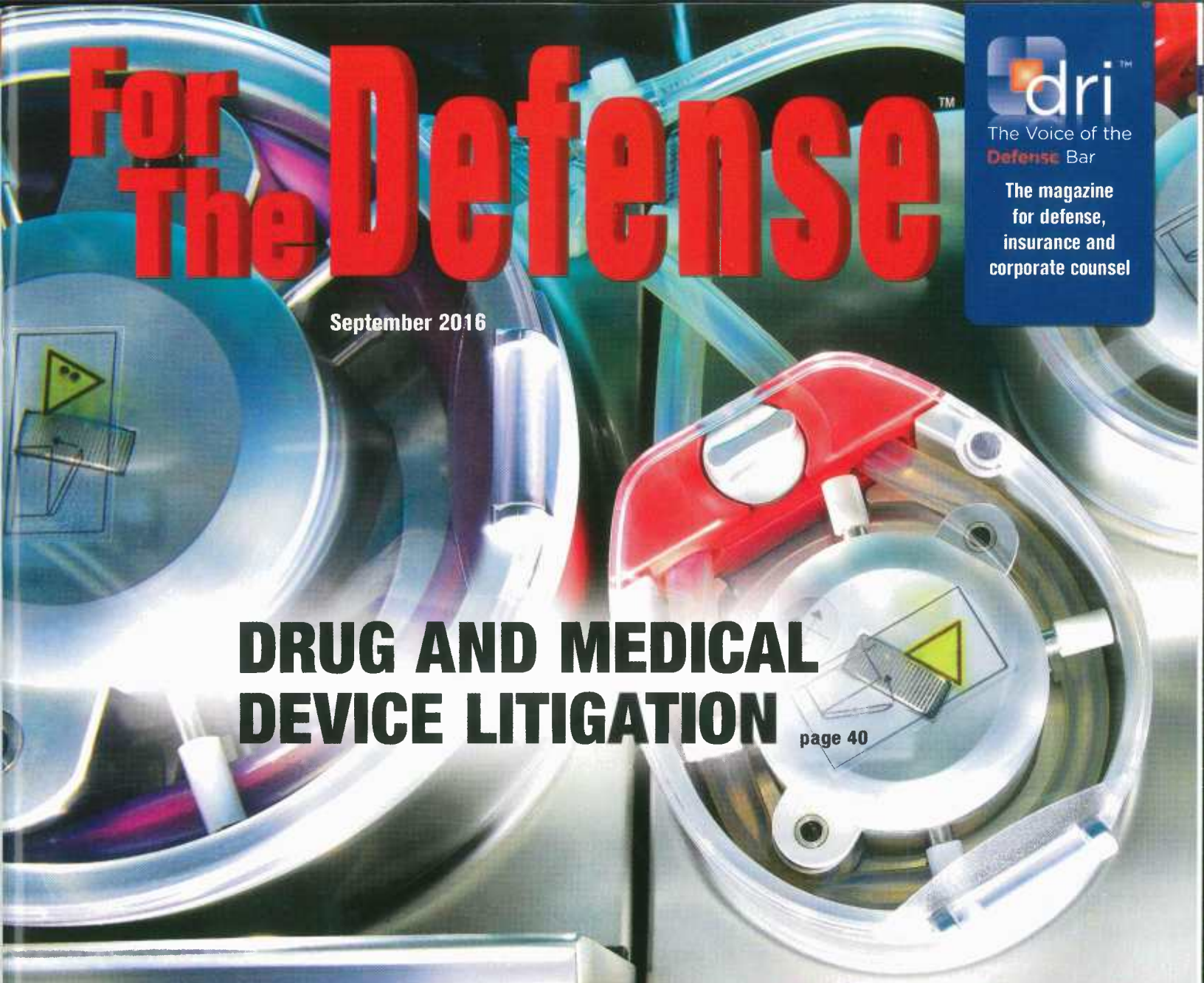

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PMA Medical Devices and Post-Approval Studies

Preemption and Other Defenses to Claims by Study Subjects

By Edward W. Gerecke and David J. Walz

Fundamental express and implied preemption principles bar these claims despite the unique situations that post-approval studies may involve.

The preemption of state law claims against medical devices approved under the premarket approval (PMA) process is now an established principle of pharma law after *Riegel v. Medtronic, Inc.*, 552 U.S. 312 (2008). Most traditional product liability claims fail due to some combination of express preemption under the Medical Device Amendments of 1976 (MDA) and implied preemption. Courts have held claims under strict liability, negligence, warranty, and other theories expressly preempted because they seek to impose state law requirements "different from, or in addition to" the applicable federal requirements. *Wolicki-Gables v. Arrow Int'l, Inc.*, 634 F.3d 1296 (11th Cir. 2011). Even if claims are "premised on a violation of FDA regulations," the claims mostly lack a "parallel" remedy under state law. *Marmol v. St. Jude Medical Center*, 132 F. Supp. 3d 1359 (M.D. Fla. 2015). At the same time, implied preemption operates as a further bar. *See* 21 U.S.C. §337(a).

In response, enterprising plaintiffs' lawyers are resorting to more nuanced arguments in their search to circumvent prevention. Recent cases have involved attempts to use U.S. Food and Drug Administration (FDA) warning letters and formal performance standards to evade preemption. *Brown v. DePuy Orthopaedics, Inc.*, 978 F. Supp. 2d 1266 (M.D. Fla. 2013) (plaintiff failed to demonstrate the necessary nexus between her claims and an FDA warning letter); *Kaiser v. DePuy Spine, Inc.*, 944 F. Supp. 2d 1187 (M.D. Fla. 2013) (holding that the plaintiff failed to plead noncompliance with a formal performance standard established by FDA). For example, one appellate court has expressly rejected claims based on a flow-rate specification

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that was stated in PMA materials without a corresponding FDA-promulgated, device-specific formal performance standard for the device involved. *Walker v. Medtronic, Inc.*, 670 F.3d 569 (4th Cir. 2012).

Given the lack of traction gained by those claims, plaintiffs' attorneys naturally will turn to other theories. One potential target concerns claims involving post-approval studies that the FDA requires when approving a PMA application. Between January 1, 2007 and February 23, 2015, the FDA ordered 313 post-approval studies. U.S. Government Accountability Office, *FDA Ordered Postmarket Studies to Better Understand Safety Issues, and Many Studies Are Ongoing* 10–11 (Sept. 30, 2015), http://www.gao/gov. The FDA ordered nearly all of these post-approval studies (94 percent) for devices approved through the PMA process. *Id.* As of February 2015, 225 post-approval studies were ongoing, with 182 "progressing adequately," and another 43 falling into the "delayed" category. *Id.* at 14–15.

While a plaintiff's attorney may attempt to frame a post-approval study as a unique situation that distinguishes his or her case from other PMA cases, fundamental principles of express and implied preemption still apply to bar the claims. Additionally, other principles based on the general nature of, and a manufacturer's role in, clinical studies operate to further bar them. This article discusses potential defenses against claims relating to PMA devices with post-approval studies.

Express Preemption Bars Claims That Impose "Different or Additional" Requirements That Are Not "Parallel"

A PMA approval order may require a post-approval study under various design protocols. The post-approval study may follow a designated number of patients from the clinical trial for a set period of time after approval with subjective (patient or surgeon assessment questionnaires) and objective (clinical and radiographic examinations) criteria. Or, the PMA approval order may outline a post-approval study with prospective patients at a designated number of investigational sites, physician investigators based upon certain criteria or training, clinical data evaluated at baseline and set intervals, collection of revision data, self-questionnaires to be completed by the investigational subjects, and other diagnostic testing.

The FDA's authority to require a post-approval study for a PMA medical device is grounded in federal requirements. It arises directly from the post-approval requirements set forth in 21 C.F.R. §814.82:

> (a) FDA may impose postapproval requirements in a PMA approval order or by regulation at the time of approval of the PMA or by regulations subsequent to approval. Postapproval requirements may include as a condition to approval of the device:
>
> ...
>
> (2) Continuing evaluation and periodic reporting on the *safety, effectiveness, and reliability* of the device for its intended use. FDA will state *in the PMA approval order* the reason or purpose for such requirement and the number of patients to be evaluated and the reports required to be submitted.

21 C.F.R. §814.82(a)(2) (emphasis added).

As a result, a post-approval study required by the FDA is a federal requirement that relates to safety, effectiveness, or "any other matter... applicable to the device." 21 U.S.C. §360k(a). Courts have concluded that this point is beyond dispute:

> There is no doubt that, as a practical reality, the PMA process imposed requirements that were specifically applicable to the [device], and that triggered preemption under §360k(a). It imposed *mandatory conditions*—created through a decades-long process of correspondence, *clinical testing* and device alteration—pertaining to the [device]....

Horn v. Thoratec Corp., 376 F.3d 163, 170 (3d Cir. 2004) (citing 21 C.F.R. Part 814) (first emphasis in original, second emphasis added).

Thus, any state law claim that seeks to impose a requirement "different from, or in addition to" the post-approval study requirements is subject to express preemption. 21 U.S.C. §360k(a).

Most plaintiffs will be unable to point to a federal regulation or a requirement specific to a post-approval study that was violated. Identifying any such requirement with the necessary nexus to the plaintiff and his or her alleged injury is even less likely. Therefore, most claims likely will attempt to create a requirement that is not imposed by federal law, and such a claim will fall due to express preemption. In *Mink v. Smith & Nephew, Inc.*, No. 15-CIV-61210-BLOOM/VALLE, 2016 WL 1045588 (S.D. Fla. Mar. 14, 2016), the plaintiff alleged various claims based on his early termination from a post-approval study. Such claims were expressly preempted because "[i]f the FDCA and its affiliated regulations do not forbid a study participant's early termination, any state law that does forbid early termination necessarily imposes a requirement that is 'different from, or in addition to' the relevant federal requirements." *Id.* at *12.

Most plaintiffs will be unable to point to a federal regulation or a requirement specific to a post-approval study that was violated. Identifying any such requirement with the necessary nexus to the plaintiff and his or her alleged injury is even less likely.

Similar reasoning applies to other claims that a manufacturer should have done something differently concerning a post-approval study. Theories of liability based on additional testing, or a different clinical plan, reporting, or selection of clinical investigators, are expressly preempted. Likewise, challenges to a study's fundamental design, whether it is a prospective cohort study comparing a group using a device with another group not using the device, or whether the study uses newly collected

data or compiles data from registries, are claims that *Riegel* expressly preempts because they impose liability under state law for actions allowed under federal law. *Wolicki-Gables*, 634 F.3d at 1301 (holding state law claims preempted because "a fact-finder could find liability even if the manufacturer had complied with the [federal requirements]"). Simply put, if a claim arises from anything other than a specific requirement of a post-approval study set forth in a PMA, then it is by definition "different from, or in addition to" the federal requirements.

In turn, implied preemption also will bar this claim to the extent that a plaintiff attempts to enforce the FDCA privately and thereby interferes with the FDA's exclusive enforcement authority because "all actions to enforce FDA requirements 'shall be by and in the name of the United States.'"

As a practical matter on this point, documents related to a post-approval study, such as the consent form signed by the study subjects, may prove helpful. These documents may undercut a plaintiff's position and demonstrate that the plaintiff's theory goes beyond any federal requirement. For example, the consent form may indicate that the FDA allows the sponsor manufacturer to alter the clinical plan or even to terminate the study altogether. If so, a state law claim seeking to impose liability for an event allowed by the FDA presents precisely the type of claim that *Riegel* preempts. *Mink*, 2016 WL 1045588, at *12.

Presuming that a plaintiff identifies a violation of an actual federal requirement, he or she still must meet the corresponding requirement that a parallel claim match a preexisting "genuinely equivalent" state law remedy. *Wolicki-Gables*, 634 F.3d at 1300; *Bausch v. Stryker Corp.*, 630 F.3d 546, 558 (7th Cir. 2010). In the context of a post-approval study, parallel state law claims should be few and far between. Absent a corresponding state law that requires a medical device manufacturer to do whatever a plaintiff alleges as a federal violation (whether to maintain the plaintiff in the study, or to fund, monitor, or keep the study ongoing), the claim is not "premised on conduct that both (1) violates the FDCA and (2) would give rise to a recovery under state law even in the absence of the FDCA." *Caplinger v. Medtronic, Inc.*, 921 F. Supp. 2d 1206, 1213 (W.D. Okla. 2013), *aff'd*, 784 F.3d 1335 (10th Cir. 2015). As an analogous example, courts reject the notion that a manufacturer must continue to supply a prescription medical product for a patient's use because no such duty exists as a matter of state law. *Lacognata v. Hospira, Inc.*, No. 8:12-CV-822-T-30TGW, 2012 WL 6962884, at *2 (M.D. Fla. July 2, 2012), *aff'd*, 521 F. Appx. 866 (11th Cir. 2013) (dismissing negligence and other claims while holding "[t]here is no authority that supports [p]laintiff's argument that a... manufacturer... has a duty to continue supplying a patient with a drug that it knows the patient relies upon for his or her medical health").

Thus, even if a federal regulation or requirement required an event claimed by a plaintiff, the alleged federal violation still may lack any parallel claim under state law.

Implied Preemption Bars Such Claims

In turn, implied preemption also will bar this claim to the extent that a plaintiff attempts to enforce the FDCA privately and thereby interferes with the FDA's exclusive enforcement authority because "all actions to enforce FDA requirements 'shall be by and in the name of the United States.'" *Brown*, 978 F. Supp. 2d at 1274 (citing 21 U.S.C. §337(a)). Any attempt at private enforcement is impliedly preempted.

For example, a claim based on a failure to report information to the FDA during a post-approval study is preempted under reasoning from *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 349, 353 (2001):

> Plaintiffs alleged that [the manufacturer] failed to provide the FDA with sufficient information and did not timely file adverse event reports, as required by federal regulations.... [T]hese claims are simply an attempt by private parties to enforce the MDA, claims foreclosed by §337(a) as construed in *Buckman*.

In re Medtronic, Inc., Sprint Fidelis Leads Prods. Liab. Litig., 623 F.3d 1200, 1205–06 (8th Cir. 2010).

Similarly, any other claim that is based ostensibly on a post-approval study, but in reality sounds in private enforcement of the FDCA, is impliedly preempted.

Defenses Other than Preemption Bar the Claims

Even if a claim based on a post-approval study survives preemption, other defenses exist. These defenses arise from the nature of clinical studies and a sponsoring manufacturer's role in such studies. Fundamentally, a study sponsor does not owe any duties to study subjects and prospective subjects for either the medical care that the study subjects receive as part of the study itself or for unrelated medical care.

The FDA's regulations and guidance provide the fundamental framework for analyzing post-approval studies. The FDA advises that all studies "should comply" with 21 C.F.R. Part 56. *See* FDA, FDA Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors, Frequently Asked Questions about Medical Devices 8 (Jan. 2006), http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127067.pdf. In turn, 21 C.F.R. Part 812 provides guidance for post-approval studies. *Id.*

A Study Sponsor Owes No Duty to a Study Subject

As a general proposition, a sponsor of a clinical trial or post-approval study owes no duty to trial or study subjects or participants. Rather, any duty owed to study subjects belongs to the physician investigator or the governing institutional review board (IRB).

The regulations that the FDA issues to govern clinical trials on human subjects set forth the responsibilities of the various

parties and place no duty upon a sponsor to the study's subjects. A "sponsor" is defined as "a person or other entity that initiates a clinical investigation, but that does not actually conduct the investigation, *i.e.*, the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual." 21 C.F.R. §56.102(j).

As the case law recognizes, "[t]he independence of the investigator from the sponsoring enterprise is necessary to ensure objectivity. . . ." *Suthers*, 441 F. Supp. 2d at 488.

In contrast to the sponsor's lack of a duty, the regulations place the duty to safeguard the study's subjects upon the governing IRB:

> Institutional Review Board (IRB) means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. *The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects.*

21 C.F.R. §56.102(g) (emphasis added).

The regulations further provide that "any clinical investigation which must meet the requirements for prior submission... to [the FDA] shall not be initiated unless that investigation has been reviewed and approved by, and remains subject to continuing review by, an IRB." 21 C.F.R. §56.103(a).

In addition to the duty that an IRB bears, the FDA defines an "investigator" as the "individual who actually conducts a clinical investigation (*i.e.*, under whose immediate direction the test article is administered or dispensed to, or used involving, a subject)." 21 C.F.R. §56.102(h). Finally, the FDA defines the "general responsibilities" of a physician investigator as the following: "An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations; *for protecting the rights, safety, and welfare of subjects under the investigator's care*; and for the control of devices under investigation." 21 C.F.R. §812.100 (emphasis added).

Under these regulations, courts routinely refuse to impose a duty upon sponsors. In *Anderson v. George H. Lanier Memorial Hospital*, 982 F.2d 1513, 1516–17 (11th Cir. 1993), the court held that "federal law did not impose a duty upon [a sponsor] to ensure that its 'investigators'" acted properly in conducting a clinical trial. In *Anderson*, three plaintiffs underwent multiple eye-implant surgeries during the study using the sponsor's medical device. They sued various defendants, including the sponsor, and alleged that the sponsor "had a legal duty to ensure" the investigator's conduct. *Id.* at 1515. The trial court and then the appellate court rejected that legal theory and agreed with the sponsor's argument "that it owed no duty under federal law" to the clinical trial's subjects. *Id.* at 1516.

Other courts agree as a matter of law. In *Sykes v. United States*, No. 1:10-cv-688, 2011 WL 3739017, at *17 (S.D. Ohio July 22, 2011), the court dismissed claims "because the pharmaceutical defendants owed no legal duty to the decedent." The appellate court affirmed the dismissal and rejected arguments that the sponsor, instead of the IRB, was "responsible for protecting the rights and welfare of clinical trial participants." *Sykes v. United States*, 507 Fed. Appx. 455, 462 (6th Cir. 2012). In holding that the sponsor owed no duty as a matter of law, the court reasoned "that 'under the FDA's regulatory scheme it is not the pharmaceutical companies that are charged with ensuring trial participants' well being [sic]. Rather, it is the [IRB] that is meant to 'protect the rights and welfare' of trial participants during a clinical trial.'" *Id.* (quoting *Abney v. Amgen, Inc.*, 443 F.3d 540, 551 (6th Cir. 2006)).

Similarly, in *Kernke v. The Menninger Clinic, Inc.*, 173 F. Supp. 2d 1117, 1124 (D. Kan. 2001), the plaintiffs attempted to pursue a negligence claim against a trial sponsor and alleged numerous duties related to the decedent. The court rejected that attempt and agreed that "[a]ll of the duties alleged by plaintiffs in this case fall within the purview of the... investigator conducting the [] study; the duties do not rest with [the sponsor]." *Id.* Therefore, the sponsor owed no legal duty to the deceased trial subject.

In short, courts around the country regularly and uniformly hold that a sponsoring manufacturer owes no duty regarding the safety or well-being of subjects in a clinical trial. *Suthers v. Amgen Inc.*, 441 F. Supp. 2d 478, 488 (S.D.N.Y. 2006) ("The[] federal regulations require that it is the investigator who recruits the subjects, determines their suitability, monitors their tolerance and reaction and reports the results.... This framework envisions the sponsoring organization maintaining its distance and detachment from the participants in the study, a status incompatible with acting as their fiduciary [for purposes of creating a duty]."). Those duties fall elsewhere, and a tort plaintiff cannot broaden a sponsor's duties contrary to the governing federal regulations. *See Cacchillo v. Insmed Inc.*, 833 F. Supp. 2d 218, 240 n.21 (N.D.N.Y. 2011) (holding that "under FDA regulations, a clinical trial's IRB, not the sponsoring pharmaceutical company, is charged with ensuring trial participates' well being [sic]").

This regulatory framework and the case law follow the underlying policy reason that the FDA applies in requiring separation between sponsors and subjects. As the case law recognizes, "[t]he independence of the investigator from the sponsoring enterprise is necessary to ensure objectivity...." *Suthers*, 441 F. Supp. 2d at 488. Under this policy rationale, "[a] legal conclusion that a sponsor is a fiduciary who owes a duty of undivided loyalty to a participant in a drug trial would have profound implications for research and new product development." *Id.* at 487. A forced separation between sponsors and subjects, including multiple intervening layers of oversight such as that undertaken by the investigators and IRB, serves the scientific goal of greater objectivity in evaluating the efficacy of the drug therapies at issue. *Id.* at 488 (holding that "the search for truth about the safety and efficacy of the drug" requires a detachment between the sponsor and study partici-