Department of Health and Human Services

# OFFICE OF INSPECTOR GENERAL

# FDA MEDICAL DEVICE REGULATION FROM PREMARKET REVIEW TO RECALL


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INSPECTOR GENERAL

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## OFFICE OF INSPECTOR GENERAL

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This report is produced by the Office of Evaluation and Inspections (OEI), one of the three major offices within the OIG. The other two are the Office of Audit Services and the Office of Investigations. The OEI conducts inspections which are, typically, short-term studies designed to determine program effectiveness, efficiency, and vulnerability to fraud or abuse.

This study used a case study approach to identify potential vulnerabilities in the Food and Drug Administration's regulatory process for medical devices.

The report was prepared under the direction of Kaye D. Kidwell, Regional Inspector General, and Paul A. Gottlober, Deputy Regional Inspector General, Office of Evaluation and Inspections, Region IX. Participating in this project were the following people:

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# EXECUTIVE SUMMARY

## PURPOSE

The purpose of this inspection was to describe the Food and Drug Administration's (FDA) regulatory process for selected medical devices that have been recalled and identify potential vulnerabilities and strengths in the regulatory system for medical devices.

## BACKGROUND

Medical devices play a vital role in health care delivery today. Technological advances in medical devices have revolutionized medical treatment. Medical devices range from the simple, such as tongue depressors, to the complex, such as artificial hearts.

Within the Department of Health and Human Services, FDA, through the Center for Devices and Radiological Health (CDRH) and district offices, regulates medical devices. The CDRH is responsible for premarket review and directs compliance and surveillance operations, such as medical device reporting (MDR) activities. The districts oversee device, food, drug, and cosmetic firms and assure the safety of biological products. Their activities include inspecting device manufacturers and monitoring recalls, which were mostly voluntary at the time this inspection was conducted.

The inspection team used a case study approach and interviews with both FDA officials and device manufacturers to analyze the regulatory system for medical devices.

## FINDINGS

- Most manufacturers consider FDA staff competent, knowledgeable, and fair.
- The FDA is unable to meet all of its regulatory responsibilities, primarily because of limited resources.
- The MDR regulation is unclear, and in some cases the MDR system may not provide early warning of device problems.
- Some regulatory actions and requirements take too much time to process and implement and therefore limit FDA's ability to enforce the Food, Drug, and Cosmetic Act.
- A significant number of recalls are due to design-related problems.

- Mandatory notification of recalls would improve the recall process.

- Some manufacturers attribute device problems to user error.

## RECOMMENDATIONS

- The FDA should develop alternative strategies, such as charging user fees, to obtain the resources necessary to meet all of its regulatory requirements.

- The FDA should clarify the MDR regulation.

- The FDA should seek legislative authority to impose civil monetary penalties and initiate recalls.

- The FDA should further develop the preproduction quality assurance recommendations and incorporate them into the Good Manufacturing Practices (GMP) regulation.

- The FDA should seek legislative authority to require manufacturers to notify FDA of recalls.

- The FDA should continue and enhance user education programs for devices that are susceptible to user error.

## AGENCY COMMENTS

The Public Health Service (PHS) concurred with the recommendations. The recommendations were presented by the Inspector General at hearings on the regulation of medical devices before the Subcommittee on Health and the Environment on July 17, 1990.

The Safe Medical Devices Act of 1990, signed by President Bush on November 28, 1990, enacted most of our recommendations. The Act authorizes FDA to initiate recalls and impose civil monetary penalties and requires manufacturers to report recalls to FDA. The Act also addresses weaknesses in the MDR system by requiring facilities to report serious problems with medical devices. In addition, the Act clarifies FDA's authority for preproduction design validation through the GMP process. The PHS submitted a legislative proposal for user fees, but the legislation failed to pass. The PHS will resubmit the proposal.

The FDA will clarify the MDR regulation and will continue to enhance its user education program.

The complete text of the comments is contained in appendix D.

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# INTRODUCTION

**NOTE:** *This inspection was completed prior to the enactment of the Safe Medical Devices Act of 1990. Therefore, many of the laws, regulations, and requirements described in this inspection have been changed.*

*The findings and recommendations of this report were presented by the Inspector General at hearings on the regulation of medical devices before the Subcommittee on Health and the Environment on July 17, 1990. The report provided essential information to Congress in developing, negotiating, and enacting the Safe Medical Devices Act of 1990, particularly the provisions concerning preproduction quality assurance (PPQA) and civil monetary penalties.*

*Many of the requirements in the new law parallel other recommendations in the report. See the "Agency Comments" section on page 22 for more details concerning the 1990 Act.*

## PURPOSE

The purpose of this inspection was to describe the Food and Drug Administration's (FDA) regulatory process for selected medical devices that have been recalled and identify potential vulnerabilities and strengths in the regulatory system for medical devices.

## BACKGROUND

For the past several years, the Subcommittee on Health and the Environment, House Committee on Energy and Commerce, has been reviewing the Medical Device Amendments of 1976 and the implementation of that legislation by FDA. We conducted this study at the request of Congressman Henry Waxman, Chairman of the Subcommittee. Congressman Waxman asked the Office of Inspector General (OIG) to track "several . . . medical devices through the entire regulatory process, from market entry to removal."

Medical devices[1] play a vital role in health care delivery today. Technological advances in medical devices have revolutionized medical treatment. Some of these advances, such as new imaging techniques and prosthetic heart valves, have fostered improvements in the diagnosis and

1 See appendix A for the legal definition of "medical device."

treatment of disease. The medical device industry has grown along with the emergence of new technologies. Although the device industry is comprised primarily of small manufacturers, it is diverse and dynamic. More than 14,000 domestic and 3,500 foreign registered device manufacturers produce approximately 1,800 types of medical devices,[2] ranging from such simple devices as tongue depressors to more complex devices such as artificial hearts.

Certain devices pose a much greater regulatory challenge than others. Many devices, such as bandages and bedpans, pose little or no medical risk and therefore require very little regulation. However, advances in complex medical devices present new risks to consumers and increasing regulatory challenges to FDA.

Within the Department, the Center for Devices and Radiological Health (CDRH) and FDA district offices regulate medical devices. The CDRH is responsible for determining device classifications, conducting premarket review, directing compliance and surveillance activities, such as medical device reporting (MDR), and providing training and education to users and device manufacturers. The FDA's 21 district offices play a critical role in the regulatory process. They have many responsibilities including inspecting manufacturers, making recall recommendations, and overseeing recalls. The FDA field offices handle food, pharmaceutical, biological, and cosmetic regulatory activities as well as device regulation.

## ➤ THE MEDICAL DEVICE AMENDMENTS

Before 1976, medical devices were largely unregulated. Congress passed the 1976 Medical Device Amendments to the Food, Drug, and Cosmetic Act (hereafter referred to as "the Act") in order to provide a comprehensive set of regulatory controls for the marketing of medical devices.

The 1976 amendments created three classes of medical devices, which are distinguished by the extent of regulation required. Class I devices are subject only to general controls such as prohibitions against misbranding. Two examples of Class I devices are tongue depressors and stethoscopes. Class II devices are subject to general controls and performance standards. Nearly 50 percent of all medical devices are classified as Class II devices. Examples are hearing aids and glucose monitors. Class III devices are also subject to general controls and in addition require premarket approval (PMA).[3] Examples of Class III devices are pacemakers and heart valves.

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2 CDRH, Activities of the Center for Devices and Radiological Health, Food and Drug Administration, February 26, 1990. A "type" of medical device is the broad, general category, such as pacemakers. This does not take into account simple variations, different models made by one manufacturer, or models made by a different manufacturer.

3 Class III device manufacturers must submit a PMA application, which includes valid scientific evidence demonstrating that their product is safe and effective.

## ➤ PREMARKET REVIEW

The 1976 amendments set forth formal criteria for manufacturers to notify FDA of their intent to market a new medical device. Section 510(k) of the Act requires that 90 days prior to marketing a medical device, the manufacturer must inform FDA of its intent. All new devices submitted to FDA for review are placed automatically into Class III[4] and are therefore subject to PMA unless the manufacturer contends that the device is "substantially equivalent" to (1) a device marketed before May 28, 1976, the date Congress enacted the Medical Device Amendments, or (2) a device marketed after that date that is classified in Class I or Class II. If FDA concurs, the device becomes subject to the same requirements as its predecessor. If FDA finds that a device is substantially equivalent to a Class I or Class II device, it allows the device to go to market with only the 90-day 510(k) notification.

During the PMA review process, FDA conducts an in-depth scientific review to ensure the safety and effectiveness of the device. Manufacturers submitting a PMA application must provide a detailed summary of safety and effectiveness data, usually from clinical trials. Before conducting clinical trials involving the use of human subjects, firms must submit an Investigational Device Exemption (IDE) application. The FDA review of the application is designed to ensure the safety and rights of patients.[5]

Currently, most devices reach the market without going through the PMA process. From 1976 through 1988, approximately 94 percent of the more than 36,000 devices and device modifications submitted to FDA for premarket clearance reached the market through substantial equivalence determinations.[6]

## ➤ POSTMARKET ACTIVITIES

***Problem Reporting.*** The FDA has two reporting systems for medical devices. Both systems are intended to provide an early warning of device-related problems. The first is mandatory medical device reporting (MDR) by device manufacturers. In 1984, FDA promulgated the MDR regulation, which requires manufacturers to submit an MDR if they receive information that "reasonably suggests" that (1) a device may have caused or contributed to serious injury or death or (2) a device has malfunctioned, and a recurrence is likely to cause or contribute to death or injury. For deaths or serious injuries, firms must notify FDA by telephone no more than 5 days after receiving the information. In addition, firms must file a written report within 15 days of the

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4 21 U.S.C. 360c.

5 An approved IDE permits a device that would otherwise be subject to marketing clearance or approval to be shipped lawfully for the purpose of conducting a clinical study.

6 U.S. General Accounting Office, Medical Device Recalls: An Overview and Analysis 1983-1988, GAO/PEMD-89-15BR, Washington D.C.: August 1989, p. 20.

initial receipt of the information. For devices that have malfunctioned but have not caused a death or injury, the written report is required, but the telephone report is not.

The FDA's second reporting system is a voluntary problem reporting program (PRP), started in 1973. The United States Pharmacopeia (USP), a nonprofit organization under contract to FDA, operates the PRP. Health care professionals, as well as other device users, may use USP's toll-free number or Medical Device & Laboratory PRP form to report device problems, which become part of the Device Experience Network and are published in brief on a monthly basis.

***Good Manufacturing Practices (GMP) Inspections.*** One of the district offices' major responsibilities is to inspect manufacturers to assess compliance with the GMP regulation, which requires that manufacturers have a quality assurance program.[7] Investigators also assess manufacturers' compliance with the MDR regulation during GMP inspections. When districts identify GMP deviations, they can issue a notice of adverse findings letter or a regulatory letter, which informs the firm that FDA is prepared to take regulatory action, such as seizure, if a firm does not attempt to correct a device-related problem.

***Recalls.*** Recalls are mostly voluntary.[8] The Act does empower FDA to require a firm to recall a device, but the criteria for exercising this provision of the law are so restrictive that the provision is impractical. The Act does not require manufacturers to report voluntary recalls to FDA. When a manufacturer learns that one of its products has problems or that FDA considers the device to have problems, the firm may choose to "recall" the product. The FDA can request that a firm initiate a recall if the company has taken no action in an urgent situation.

The FDA guidelines suggest that when a firm initiates a recall, it should notify the appropriate district office.[9] When FDA receives a recall report, the district office conducts an inspection to gather as much information as possible about the recall and sends a recall recommendation to CDRH. The recall recommendation details the firm's recall strategy, an analysis of the firm's ability to conduct an effective recall, and a recommended FDA audit program to evaluate the firm's compliance with recall guidelines.

The CDRH analyzes the recommendation, evaluates the health hazard the product presents, and classifies the recall according to the relative degree of health hazard. A Class I recall indicates that there is a strong likelihood that the device will cause serious, adverse health consequences or

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7 The Act requires FDA to conduct inspections of Class II and Class III device manufacturers every 2 years. The FDA applied this requirement to GMP inspections.

8 The FDA defines "recall" as the removal from the market of a particular device or the correction of a problem. "Correction" is the "repair, modification, adjustment, relabeling, destruction, or inspection (including patient monitoring) of a product and/or the promotional materials which cause the product to be violative, without its physical removal to some other location."

9 A recall may be initiated by a manufacturer, wholesaler, distributor, or any combination of these entities.

death. A Class II recall indicates that the device may cause temporary or medically reversible adverse health consequences or that the probability of serious adverse health consequences is remote. A Class III recall indicates that the device is not likely to cause adverse health consequences. The FDA publishes a list of recalls in its weekly *FDA Enforcement Report.*

The district office is responsible for most recall compliance activities. It prepares a recall notification, conducts audit checks, and evaluates the degree to which the recall has been successful.

The FDA's *Device Good Manufacturing Practices Manual* emphasizes that FDA "prefers to promote compliance by means other than the courts," and a voluntary recall "is generally the fastest and most effective way to protect the public."[10] The FDA may use several methods to encourage a recall, however. If an inspector identifies a violative product, the district office's compliance officer might send an official notice of adverse findings to the firm or a regulatory letter. The regulatory letter informs the manufacturer that FDA is prepared to take regulatory action (such as seizure of the device) if the firm does not correct a device-related problem. If the manufacturer fails to respond adequately to a regulatory letter, FDA may seek a court-ordered seizure or injunction to halt the marketing of a device as a last resort.

The OIG has conducted numerous reviews of FDA's programs. The OIG has evaluated both premarket review and postmarket surveillance activities.

## METHODOLOGY

The inspection team used a case study approach and interviews with officials in both CDRH and 9 district offices and representatives of 23 device manufacturers to analyze the regulatory system for medical devices. See appendix B for a more detailed discussion of the methodology.

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10 FDA, Device Good Manufacturing Practices Manual, Fourth Edition, HHS Publication FDA 87-4179, November 1987, p. 16-11.

# CASE STUDIES

The following eight case studies illustrate both strengths and weaknesses in FDA's regulatory system for medical devices. The cases reflect eight different products and device firms. For each one, we have summarized the issues and described how FDA handled the problems that emerged with the device.

## DEFIBRILLATOR/CARDIAC MONITOR

***In this case, the system worked well. The FDA became aware of the problem during a GMP inspection. Even though recalls are mostly voluntary, FDA was able to convince the firm that a recall was warranted.***

During a routine GMP inspection, FDA became aware of a problem with a company's defibrillator/cardiac monitor. Defibrillators are electronic devices that are used to provide brief electrical shock to the heart to restore the normal heart rhythm. The FDA learned that the cardiac monitor registered a 'flat line' (i.e., no heart beat) when a specific adaptor (i.e., a strap) was used at various frequencies following a defibrillator discharge of greater than 200 joules. Essentially, the strap was used to provide electrical power to both the defibrillator and monitor through a single line cord.

The company had not planned to notify customers of the potential problem. It believed that since problems occurred infrequently, customer notification was not warranted. Also, it made a hardware change in the strap to protect the cardiac monitor during discharges of the defibrillator and monitored product performance in the field.

In a December 1988 letter, the district notified the firm that CDRH considered the company's action inadequate. In January 1989, company representatives met with CDRH, which reiterated its position that the firm had not met the requirement of adequate notification. The firm agreed to attempt to work out the logistics necessary to notify its customers of the problem and to keep the district informed of its actions.

The firm acted within a week. In a letter to the district, it stated it would initiate a recall of adaptor accessories and replace them. The FDA subsequently classified the company's action as a Class II recall. By the end of the year, the firm notified the district that the recall was complete. The district then assigned audit checks to 20 district offices. As of March 1990, all but one of the audits had been completed, and the checks showed that the recall was effective.

## BALLOON DILATION CATHETER

***A lead from one of this firm's competitors led FDA to undisclosed recalls, a failure to comply with the MDR regulation, marketing without PMA, and, ultimately, seizure of this manufacturer's product.***

The balloon dilation catheter is used during the angioplasty procedure. It consists of a thin teflon-coated stainless steel tube, or wire, with a balloon at one end. During the procedure, the balloon is inflated when it reaches the clogged portion of an artery. The purpose is to compress plaque against the artery so that blood flow will increase.

Since 1987, the manufacturer has released three models of the catheter. The first catheter, which had a problem with the balloon wrapping around the wire, was replaced with a second version. Numerous cases of broken catheter tips caused the manufacturer to replace the second catheter after less than 2 months with a third version (the CDRH received only two PRPs related to broken catheter tips). The manufacturer did not designate the first two replacements as recalls and failed to submit a PMA supplement for the third catheter. The manufacturer attributed the tip breakage problems to users overrotating the catheter, but CDRH determined that the device's design was inadequate to prevent overrotation.

The FDA learned about the recall and replacement of the second catheter with the unapproved third catheter from one of the manufacturer's competitors. The competitor sent CDRH a copy of a "Dear Doctor" letter from the manufacturer indicating that because of problems with the second catheter, the catheter had been "refined." The FDA inspected the manufacturer and found more than 50 cases where the second catheter's tip had broken during the angioplasty procedure.

The CDRH determined that the manufacturer's replacement of the second catheter with the third catheter constituted a Class II recall. The CDRH later notified the manufacturer that because it had failed to file a PMA supplement for the third catheter, it was in violation of the Act and should discontinue distribution. The firm met with CDRH on two occasions to protest FDA's position but was unable to convince CDRH that PMA was unnecessary. The manufacturer submitted a PMA supplement, but FDA suggested that a recall was appropriate pending approval of the supplement.

The CDRH initially denied the district's request for a recall of the first catheter, citing manufacturer-supplied data. The district sent a recall recommendation for the first catheter, citing the balloon wrapping problem. The district office also believed that the first catheter's replacement with the second catheter constituted a recall. In the recall recommendation, the district noted that the firm had no intention of recalling the first catheter, but would continue to swap the first catheter for later models at the customer's request. The CDRH denied the district's recall recommendation, citing data provided by the manufacturer that showed that the rate of catheter failures was consistent with that of other manufacturers.

Subsequently, the district initiated another investigation of the first catheter. The purpose of this inspection was to review, evaluate, and perform a trend analysis of complaints concerning this

model. The investigator also was asked to review the manufacturer's MDR system and guidelines.

The investigator found "significant problems with relation to the firm's complaint handling system." Under the firm's MDR policy, only those complaints which led to medical intervention, such as bypass surgery, were reported to FDA. If a catheter tip broke and remained lodged in the patient or was removed, the manufacturer did not report it. The investigator found that the manufacturer had inadequate mechanisms to conduct trend analysis and failed to submit MDRs for over 200 reportable complaints.

The district recommended that FDA initiate a recall and seize thousands of catheters in the manufacturer's inventory. The seizure process took more than 5 months from initial district office review through the seizure, because this was the first time that FDA had based a seizure on noncompliance with the MDR regulation. The FDA approved the seizure recommendation, the case was filed by the U.S. Attorney's Office, and U.S. Marshals seized the catheters.

## SPINAL FIXATION SYSTEM

***This case illustrates that regulatory actions may take a long time to process. The firm promoted and marketed a device for an unapproved use.***

In 1984 and 1985, this company sought substantial equivalence determinations from CDRH for stainless steel plates and screws that an orthopedic surgeon had developed and implanted in patients' vertebrae. The CDRH determined that the spinal fixation system was not substantially equivalent and that the firm would have to obtain an approved PMA application before distributing the product commercially. The firm subsequently filed 510(k) notifications to use the plates and screws in long bones and flat bones, such as the pelvis, but not the spine. The CDRH found, in early 1986, that the devices subject to the 510(k) submissions were substantially equivalent.

In January 1986, the firm filed an IDE for the spinal plate fixation system. In July, CDRH approved the IDE protocol.

In the summer of 1989, the district inspected both the firm and the inventor who served as a clinical investigator for the IDE. It found two major violations relating to the promotion and distribution of devices that resulted from a failure to comply with the IDE regulation and the sale and use of devices for an unapproved use. Essentially, the firm never promoted the plates and screws for the use covered by CDRH's substantial equivalence findings. Instead, it marketed them for use in spinal fixation surgery through training seminars, catalogs, videotapes, and technical manuals. The company sold substantial quantities of plates and screws in the year prior to August 1989. The district found major defects with the clinical investigation in recordkeeping, adherence to protocol, review of medical records, patient selection, patient informed consent, patient follow-up, and IDE device accountability. In October 1989, the district recommended that the IDE be withdrawn. In April 1990, CDRH withdrew the IDE. The FDA currently is pursuing further action against the firm.

## HEART VALVES

***Sometimes, FDA has to pressure firms to recall products. In this case, FDA threatened to withdraw premarket approval for two heart valves if the manufacturer did not recall them.***

In August 1986, FDA granted PMA for two heart valves (aortic and mitral) to a manufacturer that subsequently sold all its assets. (The discussion that follows refers to the new firm.)

Device failures occurred both before and after PMA. The heart valves were made from pyrolitic carbon, a brittle material. Cracks or imperfections in the material could lead to the eventual failure of the valves. Two fractures of the valves were known when FDA approved the PMA application. The firm then submitted 10 more MDRs related to valve failures. All 12 of these valves were assembled from pyrolitic carbon components that were manufactured prior to January 1986. Approximately 20,000 valves were implanted in patients between 1982 and May 1988.

In early 1988, CDRH became concerned about the fracture rate of the valves and met with company representatives to discuss the problem. Initially, the firm did not believe a recall was necessary. The CDRH became convinced, however, that the problem was serious enough to warrant withdrawal of the PMA. In March, CDRH decided that the manufacturer "should . . . come in and present his reasons why FDA should not take action to remove this valve from the market."

The agency did not have to withdraw the PMA, because the firm decided to cease manufacturing and distributing the valves and to notify customers of the recall. In a May letter to physicians, the company announced that it was suspending marketing of the valve and instructed them to discontinue use and return all unused valves to the firm. The firm advised customers not to explant valves but to monitor patients who had them.

The FDA classified the company's removal of the valves as a Class I recall. In notifying the firm of the recall classification, FDA expressed concern that the firm's communication to physicians of record was "not designed to catch the attention of the reader nor to impress on the reader that immediate action should be taken." The FDA's position was that cardiologists, who monitor patients with implanted heart valves after surgery, should be made aware of the potential failure of the heart valves. One month later, the firm issued a clarifying letter to cardiologists.

The heart valves remain off the market. The company currently is preparing a PMA supplement for the device.

## KIDNEY LITHOTRIPTER

***User error, as well as problems with the design of a device, can lead to injuries and death. In this case, the firm claimed that user errors led to problems with a kidney lithotripter. However, CDRH required the firm to modify the design.***

The kidney lithotripter uses shock waves to crush kidney stones inside the body without surgical intervention. In one model, the patient rests on a stretcher placed on top of a water cushion, where the shock waves are generated and geometrically focused on the kidney stone. For several weeks after the procedure, the patient passes small sand-like fragments of the stone during normal urination. The firm also markets a lithotripter that uses a water-filled tub instead of the water cushion.

Company officials assert that incorrect use of the lithotripter can cause serious injury or even death. The most common user errors occur when physicians (1) perform the procedure on patients with risky medical or physical conditions or (2) use an excessive number of shock waves to destroy the stones.

The firm's operating manuals for both models warn physicians not to use kidney lithotripsy on patients who are pregnant, obese, have cardiac problems (especially patients with pacemakers), or receive blood thinning drugs. In December 1984, FDA approved the firm's PMA application for the first model. In January 1989, it approved a PMA supplement to expand the maximum number of shock waves from 1,800 to 3,000. The firm still stresses, however, that physicians should not use more than 2,000 shock waves to break up kidney stones. A large number of shock waves increases the risk that the lithotripter's focus may not be maintained.

The CDRH became concerned about the firm's compliance with the MDR regulation. In late 1989, CDRH requested that the district office inspect the company to assess its compliance with the regulation and failure investigations of two reports of serious injury. The investigator found that the firm did not properly document its investigation of one of the reports. He also found that the firm did not submit MDRs for other events within the regulatory time frames. The district office issued a notice of adverse findings to the firm because of the violations of the MDR regulation.

By April 1990, the firm had filed 64 MDRs for the 2 models. It blamed six deaths and four injuries on either user error or on complications resulting from undetected preexisting medical conditions.

In addition to concerns about the firm's compliance with the MDR regulation, FDA was concerned that patients might be subjected to unnecessarily high radiation doses if physicians used the high fluoroscopy mode excessively. According to the firm, this mode should be used only when visualization of the stone is difficult. In 1988, CDRH requested that the firm survey

its users to determine whether physicians were inappropriately using the higher settings. The firm found that physicians were overutilizing this mode. The CDRH ordered the firm to recall and modify the device and to educate users about proper use of the high fluoroscopy mode.[11]

This firm's lithotripters also have exhibited problems with the seat cushion and stretcher. A recall resulted from a district's MDR investigation regarding a large patient who received a second degree burn after his back was allowed to rest against the water cushion light. The district recommended a safety alert, but CDRH determined that the firm should recall both models. The CDRH considered the lithotripter to be misbranded and adulterated because the design of the cushion assembly could lead to burns when patients of a particular bulk or size are positioned against it. The firm recalled the lithotripters and made modifications.

## BALLOON INFLATION DEVICE

***In this case, design defects, which were not identified during premarket testing or review, led to a recall. Firm officials suggested that FDA's preproduction quality assurance (PPQA) recommendations might reduce future design problems.***

This recall involved a device that was fabricated by a company that manufactures coronary catheters and accessories. The recalled device was a balloon inflation device. The device was intended to inflate, deflate, and monitor the pressure of a balloon catheter, which is used in angioplasty to unclog blocked arteries.

In September 1987, CDRH reviewed the 510(k) notification for the balloon inflation device and determined that it was substantially equivalent to similar devices. The device consisted of a disposable syringe with a screw-type plunger and a pressure gauge, which was purchased from a subcontractor.

According to the manufacturer, the firm received a complaint within "days" of the device's release. The complaint concerned the gauge, which was sticking, resulting in inaccurate pressure readings. Inaccurate readings could result in a physician overinflating and possibly bursting the balloon. The manufacturer monitored the device for 2 weeks and received two more complaints. Although no injuries or deaths occurred, the company filed one MDR for the three events and decided to recall the device.

The CDRH followed the established 510(k) process when reviewing this device. However, this process is not intended to identify design flaws or safety and effectiveness. The 510(k) determination was based on the device's substantial equivalence to similar devices. Therefore,

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11 Lithotripters are also subject to regulation under the Radiation Control for Health and Safety Act, which provides CDRH with the authority to order recalls of radiological products (fluoroscopic equipment in this case).

the CDRH reviewer did not evaluate safety and effectiveness data for the device. The manufacturer also made statements about the device's accuracy in its 510(k) notification. The manufacturer claimed that the gauge would be accurate within a certain percentage throughout its operating range. Since CDRH is not required to verify data, the manufacturer did not submit any to support this claim. In the recommendation for a substantial equivalence determination, the CDRH reviewer stated that the device was accurate to that percentage.

A company official stated that the 510(k) process is "virtually worthless" for preventing potential recalls. "The 510(k) is almost like a registration, nothing more. You're not required to build prototypes. You never have . . . to show that it is reliable," he added.

The device was the manufacturer's first attempt to bring an inflation device to market. Company officials told us that a device in mass production may not perform the same as it did in a limited premarket test run and the company would probably have benefitted from a pilot test run to determine if there were any variations in quality from the premarket run.

While critical of the 510(k) process, company officials were skeptical of FDA's ability to detect product defects: "Our own engineering force even missed some things. FDA will not be able to find things that we have missed." The manufacturer had tested the device, but research and development prototypes did not exhibit the sticking problem. The problem became evident when the device went into mass production. Company officials suggested that FDA's preproduction quality assurance recommendations, which include provisions for pilot test runs, should be incorporated into the GMP regulation.

## INSULIN INFUSION PUMP

***Because GMP inspections concentrated on the manufacturer's major products and the manufacturer did not comply with the MDR regulation, FDA was unaware of the severity of problems with the insulin pump until the district office conducted a recall inspection.***

While primarily a manufacturer of cardiac devices, this firm also marketed insulin pumps for diabetics. The pump administers and regulates the amount of insulin according to the patient's needs. It is worn externally, usually in a belt pouch, and delivers the insulin through a syringe, thin tube, and needle which is inserted beneath the patient's skin.

Prior to the recall of the insulin pump, FDA had identified problems with the firm's interpretation of the MDR regulation and was aware of some problems with previous models of the pump. Both the district and CDRH had notified the manufacturer of the problems with MDRs. The manufacturer continued to apply its own criteria for submitting MDRs.

The district had conducted GMP inspections focusing on the manufacturer's cardiac devices and, to a limited extent, earlier models of the insulin pump. However, FDA was not aware of the extent of the problems with the recalled pump until the district conducted a recall inspection. During this inspection, the FDA investigator found that the problems with the pump far exceeded

those reported and targeted for correction by the manufacturer. He concluded that the pump reached the market despite the fact that totally inadequate premarket testing had been performed.

The investigator issued a report detailing a number of design deficiencies and GMP violations, including (1) inadequate safety, accuracy, design verification, and reservoir leakage testing; (2) extreme "user unfriendliness"; and (3) failure to properly assess complaints, analyze failures, and comply with the MDR regulation. Based on the results of the inspection, the district recommended that CDRH classify the recall as Class I. The pump was subsequently withdrawn from the market.

Although the manufacturer received almost 1,500 reportable complaints, it filed only 15 MDRs before the recall (the CDRH received only 7 PRPs from device users). The district's investigator questioned the small number of MDRs. During the recall, the manufacturer reiterated its disagreement with FDA over interpretation of the MDR regulation: "The industry should not be penalized for having a differing opinion from FDA. . . . We try to meet the intent of the law. "

The firm submitted a small number of MDRs primarily because (1) it did not believe that battery and keyboard failures posed safety hazards to users, and (2) it did not submit MDRs if it determined that user error caused the problem,[12] or if the pump met specifications after the event. In addition, the company was behind in logging and investigating the large number of pump complaints.

The firm believed that user error was responsible for a number of complaints that the district believed were reportable events. For example, one official stated that if users fail to follow the "therapeutic regimen prescribed, . . . high blood sugars will occur."

The CDRH requested that the manufacturer review all pump complaints for MDR reportability. The manufacturer subsequently filed MDRs for more than 1,500 unreported events. "We overreported to a certain extent," said one company official. The district recommended that a regulatory letter be sent to the manufacturer. The CDRH agreed with the recommendation, and the letter was issued approximately 5 months after the recall was initiated.

## MICROPROCESSOR VENTILATOR

***In this case, the district recommended an injunction, and CDRH denied it.***

In December 1988, a district office recommended a recall of a microprocessor ventilator, which provides gases to patients who require respiratory assistance. Two types of failures were involved. First, the watchdog timer circuit, which analyzed the functioning of the

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12 21 CFR 803.24(d)(1) requires manufacturers to submit an MDR even if they believe that the event prompting the report is due to user error.

microprocessor, failed if the electrical line voltage dropped below 100 volts. Specifically, the device ceased ventilating without audible or visual alarm. Second, the device ceased ventilating if its nebulizer were disconnected prior to an operator manually setting a ventilating time cycle.

The manufacturer received complaints related to both failures. It linked three complaints, one involving a death, to the failure of the timer circuit and was investigating three other complaints, one of which also involved a death (the firm submitted six MDRs after receiving these complaints). The company received 10 complaints (no injuries or deaths) related to the nebulizer. The firm decided to recall the devices after its failure analyses confirmed the product defects. It intended to correct each unit distributed by installing new software.

The FDA classified the firm's action as a Class I recall. In monitoring the recall, the district concluded that the recall was ineffective initially. The firm decided to recontact all of its customers by telephone and to mail another notification to those customers who did not receive the original mailing. The district then concluded that the recall was effective.

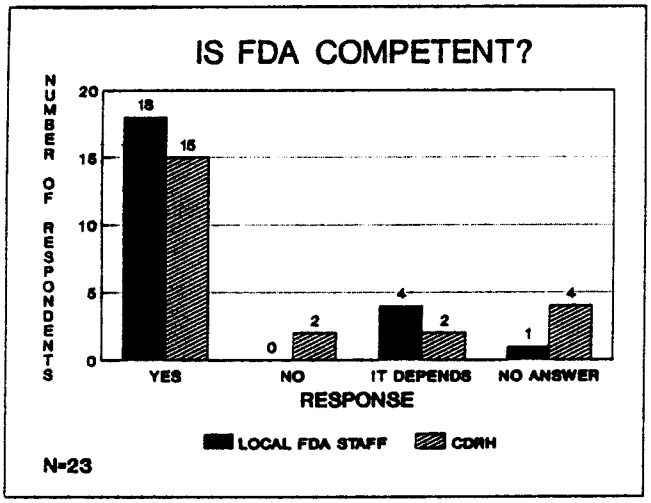
In April 1989, the district submitted an injunction recommendation to CDRH. The district believed that repeated GMP deviations demonstrated that the company would continue to manufacture unsafe ventilators. The district was particularly concerned about the microprocessor ventilator that had been recalled.

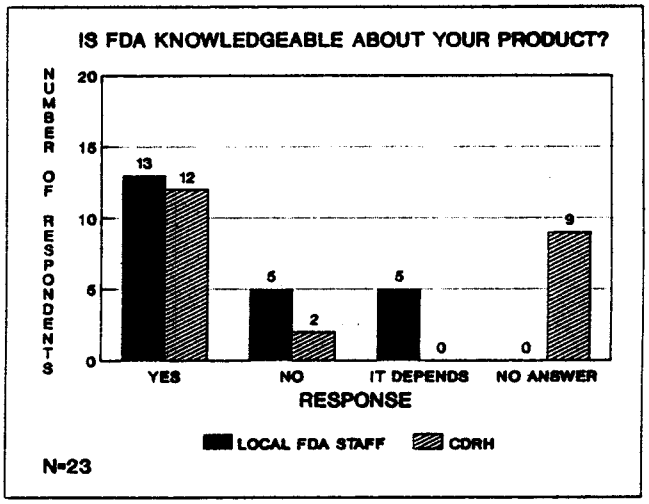
The CDRH disapproved the recommendation for injunction, stating it did not believe that the firm's GMP deviations and history of GMP compliance supported an injunction. It argued that the firm's proposed corrective actions would adequately address all but a few of the GMP deviations documented during the district's February and March 1989 inspection. As an alternative, CDRH suggested that the district issue a notice of adverse findings to the firm.

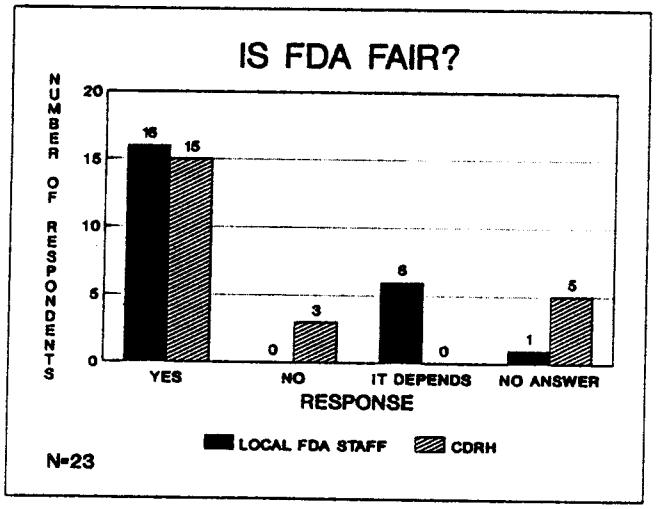
# FINDINGS

## ➤ MOST MANUFACTURERS CONSIDER FDA STAFF COMPETENT, KNOWLEDGEABLE, AND FAIR

Most companies have a favorable impression of staff in the district offices and at CDRH. Companies that reported having difficulties with FDA generally attributed the problem to certain individuals who were more adversarial than their colleagues.



One respondent said that local staff "have to deal with such a wide variety of products—it is a herculean task." Although most manufacturers believe that local staff is knowledgeable about their products, one respondent stated that "the staff needs to specialize and study medical devices. . . . Senior inspectors lack the experience to adequately understand our product." Another respondent noted that "with turnover, the level of experience has slipped. . . . Less experienced people are not as knowledgeable as others."

Regarding the staff at CDRH, one respondent noted that "the staff is underpaid given the responsibility they have. . . . Many have left for industry." Another respondent also discussed turnover at CDRH and said that "new reviewers don't have experience in [the firm's] product area."

## ➤ THE FDA IS UNABLE TO MEET ALL OF ITS REGULATORY RESPONSIBILITIES, PRIMARILY BECAUSE OF LIMITED RESOURCES

Seven districts reported that they have difficulty meeting the statutory and regulatory requirements for inspections, including those conducted to gather information about recalls and inspections conducted to assess compliance with the GMP regulation. Four districts noted that the requirement for biennial GMP inspections is particularly difficult. One respondent noted that "we have trouble with our statutory time frames for routine inspections because of higher priorities. . . . With everything a priority assignment, we can't keep up." Another respondent said that "we are absolutely behind schedule on [at least 100] GMP inspections."

One explanation for the districts' problems conducting GMP inspections may be the resources required to inspect some companies. One respondent estimated that staff in his district spent 1,500 hours at the defibrillator manufacturer over a 5-year period (e.g., 1,200 hours is 1 staff year). Another said that the manufacturer of the balloon dilation catheter "has taken up 2 staff years already. . . . Some firms need frequent inspections."

The CDRH officials are aware that districts are not meeting the biennial GMP inspection requirement. The agency's Office of Planning and Evaluation (OPE) analyzed GMP inspection data from 1981 through 1987 to determine the amount of time that elapsed between manufacturers' last two GMP inspections. The OPE found that 51 percent of all firms that FDA inspected were not reinspected within 24 months. Another finding, which was based on a different data base, was that, as of August 1988, 19 percent of all active Class II and III device manufacturers had never been inspected.

District offices would benefit from more training and less turnover of staff. Seven districts commented that their inspectors need more training to inspect device firms. One district with a large concentration of device manufacturers attributed the problem in part to turnover: "We have a 10 percent turnover rate per year making it difficult to keep our inspectors trained." One respondent commented that "When budgets are reduced, training is the first to go." Another district office official described the staffing problems due to turnover: "We may have to pull people off other jobs to get the expertise we need. . . . I don't have a lot of expertise in my office now."

We observed that the districts and CDRH are not sufficiently computerized, and the districts lack ready access to CDRH data bases. Automated equipment is in short supply in the district offices. Most investigators do not have their own personal or laptop computers to prepare investigative reports and access CDRH data bases. In response to our observations, FDA told us that the districts need regional computer centers, local area networks, and 1,500 personal computers. The FDA agreed that the shortage of computers limits districts' access to CDRH data bases.

Two districts commented that FDA needs more and better equipment not only to perform its daily tasks but also to respond to requests from the public. Officials in one district noted that when they process Freedom of Information Act requests, they purge confidential information from files. "What we need are computerized optical disc records to speed the process," said one respondent. The FDA also has problems meeting its regulatory requirements for premarket review. In a July 1990 report, the OIG's Office of Audit Services identified weaknesses in the 510(k) review process that limit the program's efficiency and effectiveness. The Office of Audit Services found that FDA does not have a management information system that tracks individual reviewer workload and productivity.

## ➤ THE MDR REGULATION IS UNCLEAR, AND IN SOME CASES THE MDR SYSTEM MAY NOT PROVIDE EARLY WARNING OF DEVICE PROBLEMS

As noted in the case studies, both the insulin infusion pump and balloon dilation catheter manufacturers had their own interpretations of the MDR regulation. These cases illustrate that failure to file MDRs may hinder FDA's ability to detect device problems. In both cases, FDA identified events that should have been reported but were not. The FDA was not aware of almost 1,500 reportable insulin pump events because of the firm's interpretation of the regulation. The FDA did not become aware of the extent of the problems with the pump until the district conducted a recall inspection. In the catheter case, FDA was unaware of dozens of catheter tip breakages because the firm did not submit MDRs unless patients underwent surgery to remove the tip. Upon investigating the firm's complaint files, the investigator found that the firm failed to submit MDRs for over 200 reportable complaints.

Twelve manufacturers said that the MDR regulation is vague or that the definitions of malfunction and serious injury are unclear. One attorney who works with the medical device industry echoed the firms' concerns when he wrote that "the definition [of serious injury in the MDR regulation] does not distinguish adequately between what is a minor injury and what is considered serious." He also echoed their concerns that the definition of malfunction does not provide adequate guidance to manufacturers about events that must be reported.[13]

Although many firms believe that the MDR regulation is vague, they do not seek guidance from FDA. Fifteen manufacturers reported that they would not contact CDRH regarding MDRs, even

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13 Edward M. Basile, Esq., "Medical Device Reporting: The Good, the Bad, and the Ugly," Food, Drug, Cosmetic Law Journal 42 (1987), pp. 91-93.

if they were unsure whether an event was reportable. A respondent said that "generally, FDA will just tell you to file it. They do not know the device, and they do not know the nature of the problem." One explanation is that CDRH cannot provide guidance over the telephone. A CDRH official noted that "you cannot make reportability decisions over the phone. You need labeling. You need to know the firm's review procedures. Firms do not want to put issues of reportability/nonreportability in writing."

In addition to the manufacturers, four districts commented that the MDR regulation is subject to interpretation. One respondent noted that "some dispute exists as to what to report—some overreport for liability reasons." Another noted that "there seems to be some confusion about the MDR by firms, district offices, and CDRH . . . . Who is responsible [for reporting]? Is it the firm whose name is on the product or the manufacturer of the product?"

Most of the districts reported that manufacturers generally comply with the MDR regulation, although three commented that some companies overreport, in part because of product liability. One district noted that although "major companies" comply, smaller firms may not.

Three manufacturers were critical of the reporting times in the MDR regulation. One respondent commented that "it is very difficult to follow up on an MDR within the regulatory time frames. We only have 5 days to investigate [a death or serious injury] and decide whether or not to report."

### ➤ SOME REGULATORY ACTIONS AND REQUIREMENTS TAKE TOO MUCH TIME TO PROCESS AND IMPLEMENT AND THEREFORE LIMIT FDA'S ABILITY TO ENFORCE THE ACT

Some regulatory actions are time consuming because they must be approved at myriad levels, both inside and outside CDRH. In one case, the district recommended seizing defective catheters in November 1989. The CDRH approved the recommendation in January 1990 and forwarded it to the Associate Commissioner for Regulatory Affairs (ACRA). The seizure was approved and took place in February. This case was unique because FDA had never attempted a seizure based on noncompliance with the MDR regulation. In another case, the district recommended an IDE withdrawal in October 1989 because of evidence that a firm was commercializing a product for an unapproved use and violating regulatory requirements. The CDRH did not withdraw the IDE until April 1990. In November and December 1989, district and CDRH officials met to discuss the case and agreed that the district would complete its investigation of the firm and prepare recommendations for an injunction and grand jury investigation. The district could not provide additional documentation to support the recommendations until March 1990. The CDRH and the ACRA approved the recommendations, which are under review by the Department's Office of General Counsel.

Two districts have used a voluntary agreement because they were frustrated with the time it took for CDRH to approve injunctions. The district notifies problem companies that it is prepared to submit an injunction recommendation to motivate firms to take corrective action. The firm signs an agreement and posts a bond for FDA's cost of supervising an injunction. When the firm has

taken corrective action, the district releases the bond. According to one district that uses this approach, the firm's bond is a "bargaining chip."

Another alternative to the lengthy legal process for some regulatory actions is civil monetary penalties. The FDA does not currently have the administrative authority to impose civil penalties on device manufacturers that violate sections of the Act.

## ➤ A SIGNIFICANT NUMBER OF RECALLS ARE DUE TO DESIGN-RELATED PROBLEMS

The FDA found that 44 percent of all quality problems resulting in recalls from 1983 to 1988 were attributable to preproduction or design deficiencies.[14] The leading cause of recalls was GMP-related problems, which accounted for 47 percent of all recalls. In seven of the eight cases we reviewed, design problems led to recalls. For example, one model of the balloon dilation catheter had a problem with the balloon wrapping around the wire. The lithotripter's problems related to the seat cushion and stretcher. The insulin infusion pump exhibited a number of design problems, including keyboard failure, incorrect battery capacitor, and numerous leakage problems.

In an attempt to reduce the number of recalls related to design flaws, FDA issued preproduction quality assurance (PPQA) recommendations for medical device manufacturers in September 1989.[15] Although not legally binding, the recommendations are intended to help manufacturers minimize design defects and improve the overall safety and effectiveness of medical devices. The recommendations outline the components of a PPQA program, such as design review and failure mode effects analysis, and provide numerous examples of device failures due to deficient design. The FDA found the examples in its recall records. One such example is the defibrillator battery packs that were recalled because one pack burst while being charged. The batteries were designed to be trickle charged, but the user charged the batteries with a rapid charge. The result was a rapid build-up of gas that could not be contained by the unvented batteries.

One of our cases illustrated the importance of PPQA. The balloon inflation device manufacturer had tested the device, but research and development prototypes did not exhibit the sticking problem that became apparent after the device went into mass production. Company officials suggested that the PPQA recommendations should be incorporated into the GMP regulation.

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14 FDA, Office of Compliance and Surveillance, Device Recalls: A Study of Quality Problems, HHS Publication FDA 90-4235, January 1990, p. 3.

15 The FDA also conducts scientific research to determine whether design-related problems explain specific device failures.

## ➤ MANDATORY NOTIFICATION OF RECALLS WOULD IMPROVE THE RECALL PROCESS

Although we did not ask manufacturers and district offices for their opinions on mandatory notification of recalls, two firms and three districts volunteered that mandatory notification is warranted. The manufacturers that suggested mandatory notification believe it is good practice to keep FDA informed. They stated that notifying FDA of recalls and allowing district offices to review firms' recall strategies are important and worthwhile actions. If a manufacturer does not notify FDA of a recall, FDA may later ask the firm to conduct another recall because the initial action was inadequate. The FDA also may publicize the recall months after it has taken place if firms do not notify FDA when they initiate the action.

Three district offices supported mandatory notification. One official called the current voluntary system "considerably difficult" and said that it results in many "after-the-fact" recalls. The official estimated that firms give FDA advance notice of recalls in only about 40 percent of the cases in his district. Another respondent noted: "Firms do not want publicity and may withhold information from FDA."

## ➤ SOME MANUFACTURERS ATTRIBUTE DEVICE PROBLEMS TO USER ERROR

In the kidney lithotripter, balloon dilation catheter, and insulin infusion pump cases, manufacturers attributed device problems to user error. The kidney lithotripter manufacturer attributed six deaths and four injuries to either user error or complications resulting from patients' undetected preexisting medical conditions. According to the balloon dilation catheter manufacturer, users' overrotation of the devices led to tip breakage. In the insulin infusion pump case, the manufacturer maintained that user error was responsible for a number of complaints that the company received.

The CDRH has conducted educational activities in numerous program areas to address the problem of user error. These areas include anesthesia machines, defibrillators, and glucose monitors. Recent educational activities included financing professional conferences, issuing press releases, and developing checklists and package inserts for users.

Four manufacturers said that FDA should play a more active role in user education. One respondent commented that "a significant amount of problems related to equipment is due to abuse or misuse of devices."

# RECOMMENDATIONS

## ➤ THE FDA SHOULD DEVELOP ALTERNATIVE STRATEGIES, SUCH AS CHARGING USER FEES, TO OBTAIN THE RESOURCES NECESSARY TO MEET ALL OF ITS REGULATORY REQUIREMENTS

Four districts reported difficulties conducting GMP inspections every 2 years. These inspections are a critical component of FDA's oversight of the medical device industry; officials in eight districts said that they often learn about recalls when they inspect firms. Districts also monitor compliance with the MDR regulation during GMP inspections.

The CDRH assessed the extent to which districts met the biennial GMP inspection requirement from 1981 to 1987. The agency should again assess compliance with the requirement and develop appropriate plans and strategies to provide staff and training for those districts that have the greatest problems meeting it.

The OIG recently issued a report that describes the underlying principles and implementation of user fees, which should supplement, rather than substitute for, an increased budget. User fees would provide FDA with additional resources only if they were not returned to the general treasury. The Office of Audit Services recommended that FDA implement its plans to redesign the management information system to capture information about the workload and productivity of individual reviewers of 510(k) submissions. The Public Health Service (PHS), which includes FDA, agreed in part. The PHS agreed that the 510(k) management information system should provide CDRH management with the information necessary to assess the efficiency and effectiveness of the 510(k) program. The PHS did not believe that tracking individual reviewers' performance would improve the efficiency of the 510(k) program.

## ➤ THE FDA SHOULD CLARIFY THE MDR REGULATION

Most manufacturers and some districts reported that the definitions of serious injury and malfunction are ambiguous. The FDA should clarify them, either in a revised "Question and Answer" document or a revised MDR regulation, and provide examples of reportable events.

## ➤ THE FDA SHOULD SEEK LEGISLATIVE AUTHORITY TO IMPOSE CIVIL MONETARY PENALTIES AND INITIATE RECALLS

The CDRH should evaluate the timeliness of the recall, seizure, and injunction processes and explore the feasibility of implementing less cumbersome procedures to remove violative devices from the market and enforce the Act. Options include initiating recalls and imposing civil monetary penalties.

➤ **THE FDA SHOULD FURTHER DEVELOP THE PREPRODUCTION QUALITY ASSURANCE RECOMMENDATIONS AND INCORPORATE THEM INTO THE GMP REGULATION**

Since design-related problems explain a large share of recalls, CDRH should continue to develop the PPQA recommendations and incorporate them into the GMP regulation.

➤ **THE FDA SHOULD SEEK LEGISLATIVE AUTHORITY TO REQUIRE MANUFACTURERS TO NOTIFY FDA OF RECALLS**

Under the current regulatory system for medical devices, manufacturers are not required to notify FDA of recalls. Consequently, the agency may not find out about a recall until it is completed. This delay compromises FDA's ability to review a firm's recall strategy and ensure that the recall is effective. Mandatory notification would strengthen FDA's ability to monitor firms' actions.

➤ **THE FDA SHOULD CONTINUE AND ENHANCE USER EDUCATION PROGRAMS FOR DEVICES THAT ARE SUSCEPTIBLE TO USER ERROR**

Although CDRH has conducted educational activities in numerous areas, it has not developed programs for all of the devices that warrant them. The CDRH should increase its educational efforts.

## AGENCY COMMENTS

The Public Health Service (PHS) concurred with the recommendations. The recommendations were presented by the Inspector General at hearings on the regulation of medical devices before the Subcommittee on Health and the Environment on July 17, 1990.

The Safe Medical Devices Act of 1990, signed by President Bush on November 28, 1990, enacted most of our recommendations. The Act authorizes FDA to initiate recalls and impose civil monetary penalties and requires manufacturers to report recalls to FDA. The Act also addresses weaknesses in the MDR system by requiring facilities to report serious problems with medical devices. In addition, the Act clarifies FDA's authority for preproduction design validation through the GMP process. The PHS submitted a legislative proposal for user fees, but the legislation failed to pass. The PHS will resubmit the proposal.

The FDA will clarify the MDR regulation and will continue to enhance its user education program.

The complete text of the comments is contained in appendix D.

# APPENDIX A

## LEGAL DEFINITION OF MEDICAL DEVICE

A medical device is defined as "an instrument, apparatus, implement, machine contrivance, implant, in vitro reagent or other similar or related article, including any component which is—

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

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

(3) intended to affect the structure or any function of the body of man or other animals,

and which does not achieve any of its principal intended purposes through chemical action within or on the body of man or other animals and which is not dependent upn being metabolized for the achievement of any of its principal intended purposes."[16]

16 21 U.S.C. 321.

# APPENDIX B

## METHODOLOGY

The inspection team used a case study approach and interviews with officials in both CDRH and 9 district offices and representatives of 23 device manufacturers to analyze the regulatory system for medical devices. The team selected a judgmental sample of eight devices from FDA's recall data base for 1988 and 1989. Three of the devices were the subject of Class I recalls; five were the subject of Class II recalls. According to our analysis of the data base, the breakdown of recalls for this 2-year period is as follows:

| Recall Classification | 1988 | 1989 |
|---|---|---|
| I | 6 | 7 |
| II | 173 | 163 |
| III | 107 | 72 |
| TOTAL RECALLS | 286 | 242 |

We limited our case studies to Class I and Class II recalls, because these classifications suggest a greater threat to public health and safety than Class III recalls.

For each case, we reviewed the 510(k) and PMA files, files pertaining to the recall, and MDRs. We also conducted face-to-face interviews with FDA officials in six district offices and at CDRH as well as the manufacturers whose products were the subject of case studies.

In addition to reviewing materials relevant to these case studies, the team interviewed a random sample of 15 manufacturers whose products had been the subject of recalls in 1988 or 1989. We asked the firms about their overall impressions of the regulatory process for medical devices. The team conducted the interviews by telephone during March and April 1990.

We also interviewed officials in three district offices that were not involved in the selected cases. We asked them about their relationship with device manufacturers and CDRH, their procedures, and their impressions of the regulatory process for devices.

# APPENDIX C

## GLOSSARY

| | | |
|---|---|---|
| ACRA | - | Associate Commissioner for Regulatory Affairs (FDA) |
| CDRH | - | Center for Devices and Radiological Health |
| FDA | - | Food and Drug Administration |
| GMP | - | Good Manufacturing Practices |
| IDE | - | Investigational Device Exemption |
| MDR | - | Medical Device Reporting |
| OIG | - | Office of Inspector General |
| OPE | - | Office of Planning and Evaluation (FDA) |
| PHS | - | Public Health Service |
| PMA | - | Premarket Approval |
| PPQA | - | Preproduction Quality Assurance |
| PRP | - | Problem Reporting Program |
| USP | - | United States Pharmacopeia |

# APPENDIX D

## AGENCY COMMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

# Memorandum

Date DEC 6 1990

From Assistant Secretary for Health

Subject Office of Inspector General (OIG) Draft Report "FDA Medical Device Regulation--From Premarket Review to Recall" OEI-09-90-00040

To Inspector General, OS

Attached are the PHS comments on the subject OIG draft report.

We concur with the report's recommendations to improve the medical device regulatory process and are taking actions to implement each of them.

James O. Mason

James O. Mason, M.D., Dr.P.H.

Attachment

| | |
|---|---|
| IG | ✓ |
| PDIG | ✓ |
| DIG-AS | |
| DIG-EL | ✓ |
| DIG-OI | ✓ |
| AIG-MP | |
| OGC/IG | |
| EX SEC | ✓ |
| DATE SENT | 12/10 |

RECEIVED
DEC 12 1990

COMMENTS OF THE PUBLIC HEALTH SERVICE ON THE OFFICE OF INSPECTOR GENERAL (OIG) DRAFT REPORT "FDA MEDICAL DEVICE REGULATION--FROM PREMARKET REVIEW TO RECALL" OEI-09-90-00040

OIG Recommendation

The FDA should develop alternative strategies, such as charging user fees, to obtain the resources necessary to meet all of its regulatory requirements.

PHS Comment

We concur. As noted in FDA's budget estimate justification documents for fiscal years 1991 and 1992, FDA developed a legislative proposal to provide specific statutory authority to collect fees for review of product applications. However, H.R. 3547, "New Drug and Device Application Fee Amendments of 1989," was not passed and died with the adjournment of the 101st Congress. PHS will resubmit the legislative proposal to the Office of the Secretary during this fiscal year. FDA continues to support the concept of user fees as one means of obtaining the resources necessary to carry out its regulatory programs. However, if the user fee legislation is enacted, the amount of the fees and the manner in which they are administered will be critical. Many medical device firms are small manufacturers and user fees could easily be an economic barrier to product development, thus having an adverse effect on public health.

OIG Recommendation

The FDA should clarify the medical device reporting (MDR) regulation.

PHS Comment

We concur. FDA has been active in its efforts to work with device manufacturers and educate them about MDR requirements. For example, since the MDR regulation was issued in 1984, FDA has published two question and answer documents on MDR, and has provided representatives at numerous conferences and workshops and worked with individual manufacturers to answer specific questions about the regulation. However, because of the large number and variety of device types, manufacturers, and health care situations to which MDR applies, FDA has initiated additional efforts to clarify the MDR requirements, and ensure a uniform understanding of the regulation.

Earlier this year, FDA's Center for Devices and Radiological Health (CDRH) formed an internal working group to examine the MDR regulation and the quality of the reports received, to (1) identify problems in the process, and (2) make recommendations to eliminate or reduce those problems. The

working group recently completed its examination work and CDRH is currently reviewing the resultant findings and recommendations. After CDRH completes its assessment of the working group's recommendations, FDA will take appropriate action to clarify the regulation.

OIG Recommendation

The FDA should seek legislative authority to impose civil monetary penalties and initiate recalls.

PHS Comment

We concur. We support the need for legislative authority to assess civil monetary penalties for violations of FDA's regulatory requirements for medical devices. We also support the need for the authority to initiate recalls to remove defective and unsafe products from the market. In that regard, the "Safe Medical Devices Act of 1990" (H.R. 3095) was passed by Congress in October 1990 and, if enacted, will allow for civil penalties to be assessed when a firm commits certain violations of the Food, Drug, and Cosmetic Act. Also, the new legislation will allow FDA to initiate recalls when there is a reasonable probability that a device would cause serious adverse health consequences or death.

OIG Recommendation

The FDA should further develop the preproduction quality assurance recommendations and incorporate them into the Good Manufacturing Practices (GMP) regulation.

PHS Comment

We concur. On June 15, 1990, FDA published an advance notice of proposed rulemaking in the Federal Register. In this notice, FDA proposed revising the GMP regulation for medical device (21 CFR, Part 820) to include requirements for preproduction quality assurance.

Under the proposed change to the GMP requirements, each manufacturer would be required to establish procedures that are appropriate for their device(s), taking into consideration (1) the maturity of the technology utilized and (2) the health hazard that is presented should the design be defective. FDA would then determine compliance with the requirements for preproduction quality assurance.

This proposed revision to the medical device GMPs was presented to the GMP Advisory Committee in June 1990. FDA will continue its efforts to affect this change to the existing regulation. In addition, H.R. 3095 (the new legislation mentioned above) will, if enacted, clarify FDA's statutory authority for including preproduction design validation under the GMPs.

OIG Recommendation

The FDA should seek legislative authority to require manufacturers to notify FDA of recalls.

PHS Comment

We concur. In May 1990, we forwarded a legislative proposal to the Office of the Secretary to modify the Federal Food, Drug, and Cosmetic Act and require firms to notify FDA of product recalls. This proposal was forwarded to the Office of Management and Budget in September 1990. We note that H.R. 3095, if enacted, will accomplish this goal for medical devices because it includes provisions requiring medical device firms to report device corrections and removals to FDA.

OIG Recommendation

The FDA should continue and enhance user education programs for devices that are susceptible to user error.

PHS Comment

We concur. We believe that educating device users is an important part of FDA's efforts to assure the safety and effectiveness of medical devices. Accordingly, FDA will continue to conduct educational activities and enhance such activities in the device area to the extent resources permit.