The Law on Cardiovascular Devices: The Role of the Food and Drug Administration and Physicians in its Implementation

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SUMMARY The Medical Device Amendments of 1976 gave the Food and Drug Administration (FDA) new authority to regulate all medical devices. This regulation requires that manufacturers provide data supporting the safety and effectiveness of new and modified devices before marketing them, and eventually provide similar data even for devices now on the market. Those working in the cardiovascular field use a device every day of their professional lives; therefore, the Medical Device Amendments will have a significant effect on everyone in the field. We must understand the law so that we can provide scientific guidance to the FDA and to the medical device industry; in this article we aim to provide the necessary information.

THE FOOD AND DRUG ACT was originally passed in 1906 to regulate the purity and safety of foods and drugs. In 1938, Congress passed the Federal Food, Drug, and Cosmetic Act, which provided regulatory authority over cosmetics, devices and drugs. This Act required that manufacturers of new drugs prove safety in applications for premarketing approval of new drugs. In 1962, the Act was amended to provide regulatory authority to assure not only the safety of new drugs through premarketing applications, but also their effectiveness. Between 1938 and May 28, 1976, the Act did not change with regard to the regulatory authority provided for medical devices. The 1938 Act prohibited the distribution of misbranded or adulterated devices in interstate commerce. Although premarket approval by the government for device safety and effectiveness was not required, devices had to be labeled properly. For example, if the device was sold in a container that was labeled "sterile," the device had to be sterile to be in compliance with the Act. However, before May 28, 1976, device manufacturers were not required to demonstrate that a device was safe and effective; the burden of demonstrating "misbranding" or "adulteration" was with the Food and Drug Administration (FDA). If the FDA had reason to believe that a device was in violation of the Act, the normal procedure was to collect a sample of the device, obtain data to show the device was actually in violation of the Act, and prove that the device was in interstate commerce in order to support any regulatory action which might ultimately be contested in the courts. Manufacturers of medical devices were not required to register with the FDA or to list their products with the FDA; therefore, the FDA was "regulating" an unknown quantity.

Medical Device Act*

The Medical Device Amendments, signed into law by President Gerald Ford on May 28, 1976, provide the FDA with expanded authority to regulate medical devices.* This Act of Congress also requires the FDA to follow certain explicit procedures for implementing this act, some of which will be discussed in detail in this presentation.

Definition of "Device"*

In the Act, the term "device" means "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related...

* A copy of the Medical Device Amendments of 1976 can be obtained from the FDA Hearing Clerk (HFA-305), Room 4-65, 5600 Fishers Lane, Rockville, Maryland 20857.
article, including any component, part, or accessory, which is —

“(1) recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them;

“(2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or

“(3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its principal intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes.”

Provisions of the Act

The Medical Device Amendments provide broad authority to the FDA to regulate medical devices. For example, the FDA may now institute a regulatory action with regard to a medical device without first determining that the device was in interstate commerce; that is, the FDA may presume that interstate commerce exists. The FDA may temporarily detain a device when it suspects that the device is in violation of the Act. It may ban a device that presents a substantial deception or unreasonable substantial risk of illness or injury. The FDA is also authorized to establish official names for devices, which is similar to the authority it has for drugs.

The Medical Device Act preempts state and local requirements for medical devices when such requirements differ from those established by the FDA. However, the FDA also has the authority to exempt a state or local requirement from the preemption provision if that requirement is more stringent than the federal requirement or if compelling local conditions require it, and compliance with the state or local requirement would not cause the device to be in violation of the Act.

The Act authorizes the FDA to restrict the sale, distribution or use of a device if its safety and effectiveness cannot otherwise be reasonably assured. However, under this provision, the FDA is not allowed to restrict the device to categories of physicians based solely on whether the physicians are “board eligible” or “board certified.” The FDA has the responsibility of regulating the advertising of restricted devices.

The Act authorizes the FDA to prescribe good manufacturing practice regulations concerning the manufacturing, packaging, storage and installation of devices. The Act requires certain record keeping and reporting for manufacturers of medical devices; for example, concerning their manufacturing operations and distribution. The law requires that manufacturers must register with the FDA and list their devices semiannually with the FDA.

The FDA may also require notification of all health professionals when a device presents an unreasonable risk of substantial harm to the public. If the FDA determines that notification alone is not sufficient to eliminate the risk, it may require the manufacturer, importer or distributor to repair or replace the device or to make a refund to the purchaser.

The Medical Device Amendments prohibit the export of devices that do not comply with certain provisions of the Act. However, these devices may be exported if they meet the specifications of the foreign purchaser; they are in compliance with the laws of the importing country; the health agency of the foreign country approves the export; the FDA determines that the export is not contrary to the public health; and the device is labeled for export only.

The Act allows for certain custom devices which are specially ordered for an individual patient or to meet the needs of an individual physician or other specially qualified person to deviate from certain performance standards and the requirements for premarket approval, as may be necessary.

The Act also allows for devices to be exempted from many of the requirements of the Act if they are intended solely for investigational use. Depending on the risk posed by the device in the investigation, the person seeking such an exemption must: (1) submit to the FDA a report of prior investigations of the device and a protocol approved by an institutional review committee (institutional review board); (2) obtain appropriate informed patient consent; and (3) maintain certain records and reports.

The Act requires that the FDA establish an office to provide nonfinancial technical assistance to small manufacturers of medical devices.

The Medical Device Amendments require that all medical devices marketed before enactment of the law (May 28, 1976) be classified into one of three regulatory categories: class I (general controls), class II (standards) or class III (premarket approval). Panels of experts must be used to classify these devices and the FDA must publish summaries of the safety and effectiveness data on which it bases its decisions for classification. The law also requires that standards be developed for all class II products and that manufacturers of all devices classified in the class III category provide scientific data to support the safety and effectiveness of the device. A product which under the new amendments meet the definition of a device, but which were previously regulated as new drugs (for example, a biological arterial graft), are automatically regulated as a class III device.

The Act requires manufacturers of devices that were first marketed after May 28, 1976, or are modified after that date, to notify the FDA about the safety and effectiveness of the device. The FDA is then required to determine whether the device is substantially equivalent in terms of safety and effectiveness to a preenactment device. Products similar to preenactment devices are regulated in exactly the same way as the devices they are equivalent to, and devices declared to be not substantially equivalent to a preenactment device or new devices must undergo premarket approval before they are marketed.

The law also provides for important procedural
mechanisms for informal hearings or hearings by special advisory committees concerning certain decisions by the FDA; for example, on premarket approval applications.

Procedures to be Followed for all Devices

Under the Act, devices marketed before and after May 28, 1976 are treated differently.

Devices Marketed Before Act of 1976

The Medical Device Amendments require that all devices marketed before May 28, 1976 be classified into one of three regulatory categories: general controls (class I), standards (class II) and premarket review (class III). The FDA had to solicit the advice of advisory committees consisting of non-FDA medical and scientific experts. The Bureau of Medical Devices of the FDA had separate advisory committees in 19 specialty areas. The Cardiovascular Device Classification Panel was formed in 1972, in 1978 it was renamed the Circulatory System Devices Panel. All panel members are listed at the end of this report. This panel has prepared a report in which they have listed all cardiovascular devices, consisting of more than 141 generic device groups, and have classified each of these groups of devices into one of the three regulatory categories.

Class I (general controls) is primarily for devices that pose no potential risk to health, and thus, can be adequately regulated without imposing standards or the need for premarket review. This category provides a broad general control. It requires that manufacturers of these devices register with the FDA; provide a listing of the products which they manufacture, which should be updated periodically; maintain and make available to the FDA, when requested to do so, adequate reports to assure that the devices that they manufacture are safe and effective; and comply with good manufacturing practices developed by the FDA after consultation with a special advisory committee established for that purpose. Manufacturers of all devices must comply with the above requirements.

Devices are to be classified in the class II (standards) category when general controls are not adequate to assure the safety and effectiveness of a device, based on the potential risk to health posed by the device. To classify a device in the class II category, the panel and the FDA must find that enough data are available on which to base adequate performance standards that would control the safety and effectiveness of these devices.

If the panel and the FDA believe that inadequate data are available on which to base a standard that would control the risks to health associated with use of a device, the device has to be classified in the class III (premarket review) category. In addition, the Medical Device Amendments also require that if a device is life-supporting, life-sustaining or an implant, then it must be classified in the class III category unless adequate justification is given for classifying it in another category.

Of the cardiovascular devices, four (surgical instruments, manual stethoscope, cardiopulmonary bypass accessory equipment and pacemaker service tools) have been recommended for classification in the class I category, 111 have been recommended for classification in the class II category and 26 have been recommended for classification in the class III category. Examples of class II devices include diagnostic intravascular catheters, vascular graft prostheses which are 6 mm or greater in diameter, electrocardiographs and vectorcardiographs. Examples of class III devices are replacement heart valves, oxygenators, pacemaker pulse generators, permanent pacemaker electrodes and arrhythmia detectors and alarms.

The cardiovascular advisory panel has submitted its report to the FDA, with recommendations for the classification of all cardiovascular devices. The FDA's proposed classification regulations were published in the Federal Register on March 9, 1979. After an appropriate period of time during which comments were received, considered, and changes made, final regulations that classified all cardiovascular devices were published on February 5, 1980.

Further Action After Classification of Devices Marketed Before May 1976

For devices classified in the class II (standards) category, the FDA may publish a notice soliciting recommendations for standards from the public, including the regulated industry. When the public does not respond or does not respond in an appropriate period of time, the FDA may develop standards for the device. Provisional standards will be published in the Federal Register for review and comment by the public; the final regulations will be published in the Federal Register, at which time the standards will become effective. The FDA is also developing a policy on the use of voluntary and mandatory standards.

For devices in the class III (premarket review) category, the FDA must also publish proposed and final regulations for each generic device group. The manufacturers of these devices are required to submit to the FDA data proving the safety and efficacy of their products. To assure the continued availability of devices already on the market, the Congress allowed a grace period for manufacturers to accumulate and submit data. A manufacturer has 30 months from the date of the final regulation classifying his device in the class III category,* or 90 days from the final regulation requiring the submission of a premarket approval application for his device, whichever time period is longer, in which to submit his application for premarket approval. Because of the limitations of resources within the Bureau of Medical Devices of the FDA, the final regulations requiring the submission of premarket approval applications for the class III

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*The 30-month grace period does not apply to devices that were previously regulated as drugs by the Bureau of Drugs or the Bureau of Biologics; for example, biologic arterial grafts.
devices may be staggered over a 3–5-year period. Consequently, manufacturers of some of the high-priority class III devices, such as replacement heart valves or oxygenators, may be required to submit their premarket approval applications within 30 months after the publication of the final regulation classifying their devices in the class III category. The FDA will probably require submission of the applications for these high-priority devices around September 1982. However, for some of the low-priority class III devices, such as pulsatile flow generators (a device used in a cardiopulmonary bypass circuit to create pulsatile flow), the FDA might not require the submission of applications for approval of these devices before 1986 or 1987. However, there is no “grandfather clause” in the medical device legislation, and eventually, all devices in the class III category that were on the market before May 28, 1976 will be required to have an approved premarket review application in order to continue to remain on the market.

Devices Marketed After May 28, 1976

The Medical Device Amendments require a manufacturer who produced a device that is a modification of, or is similar to, a preenactment device (one marketed before May 28, 1976) to notify the FDA at least 90 days before the date he intends to market that product. This is a 510(k) notification. If a manufacturer produces a new device, then a premarket approval application may have to be submitted.

The 510(k) notification, so-called because it appears under subsection k of Section 510 (the Registration Section) of the Medical Device Amendments, should include a description of the device; copies of appropriate sections of proposed labeling; a description and copies of appropriate sections of labeling for an equivalent device that was marketed before May 28, 1976; an explanation of how the new or modified device is equivalent to and how it is different from the preenactment device; and a summary of data from in vivo animal and, if appropriate, clinical testing necessary to justify the equivalence of the new or modified device.

The purpose of the 510(k) submission is to give the FDA an opportunity to determine whether the new or modified device is equivalent to a device marketed before May 28, 1976 with regard to safety and effectiveness. If it is determined to be equivalent, the manufacturer is notified that his device will be regulated in the same manner as the device to which it is equivalent. If the equivalent device is in the standards category (class II), then the new device will also be required to meet appropriate standards when they are adopted by the FDA. If the equivalent device is in the premarket review category (class III), then the new or modified device will be subject to the same grace period as the equivalent device, and the sponsor of that device will have to submit a premarket approval application for his device when such is required for all preenactment devices of the same type. If the FDA determines that the new or modified device is not equivalent to a preenactment device, the manufacturer may submit a premarket approval application to be reviewed by the appropriate panel and the FDA, and the manufacturer must receive approval before being able to market the device, or the manufacturer could petition the FDA to ask the panel to consider reclassifying his device into class II or class I.

The manufacturer who determines that the device being produced is truly a new device and who wishes to market the device would submit a premarket approval application. In addition to other information, the following are also needed in a premarket approval application: (1) a narrative summary presenting a sound basis for the requested premarket approval; (2) full information and data, published or known to the applicant, concerning investigations performed to show whether the device is safe and effective; (3) separate sections on in vitro testing, in vivo animal testing, and clinical testing, when applicable; and (4) other information which the manufacturer considers relevant to safety and effectiveness and which has been required by FDA.

In this section Congress intended the Medical Device Amendments to require early premarket review of all new devices that are not equivalent to any preenactment devices before marketing the device. This is indeed happening. The first premarket approval application for a cardiovascular device was received by the FDA on July 7, 1977. It was reviewed and discussed. Additional data were requested, changes were made in the application, which were rediscussed, and final approval was granted on December 19, 1977. Since then, the Circulatory System Devices panel has reviewed applications for biologic arterial grafts, vena caval balloon occluders, embolization device, pacemakers, heart valves and percutaneous transluminal coronary angioplasty catheters.

Investigational Device Exemptions (IDE)

The purpose of this section of the law, as stated in the Amendments, is “. . . to encourage, to the extent consistent with the protection of the public health and safety and with ethical standards, the discovery and development of useful devices intended for human use and to that end to maintain optimum freedom for scientific investigators in their pursuit of that purpose.” Without this section of the law, it would be impossible for the device manufacturers to be in compliance with the law and at the same time provide for clinical testing to establish the safety and effectiveness of devices. This section of the law allows a device to be exempted from other specific sections of the law, such as those dealing with misbranding, so that the device can be investigated clinically and data obtained to support the indications for use and provide the necessary safety and efficacy data in support of a premarket approval application or a 510(k) submission.

This section of the law was effective as of July 16, 1980. The proposed regulations were published in
August 1976. This proposal was controversial because of the studies to which it applied and the requirements it placed on the sponsor, the investigator and the institutional review committee. Because of the controversy surrounding the original proposal for Investigational Device Exemptions, another draft of that proposal was published on May 12, 1978; public hearings were held concerning this new draft of the regulation on August 7, 1978, and the final regulation was published on January 18, 1980.

This regulation provides for different requirements, depending on whether a local Institutional Review Committee determines that the device to be investigated poses a significant risk. For devices determined to be of significant risk, the sponsor of the investigation must prepare a report of prior investigations including in vitro test data, and when appropriate, in vivo animal studies, which is adequate to justify the proposed clinical testing. A clinical protocol including an informed consent form must be prepared. The sponsor must also list the investigators who will carry out the study and their qualifications. A report of prior investigations and the clinical plan, and any other relevant information concerning the investigation has to be supplied to a local Institutional Review Committee. This committee, consisting of physicians and lay members, needs to review the above information and determine whether or not the benefit-to-risk ratio associated with the study is such that it is reasonable to approve the clinical trial. After approval by the local Institutional Review Committee, the study must be submitted to the FDA. If the FDA does not deny approval of the study within 30 days after receipt of the request for an exemption, the study may commence. If the Institutional Review Committee determines that the device is not of significant risk, then the study can be initiated without prior approval of the FDA.

**FDA and Physicians and Scientists**

The views of professional societies and of individual physicians and scientists have had a significant effect on the content and implementation of the above regulations because of the desire of the FDA to receive comments. Physicians, other scientists and professional societies have had an opportunity to comment on the classification of devices; they could play the major role in the development of standards for class II devices and will be able to offer scientific opinions concerning the extent and type of preclinical and clinical testing which should be required for class III devices and in applications for premarket approval. In addition, panel members and consultants to the panel provide the FDA with scientific review and recommendations about devices that are contained in premarket review applications. These roles also provide an opportunity for physicians, other scientists and professional societies to learn more about the FDA's mandate in regulating medical devices and gives the FDA an opportunity to learn from physicians and other scientists ways in which the medical device legislation might be implemented so as to provide maximum additional benefit without unnecessarily hindering the development of devices that are necessary and desirable for the type of medical care that our society expects. Because of the sensitive issues concerning an agency that regulates, it is mandatory that consultants and panel members have no conflict of interest with regard to the regulated industry.

Anyone who wants information concerning the panel meetings and the panel's activities, has information about devices that should be known to the FDA, or wants to comment or ask questions concerning any of the FDA activities in the area of cardiovascular devices, should contact Glenn A. Rahimoeller, Director, Division of Cardiovascular Devices.

**Circulatory System Devices Panel**

*Chairmen*

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Consumer Representatives


Industry Representatives

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