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I. LEGAL HISTORY, PROCESS OF MEDICAL DEVICE REPORTING

The Medical Device Amendments to the Food, Drug, and Cosmetic Act (FDCA) were enacted in 1976 to “provide for the safety and effectiveness of medical devices intended for human use.”¹ The Amendments group medical devices into three categories—Classes I, II and III.² Class I and II devices, which require no premarket approval, are subject to fewer Food and Drug Administration (FDA) controls than Class III devices. Class III devices are typically those that “present a potential unreasonable risk of illness or injury.”³

Unlike pharmaceuticals, which all generally require extensive premarket testing, overwhelming numbers of medical devices currently in use were never required to undergo a formal premarket approval (PMA) process. It is only conceptually new devices marketed since 1976 that have been required to undergo rigorous scientific proof-of-concept and demonstration of safety and efficacy. Postmarket surveillance is thus potentially extremely important for these medical devices to ensure continued public safety, as it is the only mechanism by which FDA can determine whether a product is performing safely as per its claims.

Medical devices are subject to FDA oversight under three Class divisions.⁴ Class I Devices generally require no prior notification. Examples are tongue depressors and general use surgical instruments. These devices must be listed with FDA, and must demonstrate that they follow established good manufacturing practices (GMPs).⁵

Class II Devices may seek FDA clearance based on a “510(k)” application, where the manufacturer must demonstrate substantial equivalence to a predicate device that was on the market for the same intended use prior to the establishment of the Medical Device Amendments of 1976.⁶ Although these devices may be subject to special controls, they rarely require new supporting human clinical data to gain marketing clearance. For example, a new design for a fixation nail for hip fractures may utilize a novel compression system, but if shown to be substantially equivalent to a fixation nail in use prior to 1976, no premarket clinical testing is generally

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¹ P.L. 94-295.

² 21 C.F.R. 860.

³ 21 USC § 360c(a)(1)(C)(ii).

⁴ 21 C.F.R. 860.

⁵ 21 C.F.R. 820 et seq.

⁶ FDCA § 510(k), 21 U.S.C. § 360(k).

required before release. Commonly, however, new engineering and mechanical testing results are submitted as part of the 510(k) application.

Only Class III medical devices are required to be proven “safe and effective” by undergoing the rigorous premarket approval process before they are FDA-approved and reach patients in commercial use. This requires not only a demonstration of adequate engineering and manufacturing, but generally requires the completion of a prospective multicenter randomized control trial with minimum of two years of clinical follow-up. Non-inferiority study models have been common until 2006, but there is a new tendency for proof of superiority over the control device, often requiring more subjects to meet this higher statistical threshold.

Class III Devices are generally novel and by definition are not equivalent to pre-amendment devices. They are not appropriate to be “grandfathered” under the umbrella of a pre-1976 device by the 510(k) route. They generally require a formal Investigational Device Exemption (IDE) study to be performed. This necessitates a formal submission process to FDA, generally including novel engineering data, mechanical testing, animal testing and often small pilot studies of human trial data (frequently conducted outside the United States). The proposed clinical trial, most frequently a random comparison of the investigational device to a suitable control (i.e., conservative care or an already FDA-approved device in general use for the same clinical condition and indications) in several hundred patients, must be reviewed and approved in advance by FDA. Devices that are classified as Class III devices must be approved before being marketed, via a formal PMA application.

The PMA process requires a manufacturer to submit, among other things, reports of all clinical and non-clinical studies demonstrating the safety and effectiveness of the device, a statement of the device’s components and other details regarding any marketing of the device.⁷

After reviewing the PMA application, FDA has the authority to approve, deny, or impose modifications, in the form of either an “approvable letter” informing the manufacturer that it believes the device will be approved if the manufacturer agrees to certain conditions, or a “not approvable letter” describing the deficiencies in the application, or an order denying approval entirely.⁸ Once FDA approves a PMA application, the applicant must comply with the approval order, which contains certain conditions to approval.⁹ In addition, any subsequent changes that may affect the safety or effectiveness of the device must be submitted to FDA for approval via a PMA supplement.¹⁰

Since the 1950s, there have been examples whereby drugs and devices have undergone some type of informal postmarket surveillance. The practice began with the American Medical Association’s (AMA’s) efforts to register cases of drug-induced blood dyscrasias, most notably the antibiotic chloramphenicol’s rare side effect of aplastic anemia.¹¹ FDA soon established its own reporting system, and by 1961 both the AMA and FDA collectively studied all adverse reactions to drugs each year.¹² The AMA Registry concentrated on reports from physicians and smaller hospitals,

⁷ 21 CFR § 814.20.

⁸ 21 CFR § 814.44(c).

⁹ 21 CFR § 814.80.

¹⁰ 21 CFR § 814.39(a).

¹¹ B. Lee & WM Turner, FDA’s adverse drug reaction monitoring program. *AM J HOSP PHARM.* (1978); 35:929-932. HD Scott, A. Thatcher-Renshaw, SERosenbaum, WJ Waters, Jr., M. Green, LG Andrews & GA Faich, Physician reporting of adverse drug reactions: Results of the Rhode Island adverse drug reaction reporting project. *JAMA.* (1990); 263: 1785-1788.

¹² *Id.*

while FDA focused on collecting information from larger hospitals, universities and the federal government. In 1962, the Food and Drug Act was amended to require drug manufacturers to report adverse drug reactions to FDA. The dual reporting system continued until 1970, when the AMA dissolved its Registry, due in part to the rampant underreporting it observed.

Since its enactment in 1976, one outgrowth of the Medical Device Amendments Act that has helped resolve the underreporting problems experienced by the AMA's Registry was the creation of Medwatch, FDA's Safety Information and Adverse Event Reporting Program. MedWatch is dedicated to maintaining the safety of medical device products through MDR.¹³ The reporting requirement falls primarily on manufacturers and distributors of medical devices. Safety issues are now posted on FDA's website (www.fda.gov) as a "Safety Alert."¹⁴ The following is FDA's own summary of reporting requirements for manufacturers:

REPORTER	WHAT TO REPORT	REPORT FORM #	TO WHOM	WHEN
Manufacturer	30 day reports of deaths, serious injuries and malfunctions	Form FDA 3500A	FDA	Within 30 calendar days from becoming aware of an event
Manufacturer	5-day reports on events that require remedial action to prevent an unreasonable risk of substantial harm to the public health and other types of events designated by FDA	Form FDA 3500A	FDA	Within 5 work days from becoming aware of an event
Manufacturer	Baseline reports to identify and provide basic data on each device that is subject of an MDR report. At this time, FDA has stayed the requirement for denominator data requested in Part II, Items 15 and 16 on Form 3417.	Form FDA 3417	FDA	With 30 calendar, and 5 work day reports when device or device family is reported for the first time. Interim and annual updates are also required if any baseline information changes after initial submission. ¹

¹ <http://www.fda.gov/cdrh/devadvice/351.html>.

There are several newer "reactionary" postmarket surveillance mechanisms in place besides MedWatch, initiated as recently as 2004. The transfer of postmarket surveillance studies from the Office of Device Evaluation (ODE) to the Office of Surveillance and Biometrics (OSB) has led to further controversy, affecting medical devices and drugs, alike.¹⁵ Under OSB authority, FDA has effectively merged post-approval studies with the PMA process, making it a new condition for approval. This transfer of authority to OSB has allowed the launch of additional initiatives

¹³ FDCA sec. 519(a), 21 USC.

¹⁴ http://www.fda.gov/medwatch/SAFETY/2007/mar07_quickview.htm.

¹⁵ <http://www.sciencedaily.com/releases/2004/10/041006084449.htm>; ORTHOPEDICS THIS WEEK, *What's Up With New Post-Market Approval Studies?*, Vol. 3, issue 19, p. 10.

to strengthen post-approval study diligence.¹⁶ But generally, since 1984 all domestic manufacturers have been subject to the baseline MDR regulation noted above if they were initially required to register their product with FDA.

In 1991, FDA published a tentative final rule in the *Federal Register*, proposing to implement heightened reporting regulations for users and distributors. This included different time frames for reporting, as well as the use of standardized reporting forms. On June 16, 1992, President Bush signed into law the Medical Device Amendments of 1992, amending certain provisions of the FDCA that relate to the reporting of adverse events.¹⁷ The primary impact of the 1992 Amendments on MDR reporting was to define certain terms and to establish a single reporting standard for user facilities, manufacturers and distributors. The final rule was published in the *Federal Register* in 1995.

Following the final MDR regulation in 1995, U.S. Attorneys were given an updated overview of Medical Device Law, so they could better prosecute violators of the newly enacted law, including the charges which may be brought against offending manufacturers and distributors. One such subsection relates specifically to Reporting Requirements, including a “Medical Device Reporting” charge. The charge, in its entirety:

A device manufacturer or importer is required, within specified time periods, to submit reports to FDA whenever the manufacturer or importer receives or otherwise becomes aware of information that reasonably suggests that one of its marketed devices: 1) may have caused or contributed to a death or serious injury; or 2) has malfunctioned, and that the device or a similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.¹⁸

II. CLINICAL IMPLICATIONS—SPINE DEVICES

In the field of implants for spinal surgery, approximately 10 devices in the past 15 years have used this PMA process to gain FDA approval. For these Class III devices, manufacturing criteria are part of FDA product approval process, and are strictly monitored by FDA throughout the life of the product.

More recent FDA approvals for Class III spine devices have stipulated some type of postmarket surveillance. For both the Charite lumbar artificial disc by Johnson & Johnson, Cincinnati, Ohio, approved in October 2005, and the ProDisc-L artificial lumbar disc by Synthes, West Chester, Pennsylvania, approved in August 2006, FDA formally required postmarket surveillance as a condition of approval. Under the post-approval study requirements, each sponsor must monitor annual patient follow-up visits among the study population until five years postoperatively.¹⁹ Additionally, Class III devices require mandated structured “annual reports,” disclosing all changes in manufacturing, all adverse events that have occurred in the clinical study population, and which must support ongoing safety and efficacy of the device

¹⁶ *Id.*

¹⁷ P.L. 102-300.

¹⁸ FDCA sec. 519(a), 21 U.S.C. sec. 360i(a); *see also* 21 C.F.R. part 804.

¹⁹ JE Zigler, et al, *Results of the prospective, randomized, multicenter Food and Drug Administration Investigational Device Exemption study of the ProDisc-L Total Disc Replacement versus circumferential fusion for the treatment of 1-level degenerative disc disease*, SPINE, (2007), 32: 1155-1162.

Although only limited to five years, the postmarket surveillance requirements for these new Class III devices are significantly more rigorous than any surveillance imposed on the plethora of Class I and II devices in widespread clinical use, which have minimal annual baseline reporting requirements.

Absent the formally-required reporting process described for the Charite and ProDisc-L artificial discs, surveillance for Class I and II devices (as well as Class III devices on an informal basis) essentially falls to voluntary reporting by patients, individual physicians, and hospital staff members. In fact, 21 CFR 20.63 prohibits disclosure of confidential information by manufacturers, except in certain circumstances.²⁰ Moreover, the onus to disclose information obtained via the physician-patient relationship more often falls on FDA when it is under a court order than it does upon manufacturers, sometimes requiring disclosure in unredacted form.²¹ The issue of physicians' underreporting has been well-documented in the pharmaceutical investigational realm.²² The reasons for this, which certainly may also apply to the medical device industry, include ignorance of the reporting system, complacency, fear of medicolegal liability, personal or professional guilt about having inadvertently harmed a patient, and uncertainty as to whether the drug or device was actually the cause of the adverse event.

In Class III device studies, the clinical investigator (usually the treating physician) is responsible for reporting all "Adverse Events" and "Serious Adverse Events" to the individual hospital's Institutional Review Board (IRB), as well as to the sponsor and FDA. On the contrary, reporting of adverse events associated with Class I or II devices is voluntary for the treating physician and may be performed by informal means, as contained in published case reports, posters or presentations at scientific meetings, verbally told to manufacturers' representatives, sent as individual reports to manufacturers, or sporadically reported on a voluntary basis to FDA.

With such an unstructured system, underreporting is not surprising. Although FDA individually reviews every direct report from a physician, it is typically a highly publicized single event (a dramatic device failure or serious complication of a device in a public figure, for example) or frequent-enough adverse events that prompt multiple reports about the same device, and that are likely to prompt regulatory change based on clinical observations.

III. PREEMPTION ISSUES

One of the legal "impediments" to FDA's postmarket surveillance goals involves an issue of federalism, a "turf war" between a state's law and federal law. Under the doctrine of federal preemption, state law will be overridden if the field is sufficiently occupied by the federal government, but issues of disparate treatment among several states have arisen in the area of medical devices, which may cause confusion and, potentially, further underreporting.

²⁰ In *York v. American Medical Systems, Inc.*, U.S. App. LEXIS 30105 (1998), a district court granted plaintiff's request for disclosure, denying defendant's motion for protective order to prevent disclosure of MDR documents in unredacted form.

²¹ *Id.*

²² SA Edlavitch, *Adverse Drug Event Reporting: Improving the Low US Reporting Rates*, ARCH INT MED. (1988), 148:1499-1503; AS Rogers, E. Israel, CR Smith, D. Levine, AM McBean, C. Valente & G. Faich, *Physician Knowledge, Attitudes, and Behavior Related to Reporting Adverse Drug Events*, ARCH INT MED, (1988), 148:1596-1600.

A. *Brief History of Preemption in Medical Devices*

In addition to setting forth the procedure for obtaining PMA of medical devices, the Medical Device Amendments contain an express preemption clause, which states, in relevant part:

[N]o state or political subdivision of a State may establish or continue in effect *with respect to* a device intended for human use any requirement—

- 1) which is different from, or in addition to, any *requirement* applicable under this chapter to the device; and
- 2) which relates to the safety or effectiveness of the device or to any other matter included in a *requirement* applicable to the device under this chapter.²³

However, the Act does not define the term “requirement,” making it unclear whether Congress intended the provision to preempt state common law claims. This has led to the development of caselaw that helps remove the inherent ambiguity created by FDA’s preemption statute, but nevertheless stands as a testament to the confusion and unpredictable nature involved in such claims.

In *Cipollone v. Liggett Group*, the U.S. Supreme Court found that a state failure to warn claim was indeed preempted because Congress had sufficiently covered the labeling at issue, thus “occupying the field.” The Court deemed that the plaintiffs’ state and common law claims for failure to warn were preempted by the express preemption language contained in the Public Health Cigarette Smoking Act of 1969.²⁴ However, in *Medtronic v. Lohr*, the Supreme Court held that a Florida State statute involving a failure to warn did *not* create a direct conflict of a federal statute, and, therefore, was not preempted.²⁵ Rather, the Court examined the preemption language of the Medical Device Amendments of 1976, and interpreted much of it as having been intended by Congress to be dependent upon regulatory actions taken by FDA.

In *Lohr*, the state requirements of general applicability did not have “the effect of establishing a substantive requirement for a specific device,” nor did they threaten to interfere with a specific federal interest.²⁶ In other words, the Court held, a state’s requirements may be more stringent than the federal requirement so long as it was not developed with the specificity Congress had in mind when drafting its own statutes. Moreover, the statutory requirements at issue in *Lohr* were not specifically developed “with respect to” medical devices, and did not therefore constitute “requirements” under the preemption provision. Ultimately, the Court held that the term “requirements” under FDA’s preemption statute made federal preemption appropriate only in the case of device-specific state statute requirements.²⁷

²³ 21 USC § 360k(a) (emphasis added).

²⁴ 505 U.S. 504, 517 (1992). This case was decided before the Court determined in *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120 (2000), when FDA still controlled cigarettes and smokeless tobacco products as devices intended to deliver nicotine to the body.

²⁵ 518 U.S. 470 (1996).

²⁶ *Id.* at 474.

²⁷ *Id.* at 500.

B. *Lohr's Preemption of Claims Involving Class III Devices*

The Supreme Court did not reach the issue of whether the preemption of state claims (as per its decision in *Lohr*) also applies to devices entering the market through the PMA process. However, lower courts have attempted to address the question since *Lohr*, the majority of which have held that such claims are in fact preempted.

In *Riegel v. Medtronic*, the Second Circuit granted Medtronic's motion for summary judgment on the issue of federal preemption by section 360(k) of the Medical Device Amendments to the FDCA.²⁸ Medtronic moved for summary judgment on all claims on the ground that they were preempted by Section 360k(a) of the Medical Device Amendments to the FDCA. The court based its decision on the already-stringent PMA process, the explicit preemption provision of the Medical Device Amendments, and the Supreme Court's recent decision in *Medtronic v. Lohr*.

The Eleventh Circuit, however, is in fact the only Circuit to have held that the PMA process represents nothing more than FDA's general findings that the device is safe and effective, and does not provide any indication of any specific substantive requirements that FDA may have applied to reach its determination. In this case, *Goodlin v. Medtronic*, the court held that state claims involving PMA devices are not preempted because PMA does not constitute a federal "device-specific requirement" within the meaning of Section 360k(a). However, the Eleventh Circuit's holding in *Goodlin* is still merely an outlier case, and state common law actions alleging liability as to a PMA device generally inherently conflict with FDA's preemption requirement, and are therefore preempted.²⁹

Although the *Riegel* decision effectively precluded many common law tort claims of Class III devices, parties may still rely on the Supreme Court's federalism-based decision in *Buckman v. Plaintiffs' Legal Comm* for a similar claim.³⁰ There, the Court held that patients' state law "fraud on the FDA" claims for Class III PMA devices (pedicle screws) were impliedly preempted by section 360k(a) of the FDCA. Rather, the FDA is vested with the sole authority "to punish and deter" fraud against itself.³¹ As a general policy matter, allowing such state law claims would "inevitably conflict with the FDA's responsibility to police fraud consistently with the administration's judgment and objectives."³² Indeed, medical device manufacturers would be prohibitively burdened by having to defend among various states' individual tort systems.

The end result of all the aforementioned dissonance among the states surrounding federal preemption issues in Class III medical devices may cause manufacturers to become reluctant in fulfilling their reporting requirements, mainly because of the uncertainty of decisions based on a given state's laws. The *Buckman* decision may put some of those fears to rest for the time being, but with federal preemption in this area having been in a constant state of flux for the past fifteen years, it is no surprise that some manufacturers may wish to remain reticent in reporting adverse events.

²⁸ 451 F.3d 104 (2d Cir 2006).

²⁹ 167 F.3d 1367, 1377 (11th Cir 1999).

³⁰ 531 U.S. 341 (2001).

³¹ *Id.* at 353.

³² *Id.* at 350.

IV. MISBRANDING/ADULTERATION ISSUES

The harsh consequences for misbranding or adulteration of a given medical device under 21 C.F.R. 850 et seq., including condemnation and forfeiture, may help create an irrational fear among manufacturers, thus creating an atmosphere where they are afraid to report even minor infractions. Currently, U.S. Attorneys are advised to prosecute for a manufacturer's failure to report an adverse event resulting from a "malfunction" which it must have "reasonably known." Such requirements create a slippery slope in terms of prosecution, because a manufacturer may be held responsible for "reasonably knowing" about even minor malfunctions.

However, it should be noted that there generally must be a high incidence of adverse events associated with a given product before it can be construed to be misbranded or adulterated. Additionally, the *de minimis* doctrine has been applied to at least one district court case, which manufacturers may rely on as a defense.³³

V. CONCLUSION

Medical device reporting is no doubt necessary as a method of surveillance to ensure the safety and efficacy of FDA-approved devices after they have been released to the market. But history has taught us that in a voluntary system, underreporting can occur, having been largely responsible for the dissolution of the AMA's own internal reporting mechanism. The legal issues surrounding MDR for PMA devices, and the harsh consequences attached to even minor infractions may act as theoretical deterrents to the fullest and open reporting possible. With widespread availability of Internet access, consumers and investors alike can be made aware the moment problems with a device occur, no matter how isolated or sporadic. The posting of only a minor malfunction or drawback with a device, uploaded to the internet and immediately available for consumers to view, can have catastrophic consequences for a company. The majority of medical device manufacturers must answer to a fickle stock market, and operate in a very competitive business environment.

Ultimately, postmarket surveillance in the form of medical device reporting requires the full and willing participation of both manufacturers and clinicians, and FDA must make every effort not only to enforce compliance retroactively by prosecuting malfeasance, but also to positively incentivize future participation. This will best ensure that FDA will be made fully aware as to whether a product is performing appropriately. Although recently-approved Class III devices have been required to undergo more rigorous premarket testing as well as structured post-market surveillance, the vast majority of medical devices currently on the market have either never been primarily shown to be safe and effective (Class I), or have been demonstrated to be merely "equivalent" to a device that was marketed prior to 1976 (which itself never had to prove safety and efficacy). It would thus seem to be even more important to consider postmarket surveillance for these Class I and Class II medical devices than for the newer Class III devices, or to at least require a similar level of surveillance among all three classes.

³³ U.S. v. ... Articles of Device Consisting ... of Proplast, 800 F. Supp. 499, 502 (S.D. Tx, 1992). The *de minimis* doctrine is an equitable doctrine which mitigates against the sometimes harsh results of strict application of FDA regulations.