The Medical Device Approval Process and Related Legislative Issues

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Summary

The central medical device issue for Congress is how best to help speed medical devices to consumers if they are safe and effective, and correct them or keep them from consumers if they are not. A medical device may be anything from a tongue depressor to a pacemaker. In order to be legally marketed in the United States, medical devices must be approved by the Food and Drug Administration (FDA), the agency responsible for protecting the public health by assuring the safety, efficacy, and security of human medical devices and other products. FDA's Center for Devices and Radiological Health (CDRH) is primarily responsible for medical device review. The regulation of medical devices can affect their cost, quality, and availability in the health care system.

During reviews, FDA classifies devices according to the risk they pose to consumers. If a premarket review is warranted by the potential risk, a manufacturer must demonstrate that its device is safe and effective, or substantially equivalent to a device already on the market. FDA requires product manufacturers to register their facilities, list their devices with FDA, and follow general controls requirements. Manufacturers of FDA-approved devices are required to report serious adverse events associated with the use of their devices to FDA. In addition, tracking is required for some medical devices.

The medical device approval process is currently funded through direct FDA appropriations from Congress, and increasingly through user fees collected from applicants. FDA's authority to collect user fees, originally authorized in 2002 (P.L. 107-250), has been reauthorized in five-year increments. It will next expire on October 1, 2012, under the terms of the FDA Amendments Act of 2007 (P.L. 110-85).

A number of medical device-related topics are of interest to Members of the 111th Congress, and have prompted the introduction of legislation with pertinent provisions. Three such topics are included in major health reform bills: medical device-related taxes as a source of revenue for health reform (House-passed H.R. 3962 and Senate-passed H.R. 3590), a national medical device registry (House-passed H.R. 3962), and reporting requirements for gifts to physicians (House-passed H.R. 3962 and Senate-passed H.R. 3590).

Device-related topics addressed in other legislation include liability and preemption, as highlighted by *Riegel v. Medtronic* and *Wyeth v. Levine* (S. 540/H.R. 1346, H.R. 1086, S. 45, and S. 1324); the 501(k) clearance and device approval processes (H.R. 1321/S. 391); importation and inspection (H.R. 759 and S. 882); advertising (S. 301/H.R. 3138 and H.R. 3261); use of unapproved devices (H.R. 3261); laboratory test (*in vitro* diagnostic, or IVD) regulation; (H.R. 1699 and H.R. 1452); issues specific to certain devices, situations, diseases, or conditions (S. 717, S. 819, H.R. 1878, S. 586/H.R. 1483, H.R. 1380, H.R. 1236, H.R. 1142, S. 422/H.R. 1032, H.R. 1021, H.R. 554, S. 332, S. 254/H.R. 574, S. 236, H.R. 463, S. 21, H.R. 2088, H.Res. 577, and S. 1746); and certain other issues (H.R. 1531/S. 1089, H.R. 1737, S. 1733, S. 1591/H.R. 3560, H.R. 2454/S. 2998, H.R. 3012, H.R. 3090, H.R. 3242, and H.R. 3932).

This report contains the legislative history of medical device regulation, describes FDA's approval process for medical devices, and provides an overview of the medical device-related legislative issues facing Congress.

This report will be updated as events warrant.

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Introduction

There are many dimensions to the central medical device issue confronting Congress: how to speed medical devices to consumers if they are safe and effective, and correct them or keep them from consumers if they are not. The goals of device availability and device safety may exert opposite pulls, with implications for consumers, the health care system, and the economy. Investment in medical device development reportedly reached a high of $3.790 billion in 2007. However, investment has slowed considerably since then, reaching only $3.337 billion in 2008, and $1.197 billion in the first three quarters of 2009.[1] The products generated by the nation's venture capital-backed biotechnology and medical devices and equipment sectors supported nearly 494,000 high-skilled, high-wage jobs in 2006.[2]

Manufacturers make decisions about pursuing new devices based in part on the cost of their development. Additional regulatory requirements may escalate these costs, while other incentives, such as tax breaks or market exclusivity extensions, may diminish them. If the device development cost is too high, the eventual result may be that consumers are denied access because new products are not developed or brought to market. Access problems have led to proposals for and the enactment of incentives to develop medical devices for rare diseases and pediatric populations. However, if the regulation and oversight of device development are not stringent enough, unsafe or ineffective products may reach the market and cause harm to consumers.

Troubles related to medical devices can have serious consequences for consumers. Problems with the procedures and equipment for HIV (human immunodeficiency virus) and hepatitis C laboratory tests have led to hundreds of incorrect test results.[3] Defects in other types of medical devices, such as pacemakers, defibrillators, and coronary stents, have caused patient deaths.[4] Consequences such as these have raised questions as to whether adequate enforcement tools, resources, and processes are in place to ensure that marketed devices are safe.

The federal agency primarily responsible for ensuring the safety and effectiveness of medical devices and certain other products (drugs and biologics, for example) is the Food and Drug Administration (FDA)—one agency within the Department of Health and Human Services (HHS). A manufacturer must receive FDA permission before its device can be legally marketed in the United States. FDA's Center for Devices and Radiological Health (CDRH) is primarily responsible for medical device review. One other center, the Center for Biologics Evaluation and Research (CBER), regulates some devices—specifically those associated with blood collection and processing procedures, as well as with cellular therapies (e.g., stem cell treatments).

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[1] PriceWaterhouseCoopers/ National Venture Capital Association, "Medical Devices and Equipment," *Money Tree Report*, data provided by Thomson Reuters, at http://www.pwcmoneytree.com, searched January 26, 2010.

[2] Global Insight, "Venture Impact: The Economic Importance of Venture Capital Backed Companies to the U.S. Economy, Fourth Edition" (2008), at http://www.nvca.org/pdf/NVCA_VentureCapital07-2nd.pdf. (Note: the fifth edition, published 2009, did not contain information about jobs and the device industry.)

[3] See "Maryland Hospital Officials Resign After Patients Receive Incorrect HIV, Hepatitis C Test Results Processed in Lab," *Kaiser Network, Across The Nation* (April 22, 2004), at http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=23322.

[4] Information on recalls is available by searching the database at FDA, *Medical Device Recalls*, Database, http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm.

Jurisdiction of the centers' medical device review is governed by the FDA Intercenter Agreement between CBER and CDRH (October 31, 1991).[5]

FDA's medical device review process is funded through a combination of public money (direct FDA appropriations from Congress) and private money (*user fees* collected from device manufacturers), which together comprise FDA's total program level.[6] Since they were first collected in FY2003, the medical device user fee amounts have risen more quickly than direct appropriations for device-related activities (see **Table 1**).[7] Congress has reauthorized in five-year increments FDA's collection of medical device user fees. The authority will next expire on October 1, 2012.

Table 1. Appropriations for the FDA Devices and Radiological Health Program (DR&H), Medical Device User Fees, and Medical Device User Fees as a Percentage of Total DR&H Program Level Appropriations, FY2003-FY2011

(dollars in thousands)

	Total Program Level	Medical Device User Fees	MDUFA /Total
FY2003 Actual	$217,285	$14,838	6.8%
FY2004 Actual	$221,506	$23,875	10.8%
FY2005 Actual	$244,282	$27,161	11.1%
FY2006 Actual	$255,041	$32,069	12.6%
FY2007 Actual	$267,543	$35,202	13.2%
FY2008 Actual	$275,284	$36,422	13.2 %
FY2009 Actual	$345,311	$47,304	13.7%
FY2010 Appropriation	$368,342	$57,014	15.5%
FY2011 Request	$384,815	$61,860	16.1%

Sources: Food and Drug Administration tables for FY2005 - FY2011, "ALL PURPOSE TABLE - Total Program Level," at http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/BudgetReports/default.htm.

Notes: (1) Devices and Radiological Health (D&RH) total program level is the sum of budget authority and fees allocated from the MDUFA and MQSA authorities. The FY2011 request for the D&RH program includes $3.2 million in proposed reinspection user fees. (2) The numbers contained in this table were compiled by Susan Thaul, Specialist in Drug Safety and Effectiveness, CRS (sthaul@crs.loc.gov, 7-0562).

Medical device issues confronting the Congress arise in the context of a variety of concerns about FDA and CDRH.[8] Chief among these is that, in September of 2007, Congress passed the most

[5] FDA, *Devices Regulated by the Center for Biologics Evaluation and Research*, January 8, 2010, http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/510kProcess/ucm133429.htm.

[6] For more information on FDA's budget, See CRS Report RL34334, *The Food and Drug Administration: Budget and Statutory History, FY1980-FY2007*, coordinated by Judith A. Johnson; CRS Report RL34638, *FDA FY2009 Appropriations*, coordinated by Susan Thaul.

[7] For more information about medical device user fees, see CRS Report RL34571, *Medical Device User Fees and User Fee Acts*, by Erin D. Williams, and CRS Report RL33981, *Medical Device User Fee and Modernization Act (MDUFMA) Reauthorization*, by Erin D. Williams. FDA also funds some device and radiological health activities with fees collected under the Mammography Quality Standards Act (MQSA, P.L. 102-539), and some device user fees fund non-device specific activities at FDA.

[8] See CRS Report RS22946, *Food and Drug Administration (FDA): Overview and Issues*, by Erin D. Williams.

comprehensive FDA reform legislation in almost a decade: the Food and Drug Administration Amendments Act of 2007 (FDAAA; P.L. 110-85).[9] The impact of FDAAA for medical device regulation is discussed below in the "The History of Laws Governing Medical Device Regulation" section. In the wake FDAAA, issues related to medical devices and other products remain. These exist both in areas that FDAAA did not comprehensively address, and in areas raised by its implementation. Such issues are discussed in the "Legislative Issues" section of this report.

In order to fully understand the medical device related legislative issues that Congress faces, some background information is illustrative. This report provides an overview of the following: medical devices and their manufacturers, the history of FDAAA and other laws governing medical device regulation, and the medical device approval process. The final section surveys the device-related legislative issues of interest to Congress.

Medical Devices and Their Manufacturers

Medical device regulation is complex, in part because of the wide variety of items that are categorized as medical devices. They may be simple tools used during medical examinations, such as tongue depressors and thermometers. They may be high-tech life-saving implants like pacemakers and coronary stents. They may be machines used for diagnostic purposes, like CAT scans and EEG machines. They may even be test kits used in laboratories or by consumers at home, such as tests for pregnancy or blood glucose levels.

According to law, a medical device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, that (1) does not achieve its primary intended purposes through chemical action within or on the body of humans or other animals, (2) is not dependent upon being metabolized for the achievement of its primary intended purposes, and (3) is one of the following:

- recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them;
- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in humans or other animals; or
- intended to affect the structure or any function of the body of man or other animals.[10]

The medical device market is highly fragmented: surgical and medical supplies make up the largest sector, followed by *in vitro* diagnostic products (IVDs, which are laboratory tests), cardiovascular devices, orthopedic devices, and diagnostic imaging.[11] Although the largest companies dominate the market for devices in terms of sales, it is often the small companies that make a significant contribution to early innovation. Small companies often partner with larger

[9] See CRS Report RL34465, *FDA Amendments Act of 2007 (P.L. 110-85)*, by Erin D. Williams and Susan Thaul.

[10] Federal Food, Drug and Cosmetic Act §201(h), (21 U.S.C. 321).

[11] The Lewin Group, for AdvaMed, *The Impact of Regulation and Market Dynamics on Innovation: The State of the Industry* (Washington, DC, 2001).

companies to bring products to market, because they often lack access to capital, and the resources to conduct clinical trials and navigate the regulatory and reimbursement hurdles.

These characteristics of the medical device industry distinguish it from the drug industry, which is less fragmented, larger, and dominated by larger companies. The U.S. medical device industry as a whole is much smaller than the U.S. pharmaceutical industry. For example, the Centers for Medicare and Medicaid Services reports that the 2008 annual national health expenditures were $234.1 billion for prescription drugs, and $26.6 billion for durable medical equipment.[12] As a result, device companies often do not have the economic or financial resources of multi-billion dollar drug companies. These distinctions between device and drug manufacturers may be relevant in some regulatory discussions. Incentives and requirements placed on drug manufacturers are sometimes applied to device manufacturers as well, on which they may have a markedly different impact.

The History of Laws Governing Medical Device Regulation

Though food has been regulated since early colonial times, and drugs since the Drug Importation Act of 1848, medical devices did not come under federal scrutiny until Congress passed the Federal Food, Drug and Cosmetic Act (FFDCA) of 1938 (P.L. 75-717). At that time, few medical devices existed. In 1966, the Fair Packaging and Labeling Act (P.L. 89-755) required all consumer products in interstate commerce to be labeled accurately and truthfully, with FDA enforcing the provisions on regulated medical products, including medical devices.

The Medical Device Amendments of 1976 (MDA; P.L. 94-295) was the first major legislation passed to ensure safety and effectiveness of medical devices, including diagnostic products, before they could be marketed. The amendments required manufacturers to register with FDA and follow quality control procedures in their manufacturing processes. Some products were required to undergo premarket review by FDA, while others had to meet performance standards before marketing. Devices already on the market in 1976 (*preamendment* or *grandfathered* devices) did not have to undergo retrospective approval for marketing. Instead, they were to be broadly classified by FDA into one of three regulatory classes based on the risk they posed to the patient. Devices coming to market after 1976 had to undergo premarket review (unless they were exempt). Devices could be *cleared* by FDA if they were substantially equivalent to a preamendment device. If the device (or its use) were truly novel, it could be *approved* if it was proven safe and effective on its own merits.

In 1990, the Safe Medical Devices Act (SMD Act; P.L. 101-629) established postmarket requirements for medical devices. The SMD Act required facilities that use medical devices to report to FDA any incident that suggested that a medical device could have caused or contributed to the death, serious illness, or injury of a patient. Manufacturers of certain permanently implanted devices were required to establish methods for tracking the patients who received them

[12] Centers for Medicare and Medicaid Services, *NHE Web Tables (Historical)*, Table 2. National Health Expenditures Aggregate Amounts and Average Annual Percent Change, by Type of Expenditure: Selected Calendar Years 1960-2008, Washington, DC, p. 2, http://www.cms.hhs.gov/NationalHealthExpendData/downloads/tables.pdf. [Note that the definition of durable medical equipment (DME) (Social Security Act sec. 1861(n)), is not identical to that for medical devices (FFDCA 201(h)), but is the most similar type of expenditure tracked by CMS.]

and to conduct postmarket surveillance to identify adverse events. The act authorized FDA to carry out certain enforcement actions, such as device product recalls, for products that did not comply with the law.

In 1997, the Food and Drug Administration Modernization Act (FDAMA; P.L. 105-115) mandated the most wide-ranging reforms in FDA practice since 1938. For medical devices, provisions included measures to accelerate premarket review of devices and to regulate company advertising of unapproved uses of approved devices.

In 2002, the Medical Device User Fee and Modernization Act (MDUFMA; P.L. 107-250) amended the FFDCA to enact three significant provisions for medical devices: (1) it established user fees for premarket reviews of devices; (2) it allowed establishment inspections to be conducted by accredited persons (third parties); and (3) it instituted new regulatory requirements for reprocessed single-use devices. MDUFMA was amended and clarified by two laws: the Medical Device Technical Corrections Act (MDTCA, P.L. 108-214), and the Medical Device User Fee Stabilization Act of 2005 (MDUFSA, P.L. 109-43), and had its user fee provisions reauthorized by the Medical Device User Fee Act of 2007 (MDUFA; Title II of FDAAA).[13]

In 2007, FDAAA amended the FFDCA and the Public Health Service Act to reauthorize several expiring programs (including the medical device user fee act) and to make agency-wide changes, several of which have implications for the regulation of medical devices.[14] FDAAA created incentives as well as reporting and safety requirements for manufacturers of medical devices for children; required that certain clinical trials for medical devices and some other products be publicly registered and have their results posted;[15] created requirements to reduce conflicts of interest in advisory committees for medical devices and other products;[16] and made certain other amendments to the regulation of devices.

The Medical Device Approval Process: Premarket Review Requirements

In order for medical devices to be marketed in the United States, manufacturers[17] must register and list the devices that they commercialize with FDA, and for most devices, must obtain the agency's prior and continuing permission.[18] FDA grants this permission when a manufacturer

[13] See CRS Report RL34571, *Medical Device User Fees and User Fee Acts*, by Erin D. Williams; For historical background, see CRS Report RL33981, *Medical Device User Fee and Modernization Act (MDUFMA) Reauthorization*, by Erin D. Williams.

[14] See CRS Report RL34465, *FDA Amendments Act of 2007 (P.L. 110-85)*, by Erin D. Williams and Susan Thaul.

[15] See the Clinical Trials Databases section of CRS Report RL34465, *FDA Amendments Act of 2007 (P.L. 110-85)*, by Erin D. Williams and Susan Thaul.

[16] FDA uses advisory committees to gain independent advice from outside experts. See CRS Report RS22691, *FDA Advisory Committee Conflict of Interest*, by Erin D. Williams.

[17] The term *manufacturer* is used throughout this report for simplicity, but regulations also apply to any person, organization, or sponsor that submits an application to FDA to market a device.

[18] Certain medical devices that present only a minimal risk, such as plastic bandages and ice bags, can be legally marketed upon registration alone. These low-risk devices are deemed *exempt* from premarket review, and manufacturers need not submit an application to FDA prior to marketing them. Manufacturers of exempt devices are still typically required to comply with other regulations, known as general controls. (21 CFR 862-892).

meets regulatory premarket and postmarket requirements. The premarket requirements, which are the subject of this section, vary according to a the risk that a device presents. IVDs have their own unique premarket requirements.

FDA may grant a manufacturer permission to market a device after conducting a premarket review, based on an application from the manufacturer. There are numerous types of applications a manufacturer can submit to obtain such permission, which are described later in this section. First, however, this section presents some fundamental concepts and terms of art that will help readers to understand the details of the various application processes. These include *safety* and *effectiveness*, *approval* and *clearance* (including *substantial equivalence* to a *predicate device*), and device *classification* (including types of *controls*).

Fundamental Concepts and Terms of Art

Safety and Effectiveness

FDA has as a part of its mission to ensure that medical devices are *safe* and *effective*. The evidence required to meet the safe and effective standard varies according to the characteristics of the device, its conditions of use, the existence and adequacy of warnings and other restrictions, and the extent of experience with its use.[19] FDA considers there to be reasonable assurance of safety when it can be determined that the probable benefits to health that result from use of the device as directed by the manufacturer outweigh any probable risks.[20] Investigations for safety can include animal studies, human studies, and/or laboratory studies.[21]

FDA considers there to be reasonable assurance of effectiveness when valid scientific evidence suggests that the target population's use of the device (according to the manufacturer's instructions) provides clinically significant results.[22] Valid scientific evidence includes that from controlled clinical trials, other carefully defined clinical investigations, case histories, and other reports of significant human experience. Evidence can be collected by the manufacturer or a representative, and can be abstracted from medical literature.

Approval and Clearance

There are two paths that manufacturers can use to bring their medical devices to market with FDA's permission. One path consists of conducting clinical studies comparable to those required for new prescription drugs. This process, generally used for novel and high-risk devices, is typically lengthy and expensive. It results in a type of FDA permission called *approval*.

The other path is to demonstrate that the device is *substantially equivalent* to a device that is already on the market (a *predicate device*).[23] This type of process is unique to medical devices. It

[19] 21 CFR § 860.7(c)(2).

[20] 21 CFR § 860.7(d)(1).

[21] 21 CFR § 860.7(d)(2).

[22] 21 CFR § 860.7(e)(1).

[23] To be a predicate, a device must have either been on the market before 1976 when the MDA took effect, or it could have been cleared for marketing after 1976, but must have the same intended use as a device classified in the CFR.

is typically used for new devices that make incremental improvements or modifications to previous versions. It results in FDA *clearance,* and tends to be much less expensive and less time-consuming than seeking FDA approval.

Substantial equivalence is determined by comparing the performance characteristics of a new device with those of a predicate device. To be considered substantially equivalent, FDA must determine that the new device has the same *intended use* (also called *indication(s) for use*) as a predicate device.[24] In addition, the new device must either (1) have the same technological characteristics as the predicate, (2) have different technological characteristics that do not raise new questions of safety and effectiveness, or (3) be least as safe and effective as the predicate. The manufacturer selects which predicate device to compare with its new device. However, FDA has the ultimate discretion in determining whether a comparison is appropriate.

Here is an example of how a device might be cleared through a determination of substantial equivalence. If a manufacturer wanted to market a blood glucose test for diabetes, it could apply to FDA for a determination that the new device is substantially equivalent to a blood glucose test for diabetes that was sold in 1972. FDA has classified these devices in the Code of Federal Regulations (CFR) as follows (note, the device classification process is described at the start of the next section):

> 21 CFR 862.1345 Glucose test system.
>
> (a) Identification. A glucose test system is a device intended to measure glucose quantitatively in blood and other body fluids. Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and of pancreatic islet cell carcinoma.
>
> (b) Classification. Class II.

The manufacturer would likely ask FDA to clear the new device based on evidence that it was substantially equivalent to the device described in the CFR, rather than based on a large-scale clinical study. To obtain FDA clearance, the manufacturer would need to demonstrate two things. First, that the new device did not present new questions of safety and effectiveness. Second, that it had the same intended use as the older device (i.e., "intended to measure glucose quantitatively in blood and other body fluids"). If, based on the evidence, FDA determined that the new device was substantially equivalent to the predicate, the agency could clear the new device, and the manufacturer could market it.

Device Classification

Under the terms of the MDA, FDA has created three broad categories to describe the risk that each medical device poses to its intended patients (the *target population*) when it is used or misused.[25] The risk categories (known as *classifications*) are *Class I*, *II* , and *III*, which represent

[24] The statement of intended use is a general description of the diseases or conditions that the device will diagnose, treat, prevent, cure, or mitigate, including a description, where appropriate, of the patient population for which the device is intended. (21 CFR § 807.92(a)(5), and § 814.20 (b)(3)(I))

[25] Preamendment medical devices (those on the market prior to the passage of the MDA in 1976) were presumed to be marketable. They did not need to undergo premarket review, and could be legally unless and until FDA required their removal. As required by the MDA, FDA classified the preamendment devices and used them as the basis for creating (continued...)

low-, moderate-, and high-risk categories, respectively. (See **Table 2**.) Since the MDA was enacted, the agency has classified over 1,700 distinct types of devices and organized them in the Code of Federal regulations (CFR) in 16 medical specialties (referred to as *classification panels*), such as "cardiovascular devices" or "ear, nose, and throat devices."[26]

FDA can classify a new device based on comparison with a legally marketed device, by regulation, or by recognizing that if falls into a classification panel. If unsure what classification a product would receive, a manufacturer may make a formal request for classification to FDA.

A device's classification determines the type of regulatory requirements that a manufacturer must follow. These regulatory requirements, known as *controls*, are described in more detail in the descriptions of Class I, II, and II devices that follow.

Class I

Devices in Class I are those for which *general controls* are sufficient to ensure their safe and effective use (21 CFR § 860.3(c)(1)). General controls, the minimum regulations that apply to all FDA regulated medical devices, include five elements:[27]

- *establishment registration*—registration with FDA of companies required to do so under 21 CFR 807.20 (such as manufacturers, distributors, repackagers and relabelers, and foreign firms);
- *device listing*—listing with FDA of all devices to be marketed;
- good manufacturing practices (GMP)—manufacturing of devices in accordance with the Quality Systems Regulation (QSR) in 21 CFR 820;
- *labeling*—labeling of devices in accordance with 21 CFR 801 or 809; and
- *premarket notification*—submission to FDA of a premarket notification 510(k) (described in detail in the *Types of Device Marketing Applications* section below).

Many Class I devices are *exempt* from the premarket notification and/or the QSR requirements, though they still have to comply with the other general controls. A device is exempt if FDA determines that it presents a low risk of illness or injury to patients. (See 21 CFR 862 to 892).

Class II

Devices in Class II are those for which general controls alone are not sufficient to provide reasonable assurance of safety and effectiveness. Class II includes devices that pose a moderate risk to patients, and may include new devices for which information or *special controls* are

(...continued)

the classification panels and as the first cadre of predicate devices that could be used to demonstrate substantial equivalence.

[26] FDA, *Device Classification*, June 18, 2009, http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/default.htm.

[27] FFDCA 513(a)(1)(A); also see FDA, *General and Special Controls*, April 30, 2009, http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/GeneralandSpecialControls/default.htm.

available to reduce or mitigate risk. Most Class II devices require premarket review; however, some are exempt by regulation (21 CFR 860.3(c)(2)).

Special controls are requirements beyond general controls that FDA deems necessary to assure safe and effective use of a medical device (FFDCA 513(a)(1)(B)). They might include, for example, performance standards, postmarket surveillance requirements, or patient registries, or the development and dissemination of guidelines.

Class III

Class III medical devices include those for which general and/or special controls are not sufficient to assure safe and effective use of the device, and which require *premarket approval* (PMA; described in detail in the *Medical Device Marketing Applications* section below; FFDCA 513(a)(1)(C)). Class III includes devices which are life-supporting or life-sustaining, and devices which present a high or potentially unreasonable risk of illness or injury to a patient. New devices that are not classified as Class I or II by another means, are automatically designated as Class III unless the manufacturer files a request or petition for reclassification under FFDCA 513(f)(2). (Also see 21 CFR 860.3(c)(3).)

Table 2. Medical Device Approval Basics

Device Classification	Examples	Safety / Effectiveness Controls	Required Submission[a]
Class I	elastic bandages, examination gloves, and hand-held surgical instruments	General Controls	-*Registration only* unless 510(k) specifically required
Class II	powered wheelchairs, infusion pumps, and surgical drapes	General Controls & Special Controls	-*510(k) clearance* unless exempt -*IDE possible*[b]
Class III	heart valves, silicone gel-filled breast implants, and implanted cerebella stimulators	General Controls & Premarket Approval	-*PMA approval* unless 510(k) specifically permitted -*IDE probable*

a. Each type of required submissions is described in the *Types of Device Marketing Applications* section that follows.

b. IDE means investigational device exemption, as described below in the "Before a Marketing Application Is Submitted" section.

Medical Device Marketing Applications

As stated above, a manufacturer can market a device if FDA determines that the device is safe and effective. The agency makes that determination based on information the manufacturer submits. The information that is required—in other words, the type of marketing application the manufacturer must make (if any)—is determined based on the *risk* of that the device poses, if used according to the manufacturer's instructions. Under the terms of MDUFA, manufacturers must pay a fee for most types of submissions.[28]

[28] See CRS Report RL34571, *Medical Device User Fees and User Fee Acts*, by Erin D. Williams.

Generally speaking, according to the FFDCA, manufacturers

- are prohibited from selling an adulterated product;[29]
- are prohibited from misbranding a product;[30]
- must register their facility with FDA and list all of the medical devices that they produce or process (a process which now requires a fee under the terms of FDAAA);
- must file the appropriate premarket submission with the agency at least 90 days before introducing a *non-exempt* device onto the market; and
- must report to FDA any incident that they are aware of that suggests that their device may have caused or contributed to a death or serious injury.

Very few applications are actually denied approval. Instead, an application may be deemed "not approvable" in its current form (typically because the data that the manufacturer provides are not sufficient to demonstrate safety and effectiveness). Applications that are "not approvable" are usually withdrawn by the manufacturer before a denial is rendered.

Before a Marketing Application Is Submitted

FDAMA gave FDA the authority to establish procedures for meeting with manufacturers prior to preparing a submission.[31] The procedures aim to speed the review process by giving FDA and a manufacturer the opportunity to address questions and concerns about the device and/or the planned studies that will be used to support the marketing application before the studies are initiated and the application is submitted. For example, the "pre-IDE" process (an IDE is an investigational device exemption that allows a manufacturer to conduct a clinical trial on a medical device) is an informal "pre-submission" process. The "pre-IDE" process is so-called in name only; submitting a pre-IDE does not mean that manufacturers are required to submit subsequently an IDE application.[32] The pre-IDE process is simply a means for FDA and industry to engage in dialogue about a new device, before a study is initiated or a marketing application is submitted.

The pre-IDE process may involve sending analytical or clinical protocols to FDA for review and comment before proceeding with studies, or meeting with FDA to discuss protocols and/or possible regulatory pathways. This particular process is strictly voluntary, and not binding on either FDA or industry. The benefits to manufacturers include an opportunity to begin a dialogue

[29] A device is adulterated if it includes any filthy, putrid, or decomposed substance, or if it is prepared, packed, or held under unsanitary conditions. The FDC Act further states that a device is adulterated if its container contains any poisonous or deleterious substance, or if its strength, purity or quality varies significantly from what the manufacturer claims. For higher class devices, a device can be considered adulterated if it fails to meet performance requirements outlined in its approval, or if it is in violation of other Good Manufacturing Practice requirements.

[30] A device is misbranded when all or part of the labeling (i.e., the FDA-approved printed material providing information about the device) is false, misleading, or missing.

[31] For guidance on the procedures established, see *Early Collaboration Meetings Under the FDA Modernization Act*; Final Guidance for Industry and CDRH Staff, February 28, 2001, at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073604.htm.

[32] For more information on the IDE, please refer to the "Marketing Applications for Medical Devices" section that immediately follows this discussion.

with FDA, to promote greater understanding of new technologies, to reduce the cost of research studies by focusing on the important information needed for FDA approval (or clearance), eliminating unnecessary or burdensome studies, and to speed the review process for the future marketing application since FDA will already be familiar with the device.

Marketing Applications for Medical Devices

The following sections describe the types of premarket submissions that FDA reviews for medical devices. (See **Table 2**.)

Premarket Notification (510(k))

A 510(k) submission is required for any new, non-exempt low- or moderate-risk medical device that will be marketed in the United States. A 510(k) could also be used for currently marketed devices for which the manufacturer seeks a new indication (e.g., a new population, such as pediatric use, or a new disease or condition), or for which the manufacturer has changed the design or technical characteristics such that the change may affect the performance characteristics of the device.

The standard for clearance of a traditional 510(k) is substantial equivalence with a predicate device. A predicate device can be one of two things. It can be a previously cleared Class I or II device that does not require a PMA. It can also be preamendment Class III for which the agency has not issued regulations requiring a PMA. (PMAs, which are more rigorous submissions than 510(k)s, are discussed in the "Premarket Application (PMA)" section.)

There are several types of 510(k)s: traditional, abbreviated, special and *de novo*. In a traditional 510(k), the manufacturer submits information about the performance of the device under specific conditions of use. It also contains information about the design of the device, characteristics of device components, representations of packaging and labeling, a description and summary of the non-clinical and clinical studies that were done to support the device performance characteristics, a description of means by which users can assess the quality of the device, and information about any computer software or additional or special equipment needed. Several administrative forms are also required.[33]

Most of the studies supporting a 510(k) submission are not true clinical studies. While FDA prefers to see data on performance of the device in the actual intended population, substantial equivalence in many cases, means only that the device performs in a similar fashion to the predicate under a similar set of circumstances. As a result, many devices never have to demonstrate safety and effectiveness through clinical studies.

FDA may take any of the following actions on a 510(k) after conducting its review (21 CFR § 807.100(a)): find the device substantially equivalent to the predicate and issue a clearance letter, find the device not substantially equivalent (NSE) and issue an NSE letter prohibiting marketing, or request additional information (with the final clearance decision pending review of that information). A manufacturer generally has 30 days to provide any additional information, or

[33] FDA, *How to Prepare a Traditional 510(k)*, September 14, 2009, http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm134572.htm#link_4.

FDA may issue a notice of withdrawal of the application (21 CFR § 807.87(l)). The manufacturer may, at any time, withdraw its 510(k). FDA has 90 days to review a traditional 510(k).[34]

Abbreviated and special 510(k)s were new approaches to premarket notification that came from FDAMA of 1997, intended to streamline and expedite FDA's review for routine submissions meeting certain qualifications, thus leaving more reviewer time for more complicated submissions. An abbreviated 510(k) uses guidance documents developed by FDA to communicate regulatory and scientific expectations to industry. Guidance documents have been prepared for many different kinds of devices, and are available on FDA's website. All guidance documents are developed in accordance with Good Guidance Practices (GGP, 21 CFR § 10.115)), and many with public participation or opportunities for public comment.[35]

In addition to issuing guidance documents, FDA can either develop performance or consensus standards or 'recognize' those developed by outside parties (21 CFR Part 861). In an abbreviated 510(k), the manufacturer describes what guidance document, special control, or performance standard was used, and how it was used to assess performance of their device. Other minimum required elements are the product description, representative labeling, and a summary of the performance characteristics. FDA typically reviews an abbreviated 510(k) in 60 days.

The Quality System Regulation (QSR; 21 CFR § 820.30) is the regulation that describes the good manufacturing practice (GMP) requirements for medical devices (see the "Manufacturing" section of this report for more detail on QSR). A special 510(k) utilizes the design control[36] requirement of the QSR and may be used for a modification to a device that has already been cleared. The modifications should not affect the safety and effectiveness of the device. The special 510(k) allows the manufacturer to declare conformance to design controls, without providing the data. This type of submission references the original 510(k) number, and contains information about the design control requirements. FDA aims to review most special 510(k)s in 30 days.

Under the FFDCA, novel devices lacking a legally marketed predicate would automatically be designated Class III. FDAMA amended Section 513(f) to allow FDA to establish a new, expedited mechanism for reclassifying these devices based on risk, thus reducing the regulatory burden on manufacturers. The de novo 510(k), though requiring more data than a traditional 510(k), often requires less information than a premarket application (PMA), discussed below.

In a *de novo* 510(k) process, the manufacturer submits a traditional 510(k) for its device. However, because there is no predicate device or classification, the agency will return a decision of not substantially equivalent. Within 30 days, the manufacturer submits a petition requesting reclassification of its device into Class II or I, as appropriate. Within 60 days, FDA will render a decision classifying the device according to criteria in 513(a)(1) of FFDCA. With approval, FDA

[34] The FDA time clock (i.e., review cycle) begins when FDA receives the 510(k) and ends with the date that FDA issues either a request for additional information or a decision. More than one cycle may occur before FDA issues its final decision.

[35] FDA continually accepts public comment on any draft or final guidance document.

[36] Design controls are a series of predetermined checks, verifications, and specifications that are built into the manufacturing process to validate the quality of the product throughout the process. These can include defining the personnel responsible for implementing steps in the development and manufacturing process, defining specifications and standards for assessing the quality of the materials that go into making the product, designing specifications for accepting and rejecting different batches or lots of final product, and requirements for maintaining appropriate records.

issues a regulation that classifies the device. If the device is Class II, a special controls guidance document is also developed that then allows subsequent manufacturers to submit either traditional or abbreviated 510(k)s.[37]

Premarket Application (PMA)

A PMA is the most stringent type of device marketing application required by FDA for new and/or high-risk devices. PMA approval is based on a determination by FDA that the application contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s) (21 CFR Part 814). A PMA must contain the following information (among other things): administrative requirements; summaries of non-clinical and clinical data supporting the intended use and performance characteristics; detailed information on the design of the device and a description of the device components; instructions for use; representations of packaging and labeling; a description of means by which users can assess the quality of the device; information about any computer software or additional or special equipment needed; literature about the disease and the similar devices; information on the manufacturing process; and assurance of compliance with QSR.

In contrast to a 510(k), PMAs generally require some clinical data, but can also use studies from the medical literature (a "paper PMA"). Approval is based not only on the strength of the scientific data, but also on inspection of the manufacturing facility to assure that the facility and the manufacturing process are in compliance with the quality systems regulations (QSR: 21 CFR Part 820). FDAMA made it easier for manufacturers to submit the required sections of a PMA in a serial fashion as data are available ("modular PMA").

When a PMA is first received, FDA has 45 days to make sure the application is administratively complete. If so, FDA formally files the application. If not, the application is returned. FDA then has 75 days to complete the initial review and determine whether an advisory committee meeting will be necessary.

Advisory committees, comprised of scientific, medical, and statistical experts, and industry and consumer representatives, can be convened to make recommendations on any scientific or policy matter before FDA.[38] They allow for interested persons to present information and views at an oral public hearing before the advisory committee (21 CFR Part 14). FDA typically accepts advisory committee recommendations for an application (approvable, approvable with conditions or non-approvable); however, there have been cases where the decision has not been consistent with the recommendation (e.g., where the conditions for approval are so burdensome as to practically present a non-approvable situation). CDRH will hold joint advisory committee meetings with other centers where necessary.

After FDA notifies the applicant that the PMA has been approved or denied, a notice may be published on the Internet (1) announcing the data on which the decision is based, and (2) providing interested persons an opportunity to petition FDA within 30 days for reconsideration of

[37] FDA, *New Section 513(f)(2) - Evaluation of Automatic Class III Designation, Guidance for Industry and CDRH Staff*, February 19, 1998, http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080195.htm..

[38] For further information, see CRS Report RS22691, *FDA Advisory Committee Conflict of Interest*, by Erin D. Williams.

the decision. Though FDA regulations allow 180 days to review the PMA and make a determination (21 CFR § 814.40), in reality the review time could be much longer. Pursuant to MDUFA performance goals have been established to reduce the review time for PMAs.

Supplements to 510(k)s and PMAs

Once a device has been cleared through a 510(k) process or approved through the PMA process, the manufacturer can market the device only for the intended use that FDA cleared or approved. For example, a device, such as a stent, approved to treat coronary artery disease may not be marketed for treatment of blocked biliary ducts unless the manufacturer files additional information with FDA to demonstrate that the device is safe and effective for the new use. The information can be filed as a supplement to the original application. Supplements are required not only for new uses of a cleared or approved device, but also for design or manufacturing changes that may impact safety and effectiveness (e.g., changing the type of metal or plastic on a device, or using a different antibody for diagnosis of a disease).

Investigational Device Exemption (IDE)

An IDE allows an unapproved device (most commonly an invasive or life-sustaining device) to be used in a clinical study to collect data required to support a submission, most commonly a PMA, at some later point in time.[39] Investigational use can also include clinical evaluation of certain modifications to or new intended uses of legally marketed devices (e.g., supplemental application). All clinical evaluations of investigational devices, unless they are exempt, must have an IDE and be approved by an institutional review board (IRB), before the study is initiated.[40] The IDE permits a device to be shipped lawfully for investigation of the device without requiring that the manufacturer comply with other requirements of the FFDCA, such as registration and listing. Manufacturers of devices with IDEs are also exempt from the quality systems regulations (QSR), except for the requirements for design control.

While under investigation, manufacturers, sponsors, clinical investigators and IRBs must comply with Good Clinical Practices, including all regulations that govern the conduct of clinical studies:

- Investigational Device Exemptions (21 CFR Part 812) covering the procedures for the conduct of clinical studies with medical devices including application, responsibilities of sponsors and investigators, labeling, records, and reports;
- Protection of Human Subjects (21 CFR Part 50) providing the requirements and general elements of informed consent;
- Institutional Review Boards (21 CFR Part 56) covering the procedures and responsibilities for IRBs that approve clinical investigations protocols;

[39] FDA, *Device Advice: Investigational Device Exemption (IDE)*, July 9, 2009, http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/default.htm..

[40] An IRB is a group, generally comprised volunteers, that examines proposed and ongoing scientific research to ensure that human subjects are properly protected. For further information, see CRS Report RL32909, *Federal Protection for Human Research Subjects: An Analysis of the Common Rule and Its Interactions with FDA Regulations and the HIPAA Privacy Rule*, by Erin D. Williams.

- Financial Disclosure by Clinical Investigators (21 CFR Part 54) covering the disclosure of financial compensation to clinical investigators which is part of FDA's assessment of the reliability of the clinical data; and
- Design Controls of the QSR (21 CFR Part 820 Subpart C) providing the requirement for procedures to control the design of the device in order to ensure that the specified design requirements are met.

Devices are exempt from IDE requirements when testing is noninvasive, does not require invasive sampling, does not introduce energy into a subject, and is not stand alone (i.e., is not used for diagnosis without confirmation by other methods or medically established procedures) (21 CFR § 812.2(c)(3)).

Humanitarian Device Exemption (HDE)

An HDE is an application that is similar to a PMA, but exempt from the effectiveness requirements. An approved HDE authorizes marketing of a humanitarian use device. A humanitarian use device is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect fewer than 4,000 individuals in the U.S. per year. The exemption from proving effectiveness is designed to encourage manufacturers to develop medical devices for these small markets, assisting patients with rare diseases and conditions who might otherwise not be served.

Before submitting an HDE application, the manufacturer submits a request for a humanitarian use device designation to FDA's Office of Orphan Products Development (OOPD). The request includes (1) a statement that they are requesting a humanitarian use device designation for a rare disease or condition; (2) the name and address of the manufacturer; (3) a description of the rare disease or condition for which the device is to be used; (4) a description of the device; and (5) documentation, with appended authoritative references, to demonstrate that the device is designed to treat or diagnose a disease or condition that affects or is manifested in fewer than 4,000 people in the United States per year (see 21 CFR § 814.102(a)). In order for a device to receive marketing approval under this regulation, there should not be another legally marketed device available to treat or diagnose the disease or condition. Once a device with the same intended use as the humanitarian use device is approved or cleared, an HDE cannot be granted for the humanitarian use device.

The agency has 75 days from the date of receipt to review an HDE application. This includes a 30-day filing period during which the agency determines whether the HDE application is sufficiently complete to permit substantive review. FDA does require that a manufacturer comply with the QSR that the agency deems most relevant to the safety of the device. Alternatively, the manufacturer can request an exemption. Supplements, and sometimes even a new HDE, are required for additional indications.[41]

[41] FDA, *Guidance for Industry and FDA Staff - Humanitarian Device Exemption (HDE) Regulation: Questions and Answers*, July 18, 2006, http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071473.htm.

In Vitro Diagnostic (IVD) Products

IVD products (e.g., laboratory tests) are those reagents, instruments, and systems intended for use in diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.[42]

IVDs are medical devices as defined in Section 210(h) of the FFDCA (such as equipment used for genetic testing), and may also be biological products subject to Section 351 of the Public Health Service Act (such as biological agent diagnostic systems). IVDs may consist of general purpose reagents,[43] analyte specific reagents (ASRs),[44] general purpose or specific equipment, sometimes with computer analysis software.[45]

IVDs are different from other medical devices in that they do not act directly on a patient to produce a result like an implantable, life-sustaining or other device does. Instead, the risk to the patient is from the generation of inaccurate test results (i.e., wrong answers) that lead to mismanagement of a patient's condition.

Most IVD products that are stand-alone items of general purpose equipment, such as automated clinical analyzers, are exempt Class I devices. However, if the equipment performs a specific test, equipment plus the test becomes a test system. Test systems are considered combination devices, and they are classified according to the risk level of the highest of the two device classifications (i.e., an analyzer may be Class I exempt, but if a manufacturer wishes to market it with an HIV test kit, the system could be regulated as a Class III device and require a PMA). Most IVD products are reviewed in CDRH's Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD), and CBER's Office of Blood Research and Review (OBRR). The classification of existing IVDs can be found in 21 CFR Part 862, 21 CFR Part 864, and 21 CFR Part 866.

Like other medical devices, IVDs are subject to premarket and postmarket controls. But unlike other devices, IVDs are also subject to the Clinical Laboratory Improvement Amendments (CLIA) of 1988.[46] CLIA establishes quality standards for laboratory testing and an accreditation program for clinical laboratories that perform testing using IVD products. CLIA requirements vary according to the technical complexity in the testing process and risk of harm in reporting

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[42] 21 C.F.R. § 809.3.

[43] A general purpose reagent is "a chemical reagent that has general laboratory application, is used to collect, prepare, and examine specimens from the human body for diagnostic purposes, and is not labeled or otherwise intended for a specific diagnostic application … [General purpose reagents] do not include laboratory machinery, automated or powered systems" (21 CFR § 864.4010).

[44] Analyte specific reagents (ASRs) are "antibodies, both polyclonal and monoclonal, specific receptor proteins, ligands, nucleic acid sequences, and similar reagents which, through specific binding or chemical reaction with substances in a specimen, are intended for use in a diagnostic application for identification and quantification of an individual chemical substance or ligand in biological specimens" (21 CFR § 864. 4020(a)).

[45] In 2006, FDA's OIVD issued two draft guidance documents on IVDs: FDA, Draft Guidance for Industry and FDA Staff - Commercially Distributed Analyte Specific Reagents (ASRs): Frequently Asked Questions, September 14, 2007, http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM071269.pdf; and FDA, Draft Guidance for Industry, Clinical Laboratories, and FDA Staff In Vitro Diagnostic Multivariate Index Assays, July 26, 2007, http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM071455.pdf.

[46] FDA, *Overview of IVD Regulation*, June 18, 2009, http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm123682.htm.

erroneous results. The regulations establish three categories of testing on the basis of the complexity of the testing methodology: (a) waived tests, (b) tests of moderate complexity, and (c) tests of high complexity.

Manufacturers apply for CLIA categorization (determined by FDA)[47] during the premarket process. Postmarket, the Centers for Medicare and Medicaid Services (CMS) regulates all laboratory testing (except research) performed on humans in the U.S. through CLIA.[48] Under CLIA, laboratories performing only waived tests are subject to minimal regulation. Laboratories performing moderate or high complexity tests are subject to specific laboratory standards governing certification, personnel, proficiency testing, patient test management, quality assurance, quality control, and inspections.

CLIA categorization (defining regulatory requirements on the laboratory testing process) do not always match FDA classification (defining regulatory requirements on the tests kits or systems themselves). For example, a "waived" test under CLIA is the simplest test to perform (usually by an untrained user), with the smallest margin of error. As such, they receive little to no oversight under CLIA. However, FDA may designate such a test as Class III, so that it undergoes rigorous review to insure that it performs as advertised (i.e., with a small margin of error in the hands of an untrained user).

Most IVDs are exempt from IDE requirements. Because the benefits and risks to the patient from use of IVDs are indirect (i.e., due to the use of the test result in patient management), FDA requires that the companies demonstrate analytical test performance in patient samples that would test along the continuum of positive and negative for the marker of interest. In addition, FDA requires support for the clinical validity of the test (i.e., evidence that the biological marker that the test is detecting actually is associated with the disease or condition that the company wishes to market the test for in a predictable way).

For some of the applications seeking clearance for an IVD, biological markers that the test purports to measure may be relatively well characterized with respect to a disease and patient population (such as the link between glucose measurement and diabetes). In these cases, analytical studies using clinically derived samples (e.g., blood specimens from healthy and diabetic individuals) suffice to show that the test is actually detecting the marker. Sometimes clinical samples can be supplemented by carefully selected artificial samples, particularly if a disease, condition or marker is rare. For example, if FDA were to review a genetic test to measure genetic markers for drug metabolism, they may require the manufacturer to use actual patient samples to demonstrate that they can detect common markers. FDA may, however, allow the company to use artificial or "spiked" samples to test for rare markers so that the company would not have to test an overly burdensome number of clinical samples. In this type of submission, the manufacturer could use medical literature to support the clinical validity of the biological marker to the disease, and would not have to conduct a clinical study to demonstrate that the test measures the marker and the marker is associated with the disease.

[47] See FDA, *Find Device CLIA '88 Categorization*, July 11, 2009, http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm124103.htm.

[48] CMS, *Clinical Laboratory Improvement Amendments (CLIA) Overview*, August 26, 2009, http://www.cms.hhs.gov/CLIA/.

For other IVDs, the link between analytical performance of the test in its ability to detect a biological marker and the clinical validity of the marker is not well defined. In these circumstances, new clinical information may be required. FDA rarely requires prospective clinical studies for IVDs, but regularly requests clinical samples with sufficient laboratory and/or clinical characterization to allow an assessment of the clinical validity of a new device. For example, a company seeking to market a test for a new tumor marker may use well-characterized, archived patient samples collected as part of a completely separate study to demonstrate that their test can classify patients in a predictable way. Clinical performance is usually expressed in terms of clinical sensitivity and clinical specificity (when compared to a disease or health state) or agreement (when compared to performance of a predicate device or reference method). For most PMAs, manufacturers identify surrogate endpoints (such as tumor shrinking or reduction in a tumor marker) and establish the device performance in relation to those rather than to disease outcome (such as improved survival).

The Medical Device Approval Process: Post-Approval Requirements and Issues

Once approved or cleared for marketing, manufacturers of medical devices must comply with regulations on labeling and advertising, manufacturing, on postmarket surveillance, adverse events, a related new Sentinel Initiative, device tracking, unique device identification, compliance and enforcement. The requirements for each of these are described below.

Labeling

Like drugs and biological products, all FDA approved or cleared medical devices are required to be labeled in a way that informs a user of how to use the device in a safe and effective manner. Section 201(k) of the FFDCA defines a "label" as a "display of written, printed, or graphic matter upon the immediate container of any article." Section 201(m) defines "labeling" as "all labels and other written, printed, or graphic matter upon any article or any of its containers or wrappers, or accompanying such article" at any time while a device is held for sale after shipment or delivery for shipment in interstate commerce. The term "accompanying" is interpreted to mean more than physical association with the product; it extends to posters, tags, pamphlets, circulars, booklets, brochures, instruction books, direction sheets, fillers, webpages, etc. Accompanying can also include labeling that is connected with the device after shipment or delivery for shipment in interstate commerce. According to an appellate court decision, "most, if not all advertising, is labeling. The term 'labeling' is defined in the FFDCA as including all printed matter accompanying any article. Congress did not, and we cannot, exclude from the definition printed matter which constitutes advertising."[49]

Labeling regulations pertaining to medical devices are found in the following parts of Title 21 CFR:

- General Device Labeling (21 CFR Part 801)
- In Vitro Diagnostic Products (21 CFR Part 809)

[49] United States v. Research Laboratories, Inc., 126 F.2d 42 (9th Cir. 1942).

- Investigational Device Exemptions (21 CFR Part 812)
- Good Manufacturing Practices (21 CFR Part 820)
- General Electronic Products (21 CFR Part 1010)

All devices must conform to the general labeling requirements. Certain devices require specific labeling which may include not only package labeling, but informational literature, patient release forms, performance testing, and/or specific tolerances or prohibitions on certain ingredients.[50]

Various sections of the QSR have an impact on labeling: Section 21 CFR § 820.80(b) requires the inspection and testing of incoming materials including labeling; and 21 CFR § 820.70(f) requires buildings to be of suitable design and have sufficient space for packaging and labeling operations; 21 CFR § 820.120 deals with specific requirements for the control of labeling. This regulation applies to the application of labeling to ensure legibility under normal conditions of use over the expected life of the device; and also applies to inspection, handling, storage, and distribution of labeling. FDA considers a device to be adulterated if these requirements are not met. These requirements do not apply to the adequacy of labeling content, except to make sure the content meets labeling specifications contained in the device master record. However, failure to comply with GMP requirements, such as proofreading and change control, could result in labeling content errors. In such cases, the device could be misbranded and/or adulterated.

Manufacturing

Like drug manufacturers, medical device manufacturers must produce their devices in accordance with Good Manufacturing Practice (GMP). The GMP requirements for devices are described in the QSR, (FFDCA §520; 21 CFR 820). The QSRs require that domestic or foreign manufacturers have a quality system for the design, manufacture, packaging, labeling, storage, installation, and servicing of non-exempt finished medical devices intended for commercial distribution in the United States. The regulation requires that various specifications and controls be established for devices; that devices be designed and manufactured under a quality system to meet these specifications; that finished devices meet these specifications; that devices be correctly installed, checked and serviced; that quality data be analyzed to identify and correct quality problems; and that complaints be processed. FDA monitors device problem data and inspects the operations and records of device developers and manufacturers to determine compliance with the GMP requirements.[51]

Though FDA has identified in QSR the essential elements that a quality system should have, manufacturers have a great deal of leeway to design quality systems that best cover nuances of their devices and the means of producing them.

[50] 21 CFR §§ 801.405 to 801.437. Denture repair kits, impact resistant lenses in sunglasses and eyeglasses, ozone emission levels, chlorofluorocarbon propellants, hearing aids, menstrual tampons, chlorofluorocarbons or other ozone depleting substances, latex condoms, and devices containing natural rubber.

[51] FDA, *Medical Devices: 1. The Quality System Regulation*, June 18, 2009, http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/MedicalDeviceQualitySystemsManual/ucm122391.htm.

Postmarket Surveillance

Once their device is approved or cleared, manufacturers must conduct postmarket surveillance studies to gather safety and efficacy data for certain devices introduced into interstate commerce after January 1, 1991. This requirement applies to devices that

- are permanent implants, the failure of which may cause serious adverse health consequences or death;
- are intended for use in supporting or sustaining human life; or
- present a potential serious risk to human health.

FDA may require postmarket surveillance for other devices if deemed necessary to protect the public health. The primary objective of postmarket surveillance is to study the performance of the device after clearance or approval as it is used in the population for which it is intended—and to discover cases of device failure and its attendant impact on the patient.

Manufacturers may receive notification that their device is subject to postmarket surveillance when FDA files (i.e., accepts) the submission, and again when a final decision is made. If notified, manufacturers must submit a plan for postmarket surveillance to FDA for approval within 30 days of introducing their device into interstate commerce.

MDUFMA authorized additional appropriations for postmarket surveillance—$3 million for FY2003, $6 million for FY2004, and such sums as may be necessary in subsequent years; however, the money was not appropriated. MDUFA authorized the appropriation of $25 million per year for Postmarket Studies and Surveillance (21 USC 355 note).

Adverse Event Reporting

Section 519(a) of the FFDCA as amended by the SMDA of 1990 required FDA to establish a system for monitoring and tracking serious adverse events that resulted from the use or misuse of medical devices. The Medical Device Reporting (MDR) regulation is the mechanism that FDA and manufacturers use to identify and monitor significant adverse events involving medical devices, so that problems are detected and corrected in a timely manner. User facilities (e.g., hospitals, nursing homes, clinical laboratories) are required to report suspected medical device-related deaths to both FDA and the manufacturers within 10 working days. User facilities may report medical device related serious injuries only to the manufacturer within 10 days. Manufacturers must file a summary of all medical device reports to FDA within 30 calendar days. User facilities must file a summary report annually. Although the FFDCA gives FDA the authority to impose legal sanctions for not complying with MDR, FDA relies largely on the goodwill and cooperation of all affected groups to accomplish the objectives of the regulation. The searchable MDR database for devices is publically accessible at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmdr/search.CFM.

In August 2009, FDA published notice of a proposed rule, and a related draft guidance document, that would require manufacturers to submit MDRs to the agency in an electronic format.[52]

[52] FDA, "Proposed Rule, Medical Device Reporting: Electronic Submission Requirements," 74 *Federal Register* 42203-42217, August 21, 2009; and FDA, "Draft Guidance for Industry, User Facilities, and Food and Drug Administration Staff; eMDR—Electronic Medical Device Reporting; Availability," 74 *Federal Register* Page 42310, (continued...)

According to FDA, the proposed regulatory changes would provide the agency with a more efficient data entry process that would allow for timely access to medical device adverse event information and identification of emerging public health issues. The proposal reportedly met with some resistance from the device industry, which called for a longer timeframe to implement the changes, among other things.

In October 2009, the HHS Office of Inspector General raised questions about adverse event reporting for medical devices.[53] The report found that CDRH does not consistently use adverse event reporting and made several recommendations about how it could better do so.

The Sentinel Initiative

Some provisions related to adverse event reporting were enacted in FDAAA. One requires FDA to establish an active surveillance system for monitoring drugs, using electronic data from healthcare information holders. In response, in 2008 FDA launched the Sentinel Initiative. Its goal is to build and implement a new active surveillance system that will eventually be used to monitor all FDA-regulated products. According to FDA, the Sentinel Initiative aims to develop and implement a proactive system that will complement existing systems that the Agency has in place to track reports of adverse events linked to the use of its regulated products.

Information on the current status of the Sentinel Initiative is available at http://www.fda.gov/Safety/FDAsSentinelInitiative/default.htm.

Medical Device Tracking

Manufacturers are required to track certain devices from their manufacture through the distribution chain when they receive an order from FDA to implement a tracking system for a certain type of device.[54] The purpose of device tracking is to ensure that manufacturers of these devices can locate them quickly once in commercial distribution if needed to facilitate notifications and recalls in the case of serious risks to health presented by the devices. FDA may issue a tracking order for any Class II or Class III device:

- the failure of which would be reasonably likely to have serious adverse health consequences;
- which is intended to be implanted in the human body for more than one year; or
- which is intended to be a life sustaining or life supporting device used outside a device user facility. (21 CFR Part 821).

A current list of the devices for which tracking is required can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/MedicalDeviceTracking/default.htm#link_2.

(...continued)

August 21, 2009.

[53] Daniel R. Levinson, *Adverse Event Reporting for Medical Devices*, HHS Office of Inspector General, OEI-01-08-00110, October 2009, http://oig.hhs.gov/oei/reports/oei-01-08-00110.pdf.

[54] FDA, *Medical Device Tracking*, May 13, 2009, http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/MedicalDeviceTracking/default.htm#link_2.

Unique Device Identification

A provision in FDAAA requires the HHS Secretary to promulgate regulations establishing a unique device identification (UDI) system (FFDCA 519(f); 21 USC 360i). When implemented, this new system will require

- the label of a device to bear a unique identifier, unless an alternative location is specified by FDA or unless an exception is made for a particular device or group of devices;
- the unique identifier to be able to identify the device through distribution and use; and
- the unique identifier to include the lot or serial number if specified by FDA.

Information about the current status of the UDI System is available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/UniqueDeviceIdentifiers/default.htm.

Compliance and Enforcement

Compliance requirements apply to both the premarket approval process and postmarket surveillance. When a problem arises with a product regulated by FDA, the agency can take a number of actions to protect the public health. Initially, the agency tries to work with the manufacturer to correct the problem on a voluntary basis. If that fails, legal remedies may be taken, such as: asking the manufacturer to recall a product, having federal marshals seize products, or detaining imports at the port of entry until problems are corrected. If warranted, FDA can ask the courts to issue injunctions or prosecute individual company officers that deliberately violate the law. When warranted, criminal penalties, including prison sentences, may be sought.

Each center has an Office of Compliance (OC) that ensures compliance with regulations while pre- or postmarket studies are being undertaken, with manufacturing requirements, and with labeling requirements. The objectives of CDRH's OC's Bioresearch Monitoring (BIMO) program are to ensure the quality and integrity of data and information submitted in support of IDE, PMA, and 510(k) submissions and to ensure that human subjects taking part in investigations are protected from undue hazard or risk. This is achieved through audits of clinical data contained in PMAs prior to approval, data audits of IDE and 510(k) submissions, inspections of IRBs and nonclinical laboratories, and enforcement of the prohibitions against promotion, marketing, or commercialization of investigational devices. Any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept, can be subject to inspection. (See **Table 3**.)

Table 3. CDRH, FDA Foreign and Domestic Inspections, FY2004 – FY2008

FY	2004	2005	2006	2007	2008
Number of Inspections	2,936	2,694	2,691	2,495	2,353

Source: Prepared by the Congressional Research Service based on FDA, *The Enforcement Story* , Center for Devices and Radiological Health Enforcement Statistics, Center for Devices and Radiological Health, FDA Foreign and Domestic Inspections, Fiscal Years 2004 -2008, 2008, pp. 2-25, http://www.fda.gov/downloads/ICECI/EnforcementActions/EnforcementStory/UCM129811.pdf.

The OC also reviews the quality system design and manufacturing information in the PMA submission to determine whether the manufacturer has described the processes in sufficient detail and to make a preliminary determination of whether the manufacturer meets the QSR. If the manufacturer has provided an adequate description of the design and manufacturing process, a preapproval inspection can be initiated. Inspection is to include an assessment of the manufacturer's capability to design and manufacture the device as claimed in the PMA and confirm that the quality system is in compliance with the QSR. Postapproval inspections can be conducted within 8 to 12 months of approval of the PMA submission. The inspection is to primarily focus on any changes that may have been made in the device design, manufacturing process, or quality systems.

The compliance offices work closely with the Office of Regulatory Affairs (ORA),[55] which operates in the field to regulate almost 124,000 business establishments that annually produce, warehouse, import and transport $1 trillion worth of medical products. Consumer safety officers (CSOs) and inspectors typically have conducted about 22,000 domestic and foreign inspections a year to ensure that regulated products meet the agency's standards. CSOs also monitor clinical trials. Scientists in ORA's 13 laboratories typically have analyzed more than 41,000 product samples each year to determine their adherence to FDA's standards.

Section 516 of the FFDCA gives FDA the authority to ban devices that present substantial deception or unreasonable and substantial risk of illness or injury. Section 518 enables FDA to require manufacturers or other appropriate individuals to notify all health professionals who prescribe or use the device and any other person (including manufacturers, importers, distributors, retailers, and device users) of any health risks resulting from the use of a violative device, so that these risks may be reduced or eliminated. This section also gives consumers a procedure for economic redress when they have been sold defective medical devices that present unreasonable risks. Section 519 of the act authorized FDA to promulgate regulations requiring manufacturers, importers, and distributors of devices to maintain records and reports to assure that devices are not adulterated or misbranded. Section 520(e) of the MDA authorized FDA to restrict the sale, distribution, or use of a device if there cannot otherwise be reasonable assurance of its safety and effectiveness. A restricted device can only be sold on oral or written authorization by a licensed practitioner or under conditions specified by regulation.

Warning Letter

A warning letter is a written communication from FDA notifying a responsible individual, manufacturer, or facility that the agency considers one or more products, practices, processes, or other activities to be in violation of the laws that FDA enforces. The warning letter informs the recipient that failure to take appropriate and prompt action to correct and prevent any future repeat of the violations could result in an administrative or regulatory action. Although serious noncompliance is often a catalyst for issuance of a warning letter, the warning letter is informal and advisory. Warning letters are publically available on FDA's website at http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/default.htm. (See **Table 4**.)

[55] See ORA at http://www.fda.gov/AboutFDA/CentersOffices/ORA/default.htm.

Table 4. CDRH Warning Letters Issued, FY2000-FY2009

FY	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
# of Letters	528	498	285	205	198	182	154	155	152	136

Source: Prepared by the Congressional Research Service based on data from FDA's Office of Legislation.

Product Recall

A recall is a method of removing or correcting products that FDA considers are in violation of the law.[56] Medical device recalls are usually conducted voluntarily by the manufacturer (21 CFR Part 7), after negotiation with FDA. Under 21 CFR Part 806, manufacturers (including refurbishers and reconditioners) and importers are required to report to FDA any correction or removal of a medical device that is undertaken to reduce a health risk posed by the device. A recall may be a total market withdrawal or may be of a portion of product (such as a single lot). In rare instances, where the manufacturer or importer fails to voluntarily recall a device that is a risk to health, FDA may issue a recall order to the manufacturer (21 CFR Part 810).[57]

When a recall is initiated, FDA performs an evaluation of the health hazard presented taking into account the following factors, among others:

- Whether any disease or injuries have already occurred from the use of the product;
- Whether any existing conditions could contribute to a clinical situation that could expose humans or animals to a health hazard;
- Assessment of hazard to various segments of the population, (e.g., children, surgical patients, pets, livestock, etc.), who would be exposed to the product;
- Assessment of the degree of seriousness of the health hazard to which the populations at risk would be exposed;
- Assessment of the likelihood of occurrence of the hazard;
- Assessment of the consequences (immediate or long-range) of occurrence of the hazard.

Following the health hazard assessment, FDA assigns the recall a classification according to the relative degree of health hazard. *Class I* recalls are the most serious, reserved for situations where there is a reasonable probability that the use of, or exposure to, a product will cause serious adverse health consequences or death. *Class II* recalls are for situations where the use of, or exposure to, a product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote. In a *Class III* recall situation, the use of, or exposure to, a product is not likely to cause adverse health consequences. (See **Table 5**.)

[56] Recall does not include market withdrawal or a stock recovery. A market withdrawal is a firm's removal or correction of a distributed product for a minor violation that does not violate the law and would not be subject to legal action by FDA, e.g., normal stock rotation practices, routine equipment adjustments and repairs, etc. Stock recovery involves correction of a problem before product is shipped (i.e., is still in the manufacturer's control).

[57] CRS Report RL34167, *The FDA's Authority to Recall Products*, by Vanessa K. Burrows.

Table 5. CDRH Class I, II, and III Product Recalls, FY2004 - FY2008

	2004	2005	2006	2007	2008
Class I	36	77	76	45	131
Class II	1,235	1,351	1,252	1,102	2,178
Class III	219	170	222	132	163

Source: Prepared by the Congressional Research Service based on FDA, *The Enforcement Story* , Center for Devices and Radiological Health Enforcement Statistics, Center for Devices and Radiological Health Five-Year Total Product Recall Statistics, Fiscal Years 2004 -2008, 2008, pp. 2-26, http://www.fda.gov/downloads/ICECI/EnforcementActions/EnforcementStory/UCM129811.pdf.

In addition to a warning letter or recall, FDA may also issue a public notification or safety alert (e.g., "Dear Doctor" letter), to warn healthcare providers and consumers of the risk of the device in question. The main page for recalls, market withdrawals, and safety alerts for all FDA-regulated products is http://www.fda.gov/opacom/7alerts.html.

Legislative Issues

A number of medical device-related topics are of interest to Members of the 111th Congress. As described below, these include certain proposals in major health reform legislation, liability and preemption, 510(k) clearance and device approval, importation and inspection, the use of unapproved devices, advertising, IVD regulation, device-specific legislation, and some other issues. Note that appropriations legislation and issues are discussed in other reports.[58]

Proposals in Health Reform Legislation

Three types of device-related proposals have been included in major health reform legislation.[59] One would create device-related taxes to generate revenue for health reform. The second would require the creation of a national medical device registry. The third would create reporting requirements certain for gifts to health care providers from device manufacturers and others.[60]

Device-Related Taxes

Two of the major proposals for health reform include measures designed to generate revenue by imposing a tax related to medical devices. These have generated controversy within the device industry, with device manufacturers voicing their concern that smaller companies may suffer, and that all companies may be less able to capitalize research into the development of future

[58] CRS Report RL34638, *FDA FY2009 Appropriations,* coordinated by Susan Thaul.

[59] For further information about health reform proposals that include device-related provisions, see CRS Report R40943, *Public Health, Workforce, Quality, and Related Provisions in H.R. 3590, as Passed by the Senate,* coordinated by C. Stephen Redhead and Erin D. Williams; and CRS Report R40892, *Public Health, Workforce, Quality, and Related Provisions in H.R. 3962,* coordinated by C. Stephen Redhead.

[60] It is worth noting that various health reform proposals and certain other bills also address a fourth device-related topic: Medicare and other federal reimbursement. However, because FDA does not generally consider or regulate the cost of medical devices, this topic is beyond the scope of this report.

devices.[61] There is currently no special tax on medical devices; however, manufacturers do pay user fees to the FDA.[62]

The Patient Protection and Affordable Care Act (H.R. 3590, as passed by the Senate) would impose an annual fee on device manufacturers and importers, beginning in the calendar year 2011. The total amount of all such fees collected would be $2 billion per year ($3 billion beginning in 2018). Each manufacturer would pay a portion of the $2 billion equal to its market share; however, some sales would be excluded from the calculation, based either on the device type or the amount of gross receipts. Types of devices whose sales would be excluded from the calculation are Class II devices, typically sold to consumers at retail for $100 per unit or less, and Class I devices. Amounts of gross receipts that would be excluded are the following: for gross receipts of market sales that are not more than $5 million, all would be excluded; for gross receipts more than $5 million, but more than $25 million, half would be excluded. (For gross receipts more than $25 million, none would be excluded.)

H.R. 3590, as passed by the Senate would also place a 10% tax on indoor tanning services.

The Affordable Health Care for America Act (H.R. 3962) would place 2.5% tax on certain sales of certain medical devices. The total revenue that would be generated by this measure is estimated to be $20 billion over 10 years.[63] The tax would be applied to the first taxable sale (including certain leases and uses) of a medical device. The tax would not apply to devices sold to (or of the type an quantity typically sold to) consumers by retail establishments. Certain tax exemptions similar to those in Sec. 4221 and 4222 of the Internal Revenue Code would apply. These concern devices sold for export, and devices for use by the purchaser for further manufacture. (Other tax exemptions listed under IRC Sec. 4221(a)(3)-(6) would not apply, including those for state and local governments, nonprofit educational entities, and certain others.) Under specified circumstances involving contractually negotiated sales prices, sellers would be entitled to recover the amount of taxes paid from device producers, manufacturers, or importers. The tax would apply to sales made after December 31, 2012.

National Medical Device Registry

Concern about the safety of certain high-risk medical devices has led Congress to consider various tracking and postmarket surveillance mechanisms. Sec. 519(e) of the FFDCA permits the Secretary to order a medical device manufacturer to adopt a method of tracking for certain devices that may create risks for patients. The FDA Amendments Act of 2007 (P.L. 110-85) added a new Sec. 519(f), yet to be implemented, which requires medical devices to bear a unique identifier.[64]

[61] See, e.g., Alicia Mundy, "Drug Makers Face Tougher Measures," *The Wall Street Journal*, October 30, 2009, p. A4.

[62] For further information about user fees, see CRS Report RL34571, *Medical Device User Fees and User Fee Acts*, by Erin D. Williams.

[63] U.S. Congress, Joint Committee on Taxation, *Estimated Revenue Effects of Possible Modifications to the Revenue provisions of H.R. 3962, the "Affordable Health Care for America Act", Fiscal Years 2010-2019*, 111th Cong., 1st sess., October 29, 2009, JCX-43-09 (Washington: GPO, 2009), p. 2.

[64] For information on the implementation status of the unique device identifier, go to http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/UniqueDeviceIdentifiers/default.htm.

Two major proposals for health reform contain provisions that would require the creation of a national medical device registry. The Affordable Health Care for America Act (H.R. 3962) would require the HHS Secretary to establish a public national medical device registry to facilitate analysis of postmarket safety and outcomes data on certain devices. The registry would include Class III devices and could include, as the HHS Secretary determined appropriate and specified in regulation, a Class II device that is life-supporting or life-sustaining.

The HHS Secretary would be required to establish a procedure to link specified medical device data from manufacturers with patient safety and outcomes data from disparate sources, and integrate the registry activities with certain other postmarket risk and safety activities required by the FFDCA. In addition, acting through the HHS Office of the National Coordinator for Health Information Technology, the HHS Secretary would be required to adopt standards for the electronic exchange and use in certified electronic health records of a unique device identifier.

Gifts to Physicians and Other Health Providers

In recent years, questions have been raised over the propriety of certain financial relationships between health care professionals (e.g., physicians) and the pharmaceutical and other medical industries.[65] As part of these relationships, companies may give gifts or make payments to health care professionals as part of their marketing efforts, or for other purposes. In an effort to promote transparency and prevent inappropriate relationships, several states and the District of Columbia have enacted legislation requiring pharmaceutical companies to disclose gifts and payments made to health care professionals. While companies are free to voluntarily disclose this information, there is currently no federal requirement to do so.

The Affordable Health Care for America Act (H.R. 3962) would require certain device and other manufacturers and distributors report to the HHS Secretary of HHS certain gifts to physicians and other specified health providers. The Patient Protection and Affordable Care Act (H.R. 3590, as passed by the Senate) would create a similar requirement, but it would not apply to distributors, and would limit reporting to gifts made to physicians and teaching hospitals. These provisions also appear in a stand-alone bill, the Physician Payments Sunshine Act of 2009 (S. 301/ H.R. 3138), which is mentioned below in the "Advertising" section of this report.[66]

Liability and Preemption

Two recent United States Supreme Court cases focus on the question of whether FDA approval protects a manufacturer from liability under state tort law.[67] The first case, *Riegel v. Medtronic, Inc.*, involved a Class III medical device with FDA PMA and an express preemption provision in the FFDCA.[68] In *Riegel*, the Supreme Court held that if the FDA grants PMA for a medical

[65] This paragraph was contributed by Jennifer Staman, Legislative Attorney, CRS (jstaman@crs.loc.gov, 7-2610).

[66] For further information about gifts to physicians, see CRS Report R40790, *Requiring Disclosure of Gifts and Payments to Health Care Professionals: A Legal Overview*, by Jennifer Staman and Brian T. Yeh.

[67] For further information about product liability, see CRS Report RL33423, *Products Liability: A Legal Overview*, by Henry Cohen and Vanessa K. Burrows.

[68] *Riegel v. Medtronic, Inc.*, 522 U.S. ___ (2008). Riegel v. Medtronic, Inc., 522 U.S. ___ (2008). For a discussion of this case, please see CRS Report R40534, *Riegel v. Medtronic, Inc.: Federal Preemption of State Tort Law Regarding Medical Devices with FDA Premarket Approval*, by Vanessa K. Burrows,

device, the device manufacturer is immune from suit under state common law claims such as strict liability, breach of implied warranty, and negligence in design, testing, labeling, manufacturing, labeling, distribution, sale, inspection, or marketing of the device to the extent that such state law claims are "different from, or in addition to" federal PMA requirements.[69] The court's holding in *Riegel* suggests that to the extent that a lawsuit raises claims that "'parallel' rather than add to federal requirements," such as a state "damages remedy for claims premised on a violation of FDA regulations," such suits would not be preempted.[70]

By contrast, there was no express preemption statutory provision in the second case, *Wyeth v. Levine*, which dealt with implied preemption in the context of an FDA-approved drug label.[71] In *Wyeth*, the Supreme Court held that FDA's approval of a drug does not preempt a lawsuit against the manufacturer alleging that the drug's label failed to provide an adequate warning against significant risks. The Court did not find that the FFDCA impliedly preempted such cases. The Court drew a distinction between *Riegel* and *Wyeth* based on differences in congressional action regarding drugs and devices: "when Congress enacted an express pre-emption provision for medical devices in 1976, see §521, 90 Stat. 574 (codified at 21 U. S. C. §360k(a)), it declined to enact such a provision for prescription drugs."

Some members of Congress have proposed legislation that address what effect, if any, FDA approval should have on a manufacturer's liability, among other things. Examples of such legislation include the Medical Device Safety Act of 2009 (S. 540/H.R. 1346), the HEALTH Act of 2009 (H.R. 1086), the MCAP Act (S. 45), and the Health Care Freedom Act of 2009 (S. 1324).

510(k) Clearance and Device Approval

FDAAA (the FDA Amendments Act of 2007) required the Government Accountability Office (GAO) to study and report on the appropriate use of the 510(k) process to determine whether a new device is as safe and effective as a classified device.[72] The report, released in January 2009, made one recommendation: that FDA expeditiously take steps to issue regulations for class III device types currently allowed to enter the market via the 510(k) process (i.e., preamendment devices) by requiring PMAs or reclassifying them to a lower class. [73] The report has sparked agency action as well as legislative interest in issues related to 510(k) and preamendment devices.[74]

Some legislation has focused on separate approval-related issues. For example, the *Healthy Americans Act* (H.R. 1321/S. 391) includes approval provisions related to comparative effectiveness and device use in subpopulations.

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[69] 21 U.S.C. § 360k(a).

[70] *Riegel*, 522 U.S. ___ (2008); slip op. at 17.

[71] *Wyeth v. Levine*, 555 U.S. ___ (2009).

[72] P.L. 110-85, sec. 225.

[73] U.S. Government Accountability Office, *Medical Devices: FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process*, GAO-09-190, January 2009, http://www.gao.gov/new.items/d09190.pdf.

[74] For an example of agency action, see FDA, "Strengthening the Center for Devices and Radiological Health's 510(k) Review Process; Public Meeting; Request for Comments," 75 *Federal Register* 4402-4406, January 27, 2010.

Importation and Inspection

FDA shares its responsibility for ensuring the safety of imported medical devices with other agencies, including Customs and Border Protection. Questions raised about the safety of imported medical products have led some members of Congress to propose requiring enhanced registration for manufacturers and other establishments, the identification of prior transactions in device production, country of manufacture labeling, the hire of additional foreign inspectors, risk-based inspection, and other measures.

Examples of legislation that touch on the topics of importation and inspection include the Food and Drug Administration Globalization Act of 2009 (H.R. 759), and the Drug and Device Accountability Act of 2009 (S. 882).

Unapproved Devices

Medical devices may not be legally marketed in the United States without FDA's permission. Because FDA's evaluation takes time, there is necessarily a delay between the creation of a new medical device and FDA's evaluation of the safety and effectiveness of that device. This delay has sparked a policy debate about whether consumers and health providers should be allowed use devices lacking FDA's approval or clearance, particularly if they treat life-threatening medical conditions.

An example of legislation aimed at enhancing patient access to unapproved medical devices and other treatments is the Access to Medical Treatment Act (H.R. 3261).

Advertising

FDA has the authority to regulate the advertising of *restricted* medical devices, which are the rough equivalent of *prescription* drugs (FFDCA 502(r)). (The Federal Trade Commission regulates the marketing of non-restricted devices.) On one hand, advertising to consumers and health professionals might serve to educate them about life enhancing products. On the other, it might bias them, and raise device prices by the amount of advertising costs. Members of Congress have proposed legislation to regulate how medical device companies should promote their devices to consumers and physicians, as well as to require disclosure of companies' gifts to physicians.

Examples of legislation that touch on the topic of device promotion to physicians include the Physician Payments Sunshine Act of 2009 (S. 301/H.R. 3138) and the Access to Medical Treatment Act (H.R. 3261). The terms of S. 301/H.R. 3138 were incorporated into some health reform bills, as noted above.

IVD Regulation

FDA claims the authority to regulate all laboratory tests; however, it does not regulate all IVDs.[75] Whether FDA regulates a test depends on whether it is a laboratory-developed test (i.e., developed in-house, not for commercial distribution, also known as home brews) or a kit intended for commercial distribution. FDA regulates tests that are kits, and it does not regulate lab-developed tests in their entirety. (Certain components of lab-developed tests, called analyte specific reagents, are regulated by the FDA as Class I devices if they are commercially distributed.) While some argue that less regulation of laboratory developed tests aids consumer access to rapidly developed personalized tests, others argue that more regulation would help to ensure that the tests are accurate. Some members of Congress have proposed legislative measures that address the topic of IVD regulation.

Examples of legislation that touch on the topics of IVD regulation and reimbursement include the Patient Access to Critical Lab Tests Act (H.R. 1699) and the Medicare Clinical Diagnostic Laboratory Fee Schedule Modernization Act of 2009 (H.R. 1452).

Device-Specific Legislation

Some proposed legislation would, among other things, promote the development or availability of medical devices for particular diseases, situations, or types of research. The related legislative issues vary as widely as the topics addressed. Examples include the 21st Century Cancer ALERT Act (S. 717); the Autism Treatment Acceleration Act of 2009 (S. 819); the Global Autism Assistance Act of 2009 (H.R. 1878); the National Neurotechnology Initiative Act (S. 586/H.R. 1483); the Josh Miller HEARTS Act (H.R. 1380); the Compassionate Assistance for Rape Emergencies Act of 2009 (H.R. 1236); the Alopecia Areata Medicaid Improvement and Parity Act (H.R. 1142); the HEART for Women Act (S. 422/H.R. 1032); the Access to America's Orthopaedic Services Act of 2009 (H.R. 1021); the National Nanotechnology Initiative Amendments Act of 2009 (H.R. 554); the Lung Cancer Mortality Reduction Act of 2009 (S. 332); the Medicare Home Infusion Therapy Coverage Act of 2009 (S. 254/H.R. 574); the Longshore and Harbor Workers' Compensation Act Amendments of 2009 (S. 236); the Prevention First Act of 2009 (H.R. 463); the Prevention First Act (S. 21); the Skin Cancer Prevention, Education, and Consumer Right-To-Know Act (H.R. 2088); a House resolution to recognize the orthopedic industry for providing devices for active duty armed service members (H.Res. 577); and a bill to exempt small pharmacies from certain Medicare accreditation requirements for the purpose of providing diabetic testing strips under part B (S. 1746).

Other Issues

Medical devices are relevant to some other topics of legislative interest as well. For example, the Promoting American Agricultural and Medical Exports to Cuba Act of 2009 (H.R. 1531/S. 1089) and the Agricultural Export Facilitation Act of 2009 (H.R. 1737) would ease restrictions the exportation to Cuba of medical devices and other products.[76] The American Clean Energy and

[75] For further information, see CRS Report RL33832, *Genetic Testing: Scientific Background for Policymakers*, by Amanda K. Sarata.

[76] For further information about exportation to Cuba and other related issues, see CRS Report RL33819, *Cuba: Issues for the 110th Congress*, by Mark P. Sullivan.

Security Act of 2009 (H.R. 2454/S. 2998) and the Clean Energy Jobs and American Power Act (S. 1733) each have a mechanism for exempting devices from its hydrofluorocarbon requirements.[77] The 21st Century Global Health Technology Act (S. 1591/H.R. 3560) would promote investment in medical devices for maternal and child care.[78] The TRADE Act of 2009 (H.R. 3012) contains a measure to protect programs that would control the costs of pharmaceuticals or medical devices in trade agreements.[79] The Health Equity and Accountability Act of 2009 (H.R. 3090) and the Women's Health Office Act of 2009 (H.R. 3242) would create certain requirements for the inclusion of minorities and women, respectively, in device clinical trials. The Strengthening of FDA Integrity Act of 2009 (H.R. 3932) would apply debarment provisions currently applicable to abbreviated new drug applications to other types of applications, including those for medical devices.

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[77] For further information about clean air issues, see CRS Report R40145, *Clean Air Issues in the 111th Congress*, by James E. McCarthy.

[78] For further information about global health, see CRS Report RS22913, *Global Health: USAID Programs and Appropriations from FY2001 through FY2010*, by Tiaji Salaam-Blyther

[79] For further information on trade policy, see CRS Report RL33944, *Trade Primer: Qs and As on Trade Concepts, Performance, and Policy*, coordinated by Raymond J. Ahearn.