Regulation of Investigational Medical Devices: 
Benefits and Obstacles

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I. INTRODUCTION

Statutory provisions are in place to regulate the performance standards of investigational medical devices.1 An investigational medical device is “a medical device which is the subject of a clinical study designed to evaluate the effectiveness and/ or safety of the device.”2 Medical devices are split into three categories: Class I, Class II, and Class III.3 Examples of devices that fall into these three classifications include stethoscopes, computer tomography scanners, and pacemakers, respectively.4 Depending on the classification, the device is subject to varying levels of regulatory scrutiny before being marketed to the public.5

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Class I devices pose no potential for unreasonable risk of illness or injury, whereas Class II devices present the potential for such a risk, although the potential risk is generally not life-threatening. Class III devices have the highest likelihood that harm will occur and are subject to a process of scientific and regulatory review, known as premarket approval, because the Food and Drug Administration (FDA) has determined that the regulations for Class I and Class II devices are inadequate to ensure the safety of these Class III devices. Therefore, Class III devices are subject to more stringent FDA regulations and safeguards before they are approved for public use. These provisions are set up to ensure that medical devices are safe and effective.

Nonetheless, some groups criticize these regulations because the approval process for Class III devices raises public health concerns. Some commentators are concerned that loopholes in the current regulations for medical devices, specifically regulations (or loopholes) that create a public health risk are flawed and increase a patient’s risk for injury or death.

This article discusses research protocol, regulatory procedure, and situations which warrant exceptions to the use of investigational medical devices before formal approval, along with justification for these exceptions. This article also discusses safeguards to minimize public exposure to harmful devices and obstacles to insurance coverage.

II. STANDARD RESEARCH AND APPROVAL PROCEDURES FOR HIGH RISK INVESTIGATIONAL DEVICES

Investigational devices that are considered high risk are not exempted from the pre-market approval process. Before a high risk investigational device

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6 See Maisel, supra note 4, at 296-297.
7 Michael VanBuren, Closing the Loopholes in the Regulation of Medical Devices: The Need for Congress to Reevaluate Medical Device Regulation, 17 HEALTH MATRIX 441, 446-447 (2007) (discussing approval standards based on device classification).
9 See generally VanBuren, supra note 7, at 441-446.
10 Id. at 441.
11 FDA, IRB GUIDANCE, supra note 2.
is made available to the public, it must undergo rigorous testing to comply with FDA standards. If clinical investigators chose to conduct a clinical investigation, they must obtain an investigational device exemption (IDE) from the FDA before starting the investigation. Typically, in the case of an IDE, the device is under clinical investigation “for a serious or immediately life-threatening disease or condition in patients for whom no comparable or satisfactory alternative device or other therapy is available.” Because these are medical studies, the principal clinical investigators are usually physicians. An IDE allows the investigators to conduct the clinical trials necessary to gather data on the safety and effectiveness of the device to support market approval. An unapproved device cannot be used on human subjects until it is cleared for use in clinical trials with an IDE. Once an IDE is granted, the investigators need to obtain approval from their respective institutional review board (IRB) whose purpose is to “protect the rights and welfare of human subjects involved in such investigations.” The IRB governs research studies at institutions to ensure compliance with research protocols, and is designed to minimize the risk of harm to research participants. If the study involves a “significant risk device,” both the IRB and the FDA must approve the IDE.

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14 Id. § 812.1(a).
15 Id. § 812.36(a).
16 CDRH DEVICE ADVICE, supra note 12, at 1.
18 21 C.F.R. § 56.101(a) (2008); see also 21 C.F.R. § 56.102(f)(g) (defines IRB as “any board committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodical review of, biomedical research involving human subjects” and defines institutions as any public or private entity where the research is being conducted).
19 CDRH DEVICE ADVICE, supra note 12, at 1.
III. EXCEPTIONS AND DEVIATIONS FROM STANDARD PROTOCOL

In certain situations, investigational devices may be used on a patient who is not a subject in the clinical trial. One exception includes emergency situations where the device is necessary to “save the life of a patient…suffering from a serious disease or condition for which there exists no other alternative therapy.”20 The FDA allows the use of investigational devices for such emergencies without prior approval.21 However, the investigator must report and justify the emergency use to the FDA within five working days from the time the principal clinical investigator learns of it.22 The investigator must also notify the IRB within five working days.23

Another exception to the formal approval process, in which investigational devices may be used on subjects not in a clinical trial, is termed “compassionate use.”24 Typically, compassionate-use patients are similar to emergency-use patients in that they have a serious disease or condition and there is no alternative treatment.25 However, the compassionate-use patients do not meet preset inclusionary criteria for the clinical trials,26 but the treating physician believes the patient will benefit from the device’s use in the treatment of his or her disease or condition.27 Unlike emergency use, compassionate use requires prior FDA approval.28 Under the compassionate use exception, the FDA utilizes its regulatory discretion to grant a protocol deviation to treat the patient.29 Overall, both compassionate and emergency uses allow patients the benefit of innovative

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21 21 C.F.R. § 812.35(a)(2); see IRB MEDICAL DEVICES, supra note 17, at 9.
23 Id. § 56.104(c).
25 Id.
26 Id.
27 Id.
28 CDRH IDE GUIDANCE, supra note 20, at 19.
29 Klepinski, supra note 24, at 851; see 21 C.F.R. § 812.35(a) (2008).
care while concurrently providing quality data on the effectiveness of investigational medical devices.\textsuperscript{30}

Although the use of investigational devices in such situations can create unforeseen risks to patients, and are deviations from investigational protocols, the FDA exercises their aforementioned regulatory authority to minimize the potential of harm to patients. Furthermore, the FDA offers guidance to investigators, as well as to IRBs, to avoid confusion and maximize compliance.\textsuperscript{31} One strategy the FDA employs to monitor the risks associated with investigational devices used in clinical studies is to require investigators to report adverse events.\textsuperscript{32}

\textbf{IV. MANDATORY REPORTING}

An investigator, who has reason to believe that an investigational device caused or contributed to a serious injury or death, must report the incident to the FDA.\textsuperscript{33} The Medical Device Reporting (MDR) provisions require investigators to report deaths and serious injuries within ten working days from the time the investigator becomes aware of the incident.\textsuperscript{34} Investigators are only required to investigate and report adverse events that are “reasonably known” to them.\textsuperscript{35} Investigators must also provide to the FDA an annual report of deaths and serious injuries.\textsuperscript{36} Device manufacturers report a majority of the 80,000 to 120,000 adverse events received each year by the FDA.\textsuperscript{37} In some cases, these devices may cause \textit{an} injury, but investigators are only required to report device

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\textsuperscript{30} See Klepinski, \textit{supra} note 24, at 853.
\textsuperscript{31} See IRB MEDICAL DEVICES, \textit{supra} note 17, at 1.
\textsuperscript{32} 21 C.F.R. § 803(1)(a) (2005).
\textsuperscript{33} Id.
\textsuperscript{35} Id.
\textsuperscript{36} Id.
\textsuperscript{37} Maisel, \textit{supra} note 4, at 299.
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malfunctions that actually cause serious injury or death.\textsuperscript{38} Therefore, adverse events may be underreported.\textsuperscript{39}

Unfortunately, there is an additional factor which leads to underreporting of injuries caused by malfunctioning devices. Conflicts of interest create barriers to disclosure in investigational research, especially when financial incentives are involved.\textsuperscript{40} Manufacturers are concerned that disclosures may undermine their competitive advantage.\textsuperscript{41} Consequently, concerns have been raised about the veracity of sponsor-related research data.\textsuperscript{42} However, health care professionals and patients can also report to the FDA suspected injuries that result from malfunctioning medical devices.\textsuperscript{43} Thus, the FDA is reliant upon physicians and consumers to report adverse events.\textsuperscript{44} The FDA also takes an active role in the process by sending trained investigators to conduct routine field inspections, and to evaluate device malfunctions and irregularities.\textsuperscript{45}

As an additional safeguard to maximize reporting of adverse events, the FDA has implemented penalties for failure to comply with reporting requirements.\textsuperscript{46} Generally, the FDA will initially issue a warning letter.\textsuperscript{47} Subsequent noncompliance could result in civil (and possibly criminal) penalties.\textsuperscript{48} Although reports filed in accordance with MDR requirements are generally inadmissible in civil actions against private parties, the entities’ officials and clinical investigators can be subject to substantial fines and prison sentences for failure to comply with reporting requirements.\textsuperscript{49}

\textsuperscript{38} Rainville, supra note 34, at 10.  
\textsuperscript{39} Maisel, supra note 4, at 299.  
\textsuperscript{40} See generally Deborah A. Zarin & Tony Tse, Moving Towards Transparency of Clinical Trials, 319 SCI. 1340,1342 (2008) (discussing intellectual-property issues and data accuracy).  
\textsuperscript{41} See Id.  
\textsuperscript{42} Id.  
\textsuperscript{43} Maisel, supra note 4, at 299.  
\textsuperscript{44} Id. at 298.  
\textsuperscript{45} Id. at 299.  
\textsuperscript{46} Rainville, supra note 34, at 10-11.  
\textsuperscript{47} Id. at 11.  
\textsuperscript{48} Id.  
\textsuperscript{49} Id. at 10-11.
V. CLINICAL TRIALS: A SOLUTION OR A PROBLEM?

There is little disagreement regarding the need for rigorous clinical trials prior to public use of medical devices.\textsuperscript{50} However, due to the lengthy and costly time frames of clinical trials, there are delays in delivering these products to patients who need them.\textsuperscript{51} Consequently, the problems inherent in the design of some clinical trials increase patient mortality.\textsuperscript{52} The current standards of clinical trials typically focus on factors, such as design safety and mortality, are quite costly because they can be lengthy and require patient tracking.\textsuperscript{53} Some researchers and practitioners propose that there should be less emphasis on mortality data and greater focus on clinical efficacy.\textsuperscript{54} These researchers argue that clinical efficacy focuses more specifically on the effectiveness of the device in the treatments of the specific disease, as opposed to the current standards that focus on death and mortality factors.\textsuperscript{55} Establishing rigorous and efficient clinical trials that are consistent with FDA standards for safety and effectiveness will continue to be an ongoing challenge for research investigators.\textsuperscript{56}

VI. REIMBURSEMENT OBSTACLES

In addition to the delays in the clinical trial process, insurance coverage is another obstacle that prevents the use of investigational or experimental treatment. Even when the FDA authorizes investigators to use experimental treatments, programs like Medicare and Medicaid exclude such treatments from

\textsuperscript{51} Id. at 515-16.
\textsuperscript{52} Id. at 516.
\textsuperscript{53} Michael J. Schneck, \textit{Critical Appraisal of Medical Devices in the Management of Cerebrovascular Disease}, 4 \textit{THERAPEUTICS \\& CLINICAL RISK MGMT.} 19, 19 (2008); Henderson \\& Smith, \textit{supra} note 50, at 516.
\textsuperscript{54} See Henderson \\& Smith, \textit{supra} note 50, at 517.
\textsuperscript{55} See Id.
\textsuperscript{56} Id.
reimbursement unless it has been proven efficacious. Reimbursement obstacles can keep patients from receiving life-saving medical device treatment even after the device has been cleared for public use. Device companies do not want payment rule-issuing agencies, such as the Centers for Medicare and Medicaid Services (CMS), to “create barriers that discourage Medicare beneficiaries from accessing new treatments being studied in clinical trials or that are commercially available.” Requirements for additional evidence of device efficacy before allowing reimbursement may leave patients paying expensive medical bills for a treatment necessary to save their lives. However, some practitioners advocate that insurance companies should not provide full reimbursement until the device demonstrates unequivocal clinical efficacy.

VII. CONCLUSION

Despite the limitations in regulating investigational medical devices, there seems to be consensus regarding their benefit to the public good. Unfortunately, this seems to be where the agreement ends. Some commentators urge that stricter FDA regulations would better serve the public by minimizing the use of unapproved, and potentially harmful, devices. Others believe that more stringent clinical trials are the best solution. As discussed, there are drawbacks to both potential solutions. The emergency and compassionate use exceptions exist to maintain a balance between providing patients with life-saving treatment and ensuring patient safety prior to formal approval of investigational devices. Even after the product is finally approved and delivered to public consumers, the

59 Id.
60 See Id.
62 VanBuren, supra note 7, at 441.
63 See Schneck, supra note 53, at 19; see also Henderson & Smith, supra note 50, at 517.
64 See Klepinski, supra note 24, at 853 (discussing the compassionate use provision).
next question becomes: who pays for it? Insurance companies may not want to pay unless they are convinced of the efficacy, and some practitioners believe this is a proper standard.65 In response, other practitioners argue that these medical treatments may be expensive, and thus requiring a higher standard of clinical efficacy before insurance companies will reimburse could prevent some patients from receiving beneficial medical treatment.66 Finding a uniform solution does not appear likely in the near future, despite efforts toward such progress. Whatever the final solution becomes, it should be driven by the best interest of the patients and public health, not private interests or financial incentives.

65 Barnes & Korn, supra note 57, at 610; see also Furlan & Fisher, supra note 61, at 399.
66 Novelli, supra note 58, at 58.