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Report to the Chairman, Subcommittee on Health and the Environment, Committee on Energy and Commerce, House of Representatives

February 1989

MEDICAL DEVICES

FDA's Implementation of the Medical Device Reporting Regulation

GAO/PEMD-89-10

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GAO

United States
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Program Evaluation and
Methodology Division

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February 17, 1989

The Honorable Henry Waxman
Chairman, Subcommittee on Health
and the Environment
Committee on Energy and Commerce
House of Representatives

Dear Mr. Chairman:

In response to your letter of February 25, 1987, we are submitting this report on FDA's implementation of the medical device reporting regulation.

As agreed with your office, unless you publicly announce the contents of this report earlier, we plan no further distribution of it until 30 days from the date of the report. We will then send copies to interested congressional committees and the Department of Health and Human Services, and we will make copies available to others upon request.

This report was prepared under the direction of Michael J. Wargo, Associate Director. Other major contributors to this report are listed in appendix IV.

Sincerely yours,

Eleanor Chelimsky
Assistant Comptroller General

Executive Summary

Purpose

The ability of the Food and Drug Administration (FDA) to protect the public health has been severely limited by its lack of information on problems associated with medical devices. A previous GAO report (GAO/PEMD-87-1) found that less than 1 percent of device problems occurring in hospitals were being reported to FDA. However, FDA anticipated that its recently implemented medical device reporting regulation (MDR) would alleviate this and other shortcomings of the agency's postmarketing surveillance system. The House Subcommittee on Health and Environment of the Committee on Energy and Commerce asked GAO to examine and describe FDA's implementation of the MDR regulation. With the concurrence of the Subcommittee staff, GAO pursued four study objectives: (1) to determine the level of information generated by the MDR regulation, (2) to describe and assess the principal organizational structures and procedures of FDA's processing system for reports filed under the MDR regulation, (3) to evaluate FDA's analysis and use of the MDR data, and (4) to review FDA's efforts to assess the degree to which medical device firms are in compliance with the MDR requirements.

Background

FDA uses two overlapping systems as its principal means of ensuring the safety and effectiveness of medical devices. The first, premarketing review, is a system of checks, reviews, and controls that are intended to be applied before new devices are made available to the public. The second, postmarketing surveillance, is a monitoring system designed to provide an "early warning" of device problems after devices are in general use. The MDR regulation, implemented on December 13, 1984, requires manufacturers and importers of medical devices to report to FDA whenever they become aware that a device has been associated with the serious injury or death of a patient or that the device has malfunctioned in such a way that a recurrence of the malfunction might result in a serious injury or death. FDA established a system to process the device-problem reports that are required under the MDR regulation and procedures to monitor compliance with the provisions of the regulation.

Results in Brief

The amount of information received by FDA about problems associated with medical devices has increased more than seven-fold since the implementation of the MDR regulation. However, the system of organizational structures and procedures that FDA uses to process and analyze MDR reports was "grafted" onto the one that was designed for the voluntary problem-reporting that existed before MDR. The resulting system is not adequate to handle the volume of reports currently received, and

therefore the potential effectiveness of the MDR regulation has not been fully realized.

GAO found that the information in the MDR data base was generally accurate. However, major delays were experienced in getting critical information into the system and analyzing submitted problem reports. Additionally, using conservative estimates, GAO found that only a small proportion of the potential reporting firms have filed MDR reports during any of the first three years of the systems's operation. At most, only a quarter of those expected by FDA to report have in fact reported during any year. One-third of the establishments inspected for MDR compliance were not aware of the existence of the MDR regulation. GAO also found evidence that some medical device firms may be overreporting, while others are either not reporting at all or are underreporting.

Principal Findings

Information Flow

Prior to the implementation of the MDR regulation, FDA received approximately 2,500 problem reports annually through the voluntary problem-reporting program. During the first three calendar years after MDR implementation, FDA received approximately 18,000 problem reports annually, and there was a significant increase in the proportion of device problems associated with the death or serious injuries of patients. MDR problem reports were concentrated in a small number of medical specialties and on a few specific devices. Ten medical devices accounted for about 63 percent of all problems reported between 1985 and 1987. Cardiovascular devices accounted for 50 percent of all problem reports.

Organizational Structure and Procedures

GAO found that the operation of the MDR report-processing system was handicapped by a lack of procedural guidelines for the report analysts, by a shortage of automated data processing skills among the analysts, and by an unnecessarily complicated workflow pattern for the processing of MDR reports. In addition, the system was limited in its capacity to identify trends and anomalies associated with the occurrence of device problems. There was a resultant backlog in processing MDR reports, including more than 10,000 malfunction reports for which some portion of the FDA analysis was not complete.

Analysis and Use of MDR Data

MDR report analysis is intended to include causal evaluations and final dispositions at the time a report is closed. However, GAO found that approximately one-third of the MDR reports received between 1985 and 1987 had not been closed with one of the standard report dispositions and that 62 percent of the closed problem reports were closed as "historical reference," to be used as baseline data and background information in future analysis. The cause of device problems was tentatively identified in half the reports evaluated, and in 77 percent of these reports the device itself was found to be the cause.

The MDR data base documents few uses of the MDR data for purposes other than to record and track individual device problems. GAO found so few instances of the use of the more stringent regulatory options for dealing with device problems—such as regulatory letters or product seizures—that it was not possible to determine whether there was a relationship between the severity of problems reported and the type of action taken by FDA. (FDA has recently developed a number of case histories in which MDR reports were associated with corrective actions such as device redesign, relabeling, recall, or safety alerts.)

Coverage and Compliance

GAO found that problem reporting is concentrated in a few medical device firms. In 1987, the 12 most frequent reporters accounted for nearly 60 percent of all reports, and the composition of this group of 12 has changed only slightly over the last 3 years. These firms are manufacturers and importers of implanted devices, life-support devices, or anesthesia equipment.

FDA's program of inspections to assess whether device firms comply with MDR indicated that a third of the establishments inspected were not aware of the MDR rule. Thirty-seven percent indicated that they had received no problem reports about the medical device they manufactured or imported. Because FDA selected the establishments for inspection using a judgmental rather than a random sampling scheme, these results cannot be validly generalized to the population of all device manufacturers and importers.

Recommendations

GAO recommends that the Secretary of the Department of Health and Human Services (HHS) direct the Commissioner of the Food and Drug Administration to (1) modify the medical devices reporting regulation to require all firms that manufacture or import medical devices to submit

an annual statement indicating either that they filed no MDR reports during the calendar year because they did not receive or otherwise become aware of information concerning MDR-reportable events, or that they filed a specific number of reports on each type of reportable event and that the firm received or became aware of information concerning only these events; (2) establish a program of compliance inspections that would permit generalization of the inspection results to the universe of device manufacturers and importers (that is, select establishments for inspection on a sound statistical basis); and (3) fully document the use of MDR data in taking corrective actions on device problems, especially by ensuring that such actions are recorded in the MDR data base.

Agency Comments

HHS found GAO's draft report to be a fair and generally factual account of the MDR program. HHS concurred with our recommendation to improve documentation of the use of MDR data and described FDA initiatives addressing this and other issues raised by our findings.

HHS did not concur with our recommendation that the agency require device manufacturers to submit an annual statement affirming that the number of reports submitted covered all reportable events of which the company learned during the preceding year. The agency felt that such a requirement would be unduly burdensome for both manufacturers and the agency and would provide no additional public health benefit. HHS also did not feel that it was necessary to sample establishments for MDR compliance inspections in such a way that the results of inspections on the sample might be validly generalized to the population of manufacturers, because current plans will result in the inspection of all class II and III firms at least once every 4 years.

GAO believes that the submission of a single annual letter—which for the majority of firms would assert that they had nothing to report—would not constitute an undue burden and could be processed as part of the annual re-registration of establishments. Such a letter would ensure that all manufacturers and importers are aware of their obligation under MDR to provide early warning of any problems occurring with devices thought to be innocuous. Further, FDA's preferred judgmental selection procedure means that statistics produced before the completion of the census cannot be legitimately generalized to the population of device firms, and that many of the early inspection results may be out of date by the time the census is complete. GAO therefore continues to believe that its recommended action is warranted.

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Figures

Abbreviations

DEN	Device experience network
ECRI	Emergency Care Research Institute
EIR	Establishment inspection report
FDA	Food and Drug Administration
FD&C	Federal Food, Drug, and Cosmetic Act
FTE	Full-time equivalent
GAO	General Accounting Office
GMP	Good manufacturing practices
GQAP	Government quality assurance program
HCFA	Health Care Financing Administration
IUD	Intrauterine device
I.V.	Intravascular
MDR	Medical device reporting (regulation)
NAF	Notice of adverse findings
NEISS	National electronic injury surveillance system
OMB	Office of Management and Budget
PMA	Premarket approval application
PMS	Postmarketing surveillance
PRP	Problem-reporting program
SAS	Statistical analysis system
USP	U. S. Pharmacopeia

Introduction

Background

Medical devices include almost everything health-care professionals use to diagnose, treat, or prevent illness, improve human functioning, and support and sustain life.[1] More than 1,800 different types of medical devices are available in the United States today. They represent an industry of more than $14 billion a year. The Food and Drug Administration (FDA) is authorized to regulate medical devices during all phases of their development, testing, production, distribution, and use.

FDA formed the Center for Devices and Radiological Health in 1982 to centralize the implementation of the Medical Device Amendments of 1976 and the development of programs intended to ensure that unsafe and ineffective medical devices are not sold in the United States.[2] The Center has ten offices: management services, information systems, training and assistance, device evaluation, science and technology, compliance, health affairs, health physics, standards and regulations, and the office of the director. (The complete organization chart of the Center is in appendix I.) The office of compliance has the primary responsibility for the implementation of, and monitoring compliance with, the medical devices reporting (MDR) regulation; it investigates reported problems and recalls, monitors labels and advertising, and maintains a data bank on all devices marketed in the United States.

FDA uses two overlapping systems as its principal means of ensuring the safety and effectiveness of medical devices: premarketing review and approval and postmarketing surveillance (PMS). The premarketing review and approval processes are a system of checks, reviews, and controls that were intended to be applied before new devices are made available to the public.[3] PMS is a monitoring system designed to provide an "early warning" of problems associated with devices after they are

[1]Section 201(h) of the Federal Food, Drug, and Cosmetic (FD&C) Act of 1938, as amended by the Medical Device Amendments of 1976, defines "device" as an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is (1) recognized in the official National Formulary, or the U.S. Pharmacopeia (USP) 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 humans or other animals, or (3) intended to affect the structure or any function of the human body or bodies of other animals, and that does not achieve any of its principal intended purposes through chemical action within or on the body and does not depend upon being metabolized in order to achieve any of its principal intended purposes. The effect of the amendment was to enlarge the 1938 definition of "device" to include (1) devices intended for use in the diagnosis of conditions other than disease, such as pregnancy, (2) in vitro diagnostic products, and (3) specific products previously regulated as new drugs, including soft contact lenses, bone cement, and sutures.

[2]The Center for Devices and Radiological Health will hereafter be referred to as "the Center."

[3]See Medical Devices: FDA's 510(k) Operations Could Be Improved (GAO/PEMD-88-14, August 1988).

in general use. It is intended to promote the flow of information on problems experienced with a device back to FDA, so that the agency can act to reduce safety risks.[1]

The focus of the present study is a recently implemented component of the PMS system, the medical devices reporting regulation (MDR). Since 1973, there have been nine studies of FDA's PMS system, and five contracts to state health agencies have attempted to increase health-care professionals' knowledge and use of the problem reporting program. There are also two recent studies that focus on PMS, this one and one contracted by FDA that was still under way at the close of our review. Although the problems identified in each of the previous nine studies differed, a common thread united them all: their finding that FDA lacked a systematic approach to the identification, collection, and evaluation of adverse experience data related to medical devices. (The complete list of prior studies is contained in the "References" section at the end of this report.)

FDA's Sources of Postmarketing Surveillance Data

Prior to December 1984, FDA relied on two principal sources for PMS data: inspections used to check on compliance with good manufacturing practices, and the information contained in the device experience network (DEN). Section 520(f) of the FD&C Act, added by the 1976 amendments, authorizes FDA to promulgate regulations that specify good manufacturing practices for devices, which may include provisions for processing, packaging, labeling, manufacturing equipment, and record-keeping. Information on good manufacturing practices is used primarily for compliance purposes. FDA's policy is to inspect manufacturing facilities and operations of firms manufacturing class II and III devices every 2 years.[2] FDA also inspects manufacturers' records, particularly complaint and service files.

DEN is a centralized, automated data processing system for the collection, processing, and evaluation of device problem reports. It includes reports from the problem-reporting program (PRP); the medical device reporting regulation (MDR); government quality assurance programs (GQAP), such as those for devices used in the Veterans Administration and Department of Defense hospitals; and the national electronic injury surveillance system (NEISS), as well as radiological-testing reports and

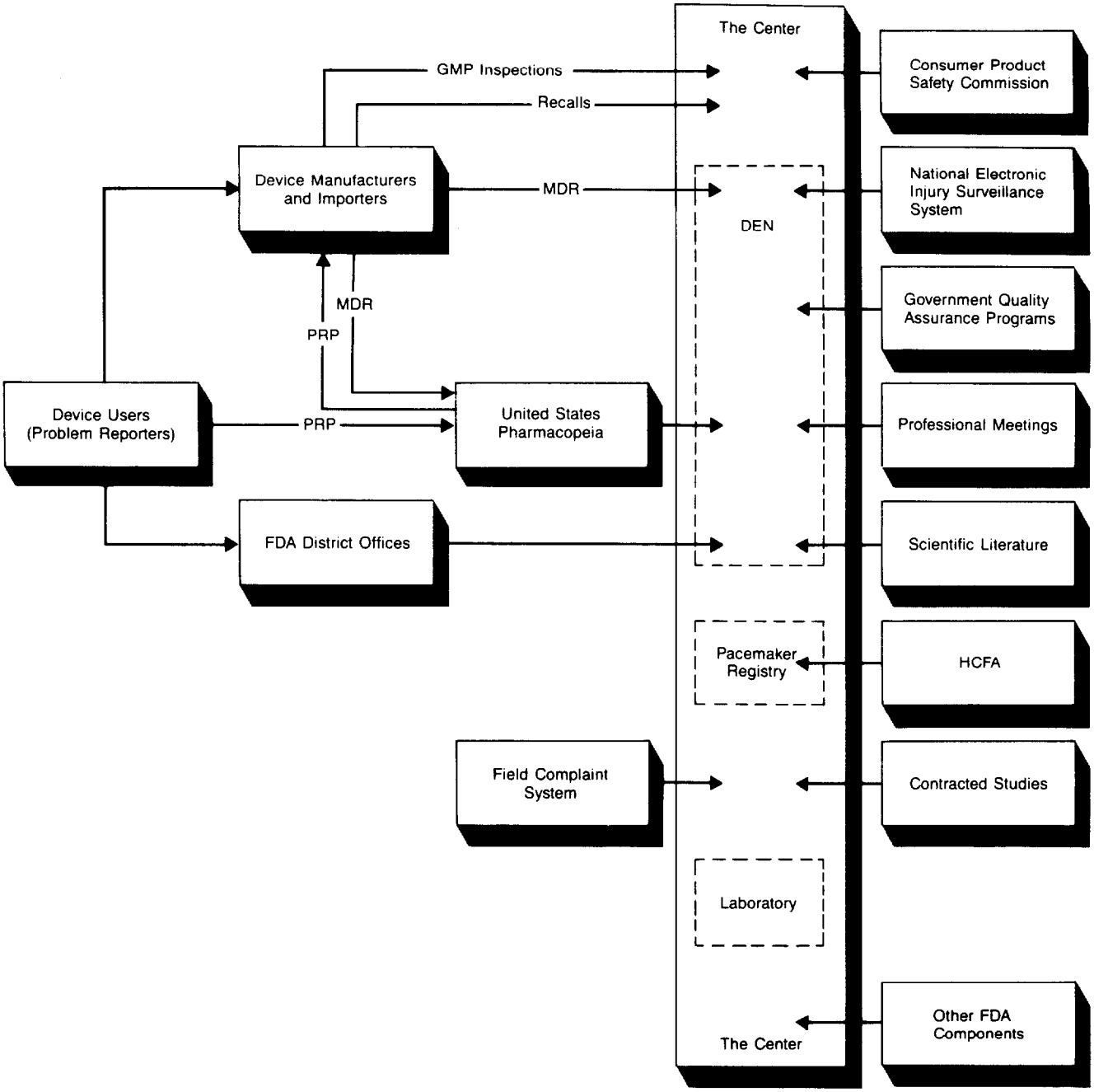
[1]See Medical Devices: Early Warning of Problems Is Hampered by Severe Underreporting (GAO/PEMD-87-1, December 1986).

[2]The three classes of medical devices are defined in the Glossary.

staff-generated reports based on articles, conferences, and other sources.

PRP is the voluntary, spontaneous reporting system currently being operated by FDA. The U.S. Pharmacopeia (USP) receives the device-problem reports—primarily from health-care professionals, through their professional associations, and from hospitals—and enters them into DEN. According to 1983 testimony by FDA officials and our own 1986 report, the program and network suffered from serious problems, especially underreporting and the use of data for little more than compliance purposes. The Center also obtains some data used in postmarketing surveillance from contracted studies, other FDA components, and the Consumer Product Safety Commission. Figure 1.1 shows the sources of PMS information.

Figure 1.1: Sources of the Center's Postmarketing Surveillance Information[a]



DEN = device experience network; GMP = good manufacturing practices; HCFA = Health Care Financing Administration; MDR = medical device reporting (regulation); PRP = problem-reporting program.

The Medical Device Reporting Regulation

The history of the MDR regulation indicates that FDA had long recognized the importance of obtaining data on the safety and effectiveness of medical devices that were in the public domain. A mandatory device experience reporting rule was first proposed by FDA on November 18, 1980. After an interval of more than a year (during which time the agency received more than 200 comments), the proposed rule was put in abeyance. The reasons FDA cited were (1) the need for further review and evaluation of the comments received, (2) OMB's advice that the proposed rule be reviewed in light of Executive Order 12291 on regulatory relief, and (3) the need to complete and analyze a study of manufacturers' complaint files to determine whether FDA inspection of these files could substitute for all or part of the proposed MDR reporting requirements. On May 27, 1983, the rule was reproposed, and a final version of the rule was published in the Federal Register on September 14, 1984. The reporting requirements of the rule in its final form were somewhat narrower in scope than those of the original proposal, but in the interim FDA had concluded that review of manufacturers' complaint files could not substitute for a reporting rule. The MDR regulation became effective on December 13, 1984.[6]

The regulation requires that a report be submitted to FDA whenever a manufacturer or an importer of a medical device becomes aware of information that reasonably suggests that its device may have caused or contributed to serious injury or death, or has malfunctioned and, if the malfunction recurs, is likely to cause or contribute to death or serious injury.[7] A manufacturer or importer may become aware of such information (1) from individuals or institutions (for example, physicians, nurses, patients, consumers, and hospitals); (2) from the medical or scientific literature; or (3) through its own research, testing, evaluation, servicing, or maintenance of its devices. MDR reports thus supplement the voluntary reports made directly to FDA under the problem-reporting

[6]A summary of issues raised in comments on the proposals is contained in the preamble to the final MDR rule, Federal Register, 49:180 (September 14, 1984), 36326-51. Comment on the persistence of some of these issues, such as problems in interpreting definitions of terms used in the rule, is contained in E. Basile, "Medical Device Reporting: the Good, the Bad, and the Ugly," Food and Drug Cosmetic Law Journal, 42 (1987), 83-100.

[7]A serious injury is defined as an injury that is (1) life threatening, (2) results in permanent impairment of a body function or permanent damage to body structure, or (3) necessitates medical or surgical intervention by a health care professional to (a) preclude permanent impairment of a bodily function or permanent damage to bodily structure or (b) relieve unanticipated temporary impairment of a bodily function or bodily structure. A malfunction is defined as the failure of a device to meet any of its performance specifications or otherwise to perform as intended. Performance specifications include all claims made in the labeling for the device.

program (PRP), by requiring that device problems reported to manufacturers be transmitted to FDA.

MDR reports were not intended to be limited to events in which there was a confirmed causal connection between a device and an adverse experience, but rather include many events in which there was an association between a device and the death or serious injury of a patient. For example, defibrillation is successful in only a small percentage of patients who experience ventricular fibrillation, even when the defibrillator works properly. However, when a defibrillator malfunctions and the patient is not resuscitated, the manufacturer is obliged to report the incident in an MDR "death report," even though there is a high probability that the patient would have died even if the defibrillator had functioned properly. If a second defibrillator is on hand when the first one fails, however (as is often the case in emergency rooms), and the patient is successfully resuscitated, the same failure of the first defibrillator is reportable as a "malfunction." Similarly, the "serious injury" category is defined in such a way as to require a report whenever surgery is necessary to remove an implanted device before the end of its anticipated life (for example, the explant of a pacemaker whose battery is failing prematurely), even though the surgery may be routine and without complications.

In cases where a device is associated with a death or a serious injury, an "initial" report is submitted to FDA by telephone as soon as possible, but no later than 5 calendar days after initial receipt of information, and by written "follow-up" report within 15 working days of initial receipt of the information. A telephone report must be followed by a written report.

In the case of a malfunction likely to cause or contribute to a death or serious injury if it recurs, a report is to be submitted to FDA in writing as soon as the necessary information for making a report is obtained, but no later than 15 working days after initial receipt of the information. A telephone report is not required. Malfunction reports are not required when (1) a death or serious injury has not occurred and (2) the device's labeling sets forth information concerning the potential for serious injury or death in case of malfunction (and the malfunction is occurring at or below the frequency and severity stated in the labeling).

Objectives, Scope, and Methodology

Objectives

On February 25, 1987, the chairman of the Subcommittee on Health and Environment of the House Committee on Energy and Commerce asked us to examine the implementation of the MDR regulation. In discussions with the Subcommittee, we agreed on four objectives, and we formulated evaluation questions for each of them.

Our first objective was to determine the information flow that has been generated as a result of the implementation of the MDR regulation. To meet this objective, we established the following evaluation questions:

1. What is the level of medical device problem reporting under the medical devices reporting regulation?

2. What are the characteristics of the problem reports that are transmitted to FDA?

We wanted to determine how much information was being generated by the regulation, the distribution of those reports according to severity, and whether that information was substantively different from that currently being obtained through PRP.

Our second objective was to provide a descriptive analysis of the structures and procedures FDA has established to collect and analyze the information required by the MDR regulation. To meet this objective, we established the following evaluation questions:

1. What are the principal organizational structures and procedures of the MDR report processing system?

2. What mechanisms are used to insure the accuracy of the MDR data base?

3. Are there major systemic problems associated with the MDR system that affect its function as a postmarketing surveillance (PMS) tool?

A critical component for the implementation of the MDR regulation is the capacity to efficiently process medical device problem information.

Therefore, we wanted to review the day-to-day operation of the MDR report processing system and the accuracy of the data it contained, and the general adequacy of the MDR report processing system as a PMS tool.

Our third objective was to describe how FDA uses the information obtained through the MDR regulation. To this end, we established the following evaluation questions:

1. What are the nature and scope of FDA's analysis and evaluation of MDR problem reports?

2. What are the types and distributions of regulatory actions FDA has taken based on the MDR problem reports?

3. What other uses has FDA made of the MDR data base?

Assuming that information of sufficient quantity and accuracy does actually reach the persons who can respond to problems associated with the use of medical devices, we intended to describe and assess the actions that FDA has taken.

Our fourth objective was to describe the scope of coverage and the degree to which medical device firms are in compliance with the MDR regulation.[8] We thus established the following evaluation questions:

1. What proportion of device firms have submitted problem reports as required by the provisions of the MDR regulation?

2. What efforts has FDA made to ensure the device firms' compliance with the reporting provisions of the MDR regulation?

We wanted to determine what proportion of device firms had submitted MDR reports as compared to the proportion that could be expected to submit reports (based on such factors as the total number of existing firms and the nature of their products), and what efforts FDA is making to ensure an acceptable level of compliance.

The general purpose of the MDR system is to expand FDA's postmarketing surveillance capabilities. Therefore, we wanted to identify any system-wide problems that could reduce the effectiveness of the MDR report

[8]As employed throughout this report, the term "firm" refers to any organization that manufactures or imports medical devices and thus is subject to the provisions of the MDR regulation.

processing system as a PMS tool. Toward this end, we conducted a review of the adequacy and usefulness of the MDR system's automated data processing component and the degree of integration of the MDR system with FDA's other PMS resources and activities.

Scope

Our fieldwork was conducted from October 1987 through June 1988. The focus of the review is the implementation of the MDR regulation during its first 3 full calendar years of operation, 1985 through 1987. We traced the internal flow of problem reports that FDA received from medical device firms and its responses to those reports.

In our earlier study of the flow of information concerning problems associated with medical devices, we found a substantial discrepancy between the characteristics and number of device problem occurrences within hospitals and those which were reported to device firms. For example, the problems that were the most likely to be reported by hospitals were manufacturer-related rather than user-related, as well as those in which the device was under warranty, service contract, or exchange agreement. Only 46 percent of the problems that occurred in hospitals were reported to device manufacturers and distributors, and a greater percentage of reports were made when an injury did not occur than when one did. We concluded that FDA's "early warning" about device problems was hampered by severe underreporting in each link of the communication network and that solutions to rectify these weaknesses should consider the network as a whole rather than trying to repair or strengthen a single link within it.

It is important to note that the MDR regulation essentially addresses one link in the network—that from device firms to FDA. It is not the intent of the regulation to address the other major links in the network: from hospitals to firms, hospitals to independent distributors, independent distributors to firms, and hospitals to FDA. For example, hospitals and independent distributors were encouraged to report device problems through the voluntary problem-reporting program, which existed before the MDR regulation was published and has continued to function since its implementation. In view of these facts, the MDR data base is unlikely to be representative of the total number or type of device problem occurrences.

Accordingly, this study does not attempt to assess possible changes in the flow of information among these other links.[1] Nor does this study attempt to determine how representative the MDR problem reports are of the universe of device problems or to evaluate the "early warning" potential of the MDR regulation problem-reporting requirements. Each of these assessments would require at minimum data from the point of origin of the device problems. Specifically, to address the question of the representativeness of the MDR reports would require a comparison of problems occurring in a representative sample of the principal users of devices—hospitals and other health-care professionals—with those contained in the MDR data base. And, to ensure that the system achieves the "early warning" goal (as opposed to the ability to track established trends), it would be necessary to include virtually all hospitals in a mandatory problem-reporting program, in order to be certain of being informed of all low-frequency but critical events occurring throughout the full range of settings, users, and device types. The result would amount to a continuous nationwide census of device problems in hospitals and other health care facilities.

Methodology

Our various objectives required different kinds of information from many sources. To understand the congressional intent and the historical background of the MDR regulation, we reviewed the legislative history, prior studies of the implementation of the regulation, and other published articles related to mandatory adverse experience reporting. We also obtained an official chart of the MDR workflow process and used this information as the basis for structured interviews focused on the day-to-day operation of the system. We interviewed FDA officials, program managers, and staff in order to clarify, supplement, and confirm the documentary evidence.

FDA provided a computer tape containing the MDR data base for January 1985 through December 1987. We used this tape to review the accuracy and completeness of the MDR data base, to tabulate the total numbers, to analyze the patterns and characteristics, and to evaluate FDA's actions in response to the medical device problem reports. We did not evaluate the internal controls of the computer system that produced the data tape.

[1]However, according to a recent internal FDA review of its device postmarketing surveillance system, it is reasonable to assume that the same disincentives to reporting by health-care professionals (of, for example, user-related problems) identified in our earlier study would continue to exist under the MDR regulation.

We reviewed MDR program documents, internal studies, and contractor reports to assess FDA's efforts to educate and ensure device manufacturers' and importers' compliance with the MDR regulation. Our discussion of the system is based on interviews with the developers, managers, problem-report analysts,[10] and other users of the MDR system within the Center; internal studies; and interim reports of a contracted comprehensive study of FDA's postmarketing surveillance (PMS) resources.[11]

The nature of the data we collected required both qualitative and quantitative analysis. We systematically reviewed the documents describing the implementation and operation of the MDR system and conducted structured interviews to clarify, confirm, and supplement what we found. We used the procedures available in the statistical analysis system (SAS) software package for analysis of the MDR data tape. Our analysis includes frequency counts of the relevant variables, crosstabulations of variables that respond to the evaluation questions, and associated statistical tests.

The final content of the report benefited from the reviews and comments provided by a panel of experts. The panel was representative of a broad cross-section of expertise in the medical device field. (The complete list of members of our review panel is in appendix II.)

Our review was conducted in accordance with generally accepted government auditing standards.

Report Organization

The remainder of the report is organized in chapters that coincide with our four objectives. Chapter 2 describes the flow of problem reports from medical device firms to FDA; chapter 3 describes the structure and procedures that constitute the MDR system and discusses the MDR system as a PMS tool; chapter 4 describes the uses that FDA has made of the MDR data; chapter 5 reviews FDA efforts to assess and ensure medical device firms' compliance with the MDR reporting requirements; and chapter 6 contains our conclusions and recommendations, followed by agency comments and our responses.

[10]Throughout this report, we refer to the FDA staff in the Product Monitoring Branch who are responsible for processing and analyzing MDR problem reports as "analysts." While 5 of the 13 analysts active in reviewing MDR reports are "consumer safety officers," 7 are "nurse consultants," and one is a "biomedical engineer." As a group, officials and staff at the Center refer to them as MDR or device-problem "analysts" or "reviewers."

[11]See Planning Research Corp., Needs Assessment Recommendations Report (McLean, Va.: May 31, 1988).

Information Flow

A critical component of the postmarketing surveillance of medical devices is the availability of performance information that can serve as an early warning of potential device problems. The purpose of this chapter is to describe the flow of information that has resulted from the implementation of the reporting requirements under the MDR regulation—that is, the level of problem reporting, characteristics of those reported problems, and the difference between the MDR data and that being submitted under the problem-reporting program (PRP).

Level of Problem Reporting

During the 3-year study period, a total of 52,863 problem reports, or an average of 17,621 reports per year (associated with the use of 1,059 medical devices), were received by FDA under the MDR regulation.[1] (See table 2.1.) Given the number of reports that were submitted during the first 4 months of 1988, FDA projects an approximate total of 15,000 reports for 1988. This represents a surge in problem reporting in the two years immediately after the MDR regulation was implemented, followed by a decline in the third year, and an estimated further decline in 1988.

Table 2.1: Overall MDR Reporting Rates by Type of Report, 1985-1987

	1985		1986		1987		All 3 years	
Type of report	No. of reports	Percent	No. of reports	Percent	No. of reports	Percent	No. of reports	Percent
Death	561	3%	513	3%	480	3%	1,554	3%
Serious injury	9,044	50	11,057	61	9,075	54	29,176	55
Malfunction	8,349	47	6,685	37	7,099	43	22,133	42
Total	**17,954**	**100**	**18,255**	**100[a]**	**16,654**	**100**	**52,863**	**100**

[a]Percentages do not total 100 because of rounding.

Source: MDR data tape provided by FDA

The most frequently reported type of device problem involved an injury to a patient that may have been caused or contributed to by a device. During this time period, 29,176, or 55 percent of all reports, were of this type. Medical device malfunctions accounted for 22,133, or 42 percent of all problem reports. Of the 52,863 problems reported, 1,554, or 3 percent, were associated with the death of a patient. The number of reports on each type of problem fluctuated over the time period. There was,

[1]The data tape we received from FDA contained some reports with missing or erroneous codes for "date received" that prevented us from including them in our analysis. There were 52,946 MDR reports in the data base with a date received between January 1, 1985, and December 31, 1987. Five of these, however, were missing a "report type," and 78 had been labeled as report type "Other," which was not one of the three categories of reportable events required under the MDR regulation.

however, a net decrease of 1,300 reports, or 7 percent, during the period 1985-1987.

Concentration of Problem Reporting

Problem reports were concentrated in a relatively small number of medical practice specialties, and within those specialties a few specific devices accounted for the majority of reports.[2] Overall, 10 medical devices accounted for about 63 percent of all problems reported during the 3-year study period.[3] The remaining 37 percent, or 19,805 reports, were associated with 1,049 separate devices. (See table 2.2.)

Table 2.2: The Ten Most Frequently Reported Devices, 1985-1987

Device name	No. of reports	Percent
Pacemaker	14,243	27%
Pacemaker electrode	5,304	10
Ventilator	4,115	8
Glucose monitor[a]	1,886	4
Anesthesia machine	1,807	3
Heart valve	1,390	3
Breast prosthesis, inflatable	1,356	3
Infusion pump	1,349	3
Intravascular administration set	972	2
Breast prosthesis, silicone	636	1
Top ten devices	33,058	63[b]
All other devices	19,805	37
Total: all devices	**52,863**	**100**

[a]Includes reports on glucose hexokinase, an in vitro diagnostic reagent used in blood glucose monitoring devices.

[b]Percentages do not add to 63% because of rounding.

Source: MDR data tape provided by FDA

Cardiovascular devices—including cardiac pacemakers, pacemaker electrodes, and artificial heart valves—accounted for nearly 50 percent of

[2]There are 19 medical specialties, as follows: anesthesiology; cardiovascular; dental; ear, nose, and throat; gastroenterology and urology; general and plastic surgery; general hospital; neurology; obstetrics and gynecology; ophthalmic; orthopedics; physical medicine; radiology; chemistry; hematology; immunology; microbiology; pathology; and toxicology.

[3]It is important to note that the lists of "top ten" devices in this chapter are based on the number of MDR reports submitted in a given time period, and that the ranking does not take account of the number of each type of device sold. The devices with the largest numbers of reports are not necessarily those associated with the greatest rate of problem occurrence, on a per-product basis. The number of implanted cardiac pacemakers, for example, is many times the number of anesthesia machines in place in hospitals, so the larger number of pacemaker MDR reports does not necessarily mean that pacemakers are more problem-prone devices than anesthesia machines.

all problem reports. Pacemakers accounted for 27 percent, nearly three times the number of reports related to any other single device. Anesthesiology devices, including ventilators and anesthesia gas machines, accounted for 15 percent of all problem reports. No other single device or group of related devices accounted for more than 7 percent of all problem reports submitted to FDA between 1985 and 1987.

Characteristics of Problems Reported

The concentration of problem reports on a relatively small number of medical devices and medical specialties was repeated in the distribution of problem types. Between 1985 and 1987, there were 1,554 patient deaths reported as having been associated with a medical device. Ten devices accounted for 936 death reports, or 60 percent of all reports related to the death of patients.

Cardiovascular device problem reports accounted for 708 death reports, or 46 percent of all problem reports associated with patients' deaths over the 3-year period. Heart valves and defibrillators, ranked one and two, had nearly the same number of reports over the 3-year period and together accounted for 31 percent of all death reports in the MDR data base. Each had roughly three times the number of reports of the next most often reported device, the ventilator. (See table 2.3.)

Table 2.3: The Ten Devices Most Frequently Reported as Associated With the Death of Patients, 1985-1987

Device	No. of Reports	Percent
Heart valve	244	16%
Defibrillator	240	15
Pacemaker	90	6
Ventilator	88	6
Pacemaker electrode	60	4
Anesthesia machine	53	3
Intravascular diagnostic catheter	50	3
Infusion pump	47	3
Tampon	40	3
Intra-aortic balloon	24	2
Top ten devices	936	60[a]
All other devices	618	40
Total: all devices	**1,554**	**100**

[a]Percentages do not add to 60% because of rounding.

Source: MDR data tape provided by FDA

Ventilators and anesthesia gas machines, both of which are used in anesthesiology, accounted for 141 deaths, or 9 percent of all death

reports received by FDA from 1985 through 1987. No other single device or group of related devices accounted for more than 3 percent of device problems that involved a patient's death.

As has been the pattern for all reports, reports of death were concentrated on only a few devices. Ten devices accounted for 60 percent of all reports of death. Six of the 10 were cardiovascular devices, and these accounted for about 46 percent of all death reports. Overall, reports of death decreased slightly.

Patient injury was associated with 29,176 problem reports, or 55 percent of all reports in the MDR data base. Ten devices accounted for 73 percent of all reports of injuries. (See table 2.4.)

Table 2.4: The Ten Devices Most Frequently Reported as Associated With Injuries to Patients, 1985-1987

Device name	No. of reports	Percent
Pacemaker	11,985	41[a]
Pacemaker electrode	4,431	15
Ventilator	1,267	4
Heart valve	1,038	4
Breast prosthesis, silicone	601	2
Tampon	513	2
Intraocular lens	421	1
Contact lens	392	1
Intrauterine device	341	1
Infusion pump	322	1
Top ten devices	21,311	73
All other devices	7,865	27
Total: all devices	**29,176**	**100**

[a]Percentages do not total 73 because of rounding.
Source: MDR data tape provided by FDA

Cardiovascular device problems accounted for 17,454 reports, or nearly 60 percent of all reports of injuries. Patient injury was more often associated with problems involving pacemakers (41 percent) than any other single device. There were 11,985 pacemaker reports over the 3-year period. Pacemaker electrodes accounted for 4,431 reports, or 15 percent, and heart valves for 1,038, or 4 percent of all injury reports. No other single device accounted for more than 4 percent of the injuries reported to FDA.

Reports of device problems associated with injury exhibited a pattern similar to reports involving death. Injury reports were dominated by a

few devices. However, the degree of concentration was greater for injury reports than for reports of deaths.

There were 22,133 reports, or 42 percent of all reports in the MDR data base, that related to malfunctions. Similar to reporting patterns for devices associated with deaths and injuries, reports about malfunctions were concentrated on a small number of devices. Anesthesia devices—including ventilators, anesthesia gas machines, and respiratory gas humidifiers—accounted for 27 percent of all malfunction reports. Cardiovascular devices—including pacemakers, pacemaker electrodes, and intra-aortic balloons—accounted for 3,458 reports, or 13 percent of all malfunction reports. (See table 2.5.)

Table 2.5: The Ten Devices Most Frequently Reported as Malfunctioning

Device name	No. of reports	Percent
Ventilator	3,972	18%
Pacemaker	2,136	10
Anesthesia machine	1,693	8
Glucose monitor	1,672	8
Infusion pump	980	4
Intravascular administration set	811	4
Pacemaker electrode	805	4
Intra-aortic balloon	517	2
Respiratory gas humidifier	365	2
Peritoneal dialysis administration set, disposable	348	2
Top ten devices	13,299	60[a]
All other devices	8,834	40
Total: all devices	**22,133**	**100**

[a]Percentages do not add to 60 because of rounding.
Source: MDR data tape provided by FDA

The 10 most frequently reported devices accounted for 13,299 reports, or 60 percent of all reports of malfunctions, and the top 4 devices accounted for 9,473, or 43 percent of malfunction reports. Ventilators were the most frequently reported single device in the malfunction category of report. Nearly 1 of every 5 malfunction reports was about ventilators; they accounted for 3,972 reports, or 18 percent of all malfunction reports.

Pacemakers were the devices with the second largest number of malfunction reports with 2,136, or 10 percent of the reports in the data base. Anesthesia machines, with 1,693 malfunction reports, accounted for 8 percent of such reports. Glucose monitors generated the fourth

largest number of malfunction reports with 1,672, or 8 percent of all malfunction reports in the period covered by this analysis. No other single device accounted for more than 4 percent of all malfunction reports.

The net decrease in the number of malfunction reports was more pronounced than the changes recorded for injury or death reports. Malfunction reports decreased by 1,250, or 15 percent, from 1985 to 1987, compared with an increase of less than 1 percent for injuries and a decrease of 81, or 14 percent, for deaths.

Comparison of MDR and PRP Problem Reports

In contrast to the large number and many types of reports submitted under the MDR regulation, the problem-reporting program (PRP) received an average of only 2,600 reports annually in the 3 years after implementation of the MDR regulation. These reports were in addition to the reports submitted under the MDR reporting requirements.[1] Eighty-eight percent concerned medical device malfunctions, 11 percent were associated with injury to a patient, and 1 percent were associated with the death of a patient.

Conclusions

The purpose of this chapter was to describe the level of reporting and the characteristics of the problems that were reported to FDA under the medical device reporting (MDR) regulation. The MDR regulation increased the number of device-problem reports made to FDA approximately sevenfold, from 2500 to more than 17,500 per year. During the first three full calender years after the implementation of the MDR regulation, FDA received 52,863 device-problem reports on 1,059 separate devices. During this same time period, there was also a slight increase in the average annual number of problem reports received through the problem-reporting program (PRP) during the previous 3-year period (from 2500 to 2600 reports).

There was a net decrease in MDR reporting between 1985 and 1987. In 1985, there were 17,954 reports; however, this figure dropped to 16,654 in 1987, a reduction of 7 percent. This decline included 81 fewer device problems associated with deaths and 1,250 fewer device malfunctions. If the pattern of reporting exhibited during the first quarter of 1988 continues, the number of reports in 1988 will drop to about 15,000. This

[1]During the first year after the implementation of the MDR regulation, FDA engaged a private sector contractor to determine the degree of overlap of reports between the MDR system and PRP—that is, identify problem reports submitted under both systems that referred to the same event. The study found that there was "a minimal overlap" of about 100 reports out of approximately 20,000.

would be a net decline of 15 percent compared to 1985, which would mean that over 2,600 fewer reports were received in 1988 than in 1985.

Problems associated with patient injury accounted for most of the reports in the MDR data base with 29,176, or 55 percent; device malfunctions totaled 22,133 reports, or 42 percent; and patient deaths generated 1,554 reports, or 3 percent. An FDA study of the first year of MDR implementation tentatively attributed the large proportion of serious injury reports under the MDR system to the large number of reports involving explants of pacemakers that had been previously recalled. Pacemaker explants may continue to account for a large proportion of serious injuries, as is suggested by the total number of MDR injury reports associated with pacemakers and pacemaker electrodes. Overall, the nature and characteristics of the problems reported to FDA under the MDR regulation were more serious than the problem reports FDA received through the problem-reporting program (PRP). Nearly 90 percent of the PRP reports were related to device malfunctions, and about 1 percent were associated with the death of a patient.

MDR reporting was concentrated on relatively few devices. Ten devices accounted for 63 percent of all MDR reports. This concentration held across all types of problem reports: 10 devices accounted for 60 percent of all deaths, 73 percent of all injuries, and 60 percent of all malfunctions. Pacemakers alone accounted for 27 percent of all reports, and pacemaker electrodes accounted for another 10 percent of all reports. Combined, these two devices were involved in over one-third of all MDR reports.

Over 75 percent of all reported deaths were related to devices in the anesthesiology and cardiovascular medical specialties. Heart valves and defibrillator reports combined to account for nearly one-third of all reports of death. About 56 percent of the reports of injuries involved pacemakers and electrodes. Although malfunction reports were somewhat less concentrated than other kinds of reports, ventilators and pacemakers were involved in over one-quarter of all such reports.

The fluctuations observed in the rate of problem reporting may be explained by several factors. Specifically, during the first two years of operations, some manufacturers and importers did not fully understand the reporting requirements of MDR and may have been "overreporting." One firm, for example, appeared to consider each routine service call or repair of a ventilator a "malfunction" whose recurrence could cause a

death or serious injury, and treated all of these routine events as reportable under the MDR rule. FDA officials stated that the decline in reporting may be attributable to their subsequent efforts to "educate" manufacturers and importers about reporting requirements. They also suggested that there might actually be fewer occurrences of problems associated with medical devices. FDA officials point to the increased frequency of device firms' preventive actions (such as voluntary medical device recalls and safety alerts) since the implementation of the MDR regulation as support for this contention. However, although these are plausible explanations of the shift we observed in MDR reporting rates, there is no direct evidence that these factors caused the observed changes.

It was beyond the scope of this study to systematically determine whether the data base was an accurate reflection of the total number of medical device problems that occurred during the study period. However, there was evidence that a proportion of the reports that manufacturers claimed had been submitted to FDA, as well as a number of FDA's actions or responses to reports, had not been included in the data base at the time of MDR compliance inspections. Several examples of data that were not entered into the data base are discussed in chapters 3 and 5.

The Structure and Process of the MDR Reporting System

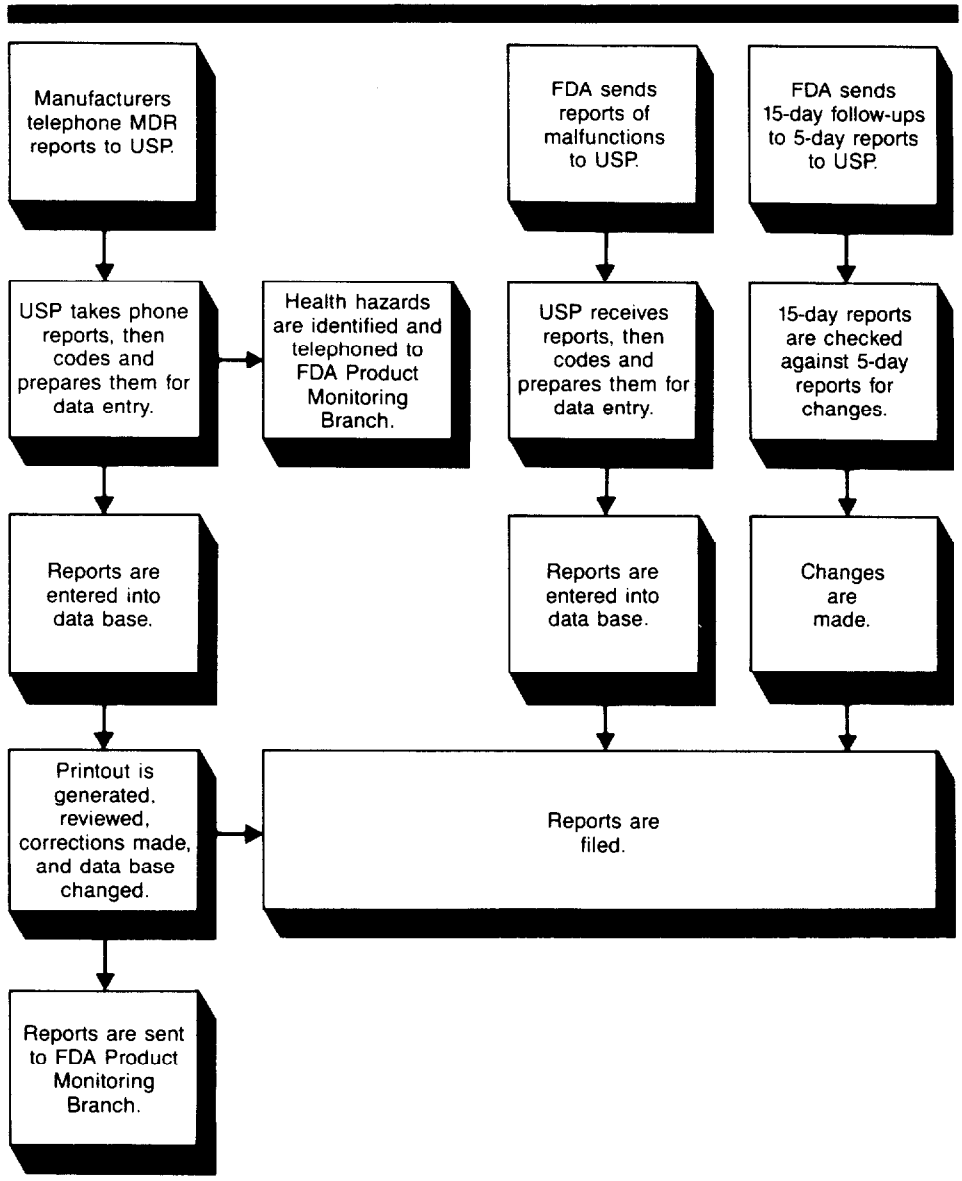
The MDR regulation describes seven items of data that medical device firms should submit to FDA for each problem report.[1] This chapter describes the organizational structures and operational procedures of the system established by the Center to process MDR reports and FDA's efforts to improve the overall MDR report processing system and its postmarketing surveillance (PMS) capabilities. FDA contracted with U.S. Pharmacopeia (USP) to receive, computerize, and forward to the Center for Devices and Radiological Health the initial and follow-up MDR reports that are associated with deaths and serious injuries of patients. (Malfunction reports are submitted directly to the Center.)

Initial Report Processing at USP

Prior to the implementation of the MDR regulation, U.S. Pharmacopeia (USP) had been contracted by FDA to prepare and enter information—such as premarket approval applications (PMAS), problem-reporting program (PRP) data, and other reports issued by the Center—into the Center's data bases. In December 1984, USP began processing reports submitted to FDA under the MDR regulation. Reports received at USP are analyzed, coded, edited, and otherwise prepared for entry into the data base by its analysts and coders. This included computer processing of initial and follow-up death or serious injury reports, and of the written malfunction reports. (See figure 3.1.)

[1] MDR data items are as follows: (1) identity of the device; (2) identity of the manufacturer, or in the case of an imported device, the importer and the foreign manufacturer; (3) identity of the individual making the report to FDA; (4) description of the event giving rise to the report, including (a) whether any deaths or serious injuries occurred and (b) the number of persons who died or were seriously injured; (5) identity of the person who provided the information to the manufacturer or importer; (6) whether the manufacturer or importer intends to submit additional information, and if so, when such information will be submitted; and (7) whether the reported event has occurred or is occurring more frequently or with greater severity than is stated in the labeling or than is usual for the device, if there is no pertinent statement in the labeling and if such information is available.

Figure 3.1: Overview of MDR Workflow at USP



Sources: USP final contract and MDR flowcharts 1 and 2, provided by the Center.

The role of USP has been significantly expanded since the implementation of the MDR regulation. A large backlog of reports resulted from the quantity of reports that manufacturers and importers submitted during the first months of implementation. By October 1985, USP had coded and entered all backlogged reports. At the same time, USP assumed increased responsibility for quality control checks and the coordination of report

processing (consisting of triage, jacketing, and the maintenance of files of original MDR malfunction reports). In February 1986, USP began to provide data entry for final and interim MDR report tracking and closing, previously done by FDA, and entry of reports that were submitted in batches according to the alternative reporting program.[2]

In May 1987, USP assumed the responsibility for receiving the MDR death and serious injury reports by telephone. USP maintains a 24-hour telephone system (with four lines) for receipt of the initial reports. This system also handles reports submitted by telephone facsimile transmission. Telephone calls are received via an automatic answering device until 1:00 p.m. Eastern time, at which time the taped calls are returned and incoming calls are answered by USP staff until 4:30 p.m. The jacketed reports and a daily log are then forwarded to the Center for additional analysis and actions.

Data Accuracy

The accuracy of the data items entered into the MDR data base is monitored through error-and-omission checks performed by the USP analysts and coders after the data have been entered and automated error-checking routines have been run within the system.

Macro Systems, Inc., a contractor engaged by FDA to perform a statistical evaluation of trends in the medical devices reporting, evaluated the MDR data base in 1986. It concluded that "the frequency distributions of certain MDR variables reveal a significant number of inconsistencies which may be the result of coding and keying errors." The contractor's report indicated that the most serious problems were misspecification of manufacturers' "short names" and illegal values for date variables.[3] There were also many variations in the manufacturers' full names because of misspellings and differences in punctuation.

We examined several internal indicators of inaccurate coding or data entry, such as impossible dates and other out-of-range codes, as well as

[2]Under the MDR Alternative Reporting Program, selected device manufacturers and importers have been granted variances in their reporting timetable for specific, well-known problems with specific brands and models (for example, a particular model of pacemaker lead which is being monitored because of a previous recall). For these, the initial and follow-up reporting requirements are waived, and a monthly, quarterly, or yearly "batch" reporting schedule is instituted.

[3]A manufacturer's "short name" is an abbreviated version of the manufacturer's full name and serves as a unique identifier in the data base. For example, Astrophysics Research Corporation is abbreviated to ASTRRESE. Examples of illegal date values include years for "date received" prior to the implementation of the program and those after the current year.

variable categories that would always be expected to contain data (for example, the dates on which a report was received and entered into the data base).[4] We also interviewed the Center staff responsible for managing the MDR data base. They indicated that subsequent to the Macro System's report in 1986, several quality control routines had been added to the data base, including validation of manufacturers' short names and rejection of illegal date values. We confirmed the operation of the short name edit as applied to the computer tape of the MDR data base we obtained from the Center for this analysis. We found that the MDR data base contained relatively few obvious coding and data entry errors (such as dates on which a report was received being beyond the present or other out-of-range codes).

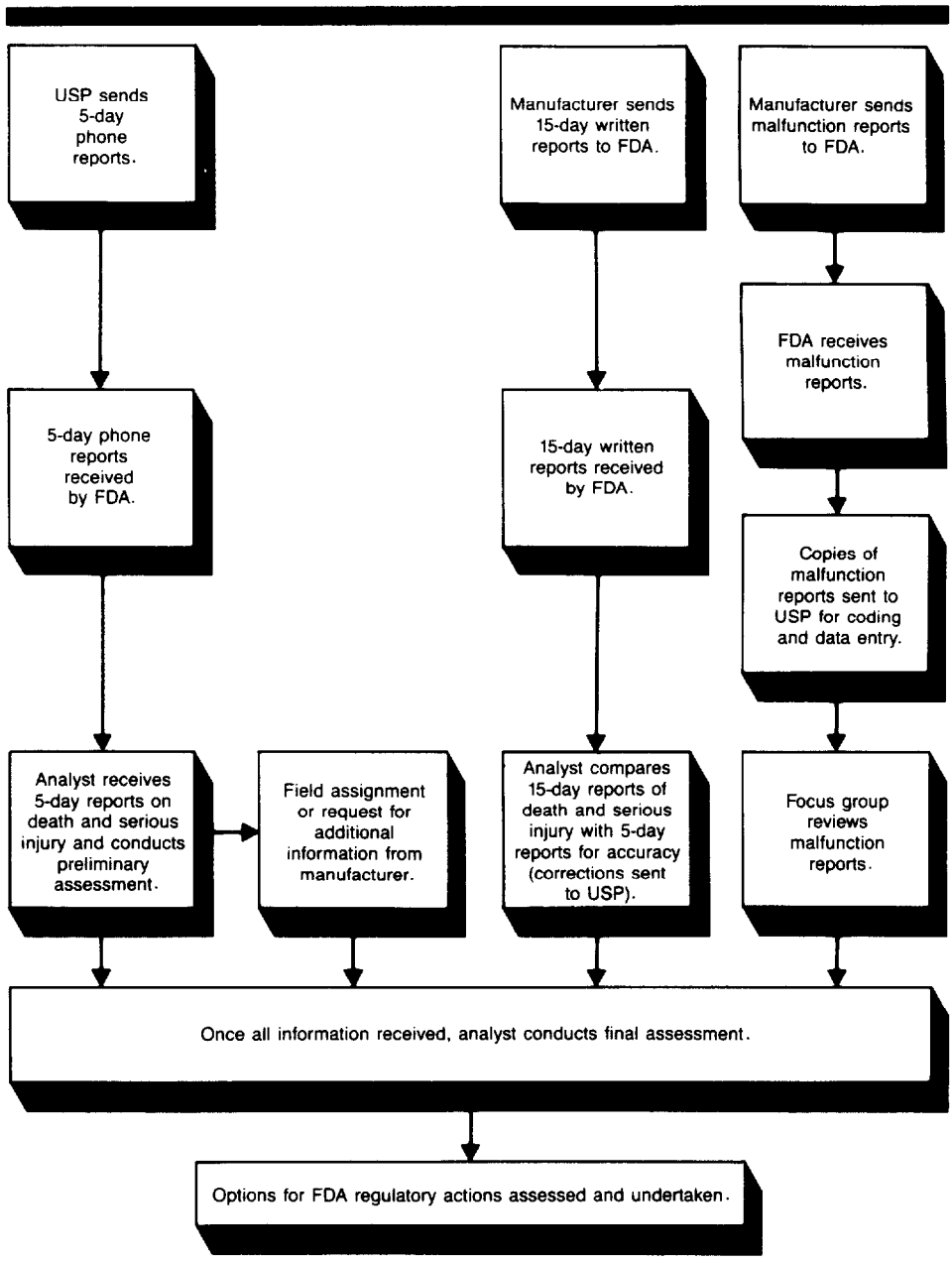
MDR Report Processing at the Center

MDR reports that are received by the Center's operations and product monitoring branches are entered into a system of reviews and analysis to determine the nature and scope of the problem identified and to initiate problem-solving actions.[5] Figure 3.2 provides an overview of the Center's processing of MDR reports.

[4]Since it was beyond the scope of this study, we did not attempt to verify the accuracy of the information in the data base against external sources such as coding forms or written reports.

[5]There are 73 full-time equivalent (FTE) staff assigned to the MDR program in the following capacities: 25 for processing and analysis (including 12 full-time analysts), 27 for support personnel and office overhead, 9 for field investigators and follow-up, and 12 coding and data entry specialists for the USP contract.

Figure 3.2: Overview of MDR Work Flow at FDA



Sources: Figure 3.1, "Overview of MDR Work Flow," and MDR flowcharts 1 and 2, provided by the Center.

Death and serious injury reports are distributed to one of 12 analysts, according to the medical specialty associated with the device. MDR program managers stated that there were neither formally documented procedures nor decision criteria for processing MDR reports, nor is there a formal training program for the analysts. On-the-job training, with supervisory review, was the predominant training mode. Each analyst uses some combination of the information contained in the jacketed report, data from one or more of the Center's automated data bases, consultation with knowledgeable others, and his or her own professional judgment to make an initial problem assessment (that is, health risk, level of severity) and then a decision on a course of action.[6]

A contractors's recently completed analysis of the analysts' workload found that they handle an average of 16 reports daily. Given that the Center receives an average of 17,621 new reports a year and must review each report at least twice, and based on the fact there are twelve reviewers, we find that the analysts must review an average of 12 reports daily. On average, this means that 30 to 40 minutes is spent on each review. While some reviews can take several days of investigation, others do not require this much time, especially the review of the initial report in which very little information may have been provided. In addition, batches of similar reports received under the alternative reporting program are handled as a single unit. Many of these concern devices previously subject to a recall. As a matter of routine, they are immediately processed and closed on the basis of the previous recall.

An analyst may initiate an "assignment to the field" for an on-site inspection when it is believed that the incident is a sufficient threat to the public health. Our analysis of the MDR data base indicated that 1,048 such field assignments were made in connection with the 52,863 MDR reports received between 1985 and 1987.

If the incident is not a sufficient threat to the public health to require immediate action, the analyst holds the initial report from the device firm until the follow-up written report is received. The analyst then conducts an interim or final assessment to determine data adequacy by evaluating all information received to date. The information includes the

[6]The Center for Devices and Radiological Health collects information and maintains several PMS-related data bases throughout the Center, including those associated with the following processes: 510(k), PRP, recall, PMA, and registration and listing. Most of the analysts whom we interviewed indicated that in addition to the information contained in the MDR data base, they would routinely cross-check problems with information contained in the PRP data base and the medical devices recall data base.

initial report, the follow-up report and the establishment inspection report, and all additional information received from the device firm.[7]

The Center's staff indicated that the completeness of a given MDR report varied with the type of device and the particular manufacturer. Some manufacturers submit the minimal amount of information required under the regulation, while others submit much more than is required. When the information submitted is not sufficient for a determination of the problem's cause, scope of the problem, or the risk to public safety, additional information has to be requested from the reporter. The analysts indicated that many times manufacturers may not yet have the needed information in their possession at the time the initial report must be made to FDA. They also reported that they believed that some information (for example, device failure analysis and the company engineer's causal attribution) is not submitted because of concerns about subsequent liability claims against the company. Several analysts indicated that unless it is an obviously critical situation, they wait until they receive the written follow-up report before analyzing the case. They also indicated that some follow-up reports require a request for additional information. This procedure results in their handling many reports several times before they can be closed, which helps contribute to a backlog and thus delays the processing of incoming reports—thereby impairing the "early warning" function of the MDR problem reports.

MDR reports that are determined to contain adequate data are assessed for the effect of the incident described upon the public health and are provided with a closure determination. This assessment involves a causal evaluation of the adverse event and a final report disposition.

Malfunction reports are not subject to the 5-day reporting requirement that applies to reports of deaths and serious injuries. Instead, they are submitted directly to FDA no more than 15 working days after the incident. A preliminary screening is conducted to determine if the malfunction reports require an upgrade to the death or serious injury category. When a malfunction report has been authorized for upgrade, it is jacketed and sent to the appropriate analyst for review. If a determination is made that the report does not warrant an upgrade, it is entered in the

[7] Additional information to follow-up and malfunction reports can be voluntarily sent by the device firm or can be requested by FDA (that is, be nonvoluntary). Any such information request must be in writing, must state the reason or purpose for which the information is being requested, and specify a due date. Approximately 1,724 additional information reports were listed in the MDR data base as having been requested by FDA in connection with MDR reports between 1985 and 1987. In addition, analysts indicated that they make many additional information requests by telephone, but that these are not recorded in the MDR data base.

data base as a malfunction. A monthly printout of malfunction reports is generated, covering the most recent 30-day period, and sent to the appropriate focus group.[5] The focus group reviews the report and determines whether the report requires further review or is closed out. At the time of our review, we found that there was a backlog of at least 10,000 malfunction reports, many more than 2 years old, that had not yet been closed out.

Malfunction reports may be the best early warning of medical device problems. They describe problem occurrences that were not associated with the injury or death of a patient. However, if the problem should recur, it may result in the injury or even death of a patient. Conversely, many reports of the death or serious injury of a patient may in fact concern events that occurred in association with life-supporting devices but were not caused by those devices. In addition, many of the "serious injuries" recorded in the MDR data base are caused by explants of previously recalled pacemakers and leads whose problems are now well understood.

Problems of the MDR Report Processing System

The MDR reporting requirements have resulted in FDA's receiving almost seven times as much information as it received through PRP, and the events being reported under the new requirements are more serious. Nevertheless, more than three years after implementation, FDA is still operating with a "makeshift" MDR report processing system, a system that was "grafted" onto the system developed for the problem-reporting program (PRP).

The ability to obtain information about a particular device from the Center's other data bases (for example, PRP, recall, 510(k), and PMA) is essential to establishing a complete and accurate record of a medical device's performance. It is largely on the basis of this record that analysts must make their risk assessment of the problem being reported through the MDR system. There are, however, several barriers to access to the Center's data as the system now exists across several computer systems. The principal barriers are user training, hardware difference and incompatibilities, and the variety of data base management software in use. Although the MDR system has the ability to interact with

[5]Focus groups are composed of analysts from the Center in each medical specialty. They meet periodically to discuss device problems—especially malfunctions reported in the MDR system—and to reach a consensus on actions to be taken. Their recommendations then are forwarded to analysts.

other of the Center's systems, no programming presently links it with them.

A comprehensive review of the Center's existing postmarketing surveillance (PMS) data bases and computer capabilities was recently completed.[9] One of the findings of that review was that there is no menu-directed access to the MDR data base, so that a user is required to enter six successive commands with no system direction to retrieve data at a remote terminal.[10] In addition, some analysts stated that they "often did not conduct a search on the on-line systems since the trouble involved was considered more costly than the value of any retrieved data." We were also told by a device expert at the nonprofit Emergency Care Research Institute (ECRI) that one office at the Center routinely gets the data base searches it needs from ECRI, because it is easier than using the Center's data bases. This is so because ECRI obtains a monthly MDR/PRP tape from the freedom-of-information office at FDA, reviews each entry, and categorizes it (using ECRI's own nomenclature for device categories, which is more specific than FDA's).

Some of the analysts we interviewed confirmed the existence of these problems and noted several specific problems they had experienced after having gained access to the system (such as difficulties in preparing data requests, unexpected results from data requests, and text fields that contained insufficient detail to conduct their analyses).

The analysts also reported problems in using MDR data caused by inconsistencies in the terminology used to refer to a particular device. The problems included failure to identify some device problems in data summaries and difficulties in matching some of the terms used in related data bases maintained by the Center.

They also expressed their desire to correct obvious errors and update and close reports on-line. Currently, analysts can only review and retrieve data from the MDR system; they cannot add to or change the information in the reports. This restriction increases the time and resources required to process each report since the printed-out copy must be sent back to USP for correction and further processing.

[9]Planning Research Corporation, Needs Assessment Recommendation Report (McLean, Va.: May 31, 1988).

[10]Several of the analysts we interviewed indicated that they had received very little formal training in the use of the computer system and the Model 204 data base management system software used to store and retrieve MDR data. Training was for the most part informal, and much of it had been a matter of the sharing of knowledge, as needed, by more experienced or skilled analysts.

The Model 204 software used with the medical device reporting (MDR) regulation is unique to International Business Machine computers and is therefore not compatible with the computing resources at the Center's main computer center. In addition, although the MDR system has the capability to interact with other of the Center's systems, no software program presently links the systems. Manual processes using printed reports as references to coded data elements are currently the primary "link" between the systems. According to the analysts we interviewed, the problem-reporting program (PRP) and recall data bases are routinely accessed as part of their initial MDR report review. Several said that the recall data base was incomplete and not integrated for efficient use. They reported that the computerized data base itself contains very little information, and to understand a recall it was necessary for them to walk over to the recall section and physically sort through the information contained in file folders.

Because most medical devices first marketed before the 1976 device amendments have not been approved by FDA as safe and effective through the premarket approval process, even one report, or a sudden increase in the frequency of problems with device types that are not generally related to a patient's death or serious injury (such as hospital beds), may serve as an early warning and provide a basis for FDA actions. However, the early warning function of the system is severely hampered by the system's limited capability to identify "spikes" and statistically valid trends in the MDR reports.[11]

A Model 204 software package was developed at the Center as an interim device until a formal trend analysis package becomes available. Analysts who indicated that they used the interim trend analysis programs said they seem to be functioning adequately for their individual specialized requests and are able to provide a more general report comparing "blips" in the previous 30 days of reporting to those in the previous 360 days, both for devices and manufacturers. The interim package is limited in its capacity to statistically assess spikes or trends; it is mainly a way of presenting reporting rates over time descriptively.

Finally, our review found that overall there appeared to be a fragmented approach to postmarketing surveillance (PMS) problem solving. Many issues that come before individual offices in the Center are handled by that office in isolation. For example, the collection of MDR data is

[11] A "spike" refers to a sudden jump in the reporting pattern for any given medical device, and a trend to the pattern of reporting over a period of time.

primarily the responsibility of the office of compliance, but other offices—such as science and technology and training and assistance—also respond to device problems and use MDR data. This lack of coordination sometimes results in an inefficient use of PMS resources and a duplication of effort at the Center. For example, we found that there had been at least two separate studies of the implementation of the MDR regulation and that three intravascular infusion pumps studies had been conducted at the same time. All these efforts were independent, involved no coordination, and basically came to similar conclusions.

A conclusion similar to ours was reached by an internal postmarketing surveillance (PMS) work group at the Center. In their 1987 report, the work group concluded that "the major postmarketing surveillance problem was the failure of the Center to develop a Center-wide policy and program for managing the collection, utilization, and analysis of information on adverse experiences"; that the Center had emphasized improving the premarket approval process and that only minor attention had been paid to upgrading PMS; that most of the Center's actions under the current system involve reaction to individual reports based on perceived risk to the public health and violations of FDA regulations; and finally that the Center was making do with an inadequate problem-reporting system.

Based on the recommendations of the PMS work group, the Center has implemented three major initiatives to correct some of the major medical device reporting (MDR) system deficiencies and improve overall PMS activities. First, the Center has established a centralized planning and administrative unit for PMS activities. Second, the Center has outlined a project to develop a comprehensive and integrated data collection and management capability for PMS. The project is divided into four phases: (1) define requirements, (2) design a new system, (3) implement the new system, and (4) train users and systems personnel who are going to maintain it.[12]

The first phase of the project is composed of an analysis of the current PMS information system; a list of the Center's expectations for a new system, including a users' survey; development of a conceptual model of an optimal system, consisting of a basic system plus add-on modules

[12]To date, the first phase of the project has been completed by a contractor, the Planning Research Corporation. In comments on a draft of this report, FDA indicated that phases two through four have been placed on hold for several years and that the Center has decided to do the needed revisions without contracting.

that will be optional; and a detailed identification of the functional requirements of the new system.

The third initiative was a 1986 FDA contract with Macro Systems, Inc., to develop a trend analysis software package for use with the MDR data base. Center officials told us that they expected to have a formal trend analysis package in place and fully functional by the end of 1988. The program will perform device-specific and overall analyses, including statistical tests of spikes and trends associated with reported device problems.

Conclusions

The purpose of this chapter was to describe the organizational structures and procedures of the MDR report processing system and the mechanisms that are used to ensure the accuracy of the MDR data base, and to determine if there are systemic problems associated with the MDR system that affect its function as a postmarketing surveillance (PMS) tool.

The current MDR report processing structure and procedures are complex, involving more movement and handling of paperwork than is judged efficient by Center officials. This systemic inefficiency has had certain negative consequences (such as the failure to enter the final evaluations and dispositions of some closed reports into the MDR data base for use in future report analysis) as well as contributing to an uncertain degree to the report processing backlog.

The Center's analysts are responsible for analyzing MDR reports, gauging the potential public heath risk, and initiating appropriate remedial actions. The validity of the risk assessment process is dependent on the professional judgment of individual analysts, who often function without the benefit of either formal written report procedures or adequate training in the use of the MDR automated data base. On-the-job training, with supervisory review, was the predominant training procedures at the time of our review.

Overall, the data collection and analysis system that supports the MDR reporting requirements was designed for another purpose and is not adequate for the current level of reporting. Many problems that we identified in this review, such as the lack of a standardized terminology and of an automated device-thesaurus, have been repeatedly identified as problems, dating back at least to a 1975 planning study for the device

experience network and including our own 1983 report.[13] Other problems—for example, the lack of integration and accessibility of the Center's data bases, the lack of "user-friendly" automated data processing facilities, and the failure to move beyond recording and tracking essentially separate problems to include trend analysis—increase the analysts' workload, further complicate the flow of work within the office, and severely limit the analysts' ability to move beyond processing and tracking separate device problems to more global and considered types of analyses. However, the Center has recently undertaken initiatives to address a number of the deficiencies in the current MDR report processing system and its overall postmarketing surveillance (PMS) capabilities. These include creating a centralized planning and administrative unit for PMS activities, outlining a project to develop a comprehensive and integrated data collection and management capability, and contracting for statistically valid trend analysis software. These initiatives had not been implemented or were not fully operational during our review, and we are therefore unable to determine how effective they will be.

[13]See U.S. General Accounting Office, Federal Regulation of Medical Devices—Problems Still to Be Overcome (GAO/HRD-83-53, September 1983).

The Analysis and Use of MDR Data

The collection of complete and accurate PMS data on medical device problems is a primary objective of the medical device reporting regulation (MDR), but the application of that information to problem solution is of equal importance. We therefore reviewed the Center's analysis of the medical device problem reports and examined evidence of FDA's employment of MDR data in taking regulatory and other corrective actions.

Causal Analysis of Reported Problems

A primary analysis of MDR problem reports is of their causal evaluation. These evaluations are based on the information contained in the initial report, additional information obtained from the manufacturers, and the analyst's professional judgement. When an MDR report is given a final disposition at closeout, analysts also assign a definite causal factor to the problem, a "probable" causal factor, or no determination of causality, with a note to require periodic monitoring of the frequency and severity of the reported problem as well as similar ones.[1]

There are three general causal categories, each of which includes several more specific causal factors that analysts may assign to MDR reports. The general categories are the design and manufacturing of the device, the use of the device, and the physiological or procedural factors associated with the patient or the environment in which the device is applied.

A causal evaluation was performed on 61 percent (32,130) of the 52,863 MDR reports submitted to FDA between 1985 and 1987 and subsequently closed with "final dispositions." Forty-eight percent, or 15,424 of the reports that were evaluated, were assigned to one of the three general causal categories. In 77 percent, or 11,832 of these submissions, the cause assigned was the device itself, including its labeling, expected wear, and flaws in design; in 15 percent, or 2,388 of the submissions, the problem was attributed to a variety of user errors, including reuse, misapplication, and failure to service; and in 8 percent, or 1,204 reports, the problem was attributed to the patient's condition, inherent risk factors, environmental factors, or anticipated adverse reactions.

The remaining 16,704, or 52 percent of the reports that were evaluated for causal attribution, were not assigned to one of the general causal categories. For 7,912 of these, or 22 percent of the reports evaluated, a focus group determined that no further action was necessary at the

[1] A report may also be reviewed and a determination made that the product is not regulated by the Center. This results in a recommendation that the report be forwarded to the appropriate FDA center or federal agency for follow-up.

time; for 4,243, or 13 percent, the analysts could not determine a cause and noted that the available frequency and severity data did not indicate that any further investigation was necessary at the time; and in 9 percent, or 2,733 reports, the problem was identified as an adverse effect that FDA had previously associated with the device. Each of these three evaluations included a statement that the frequency and severity of the reported event should be periodically monitored to determine if any follow-up or other action was indicated. In 6 percent, or 1,789 of the evaluated reports, it was concluded that the medical device did not malfunction and thus the incident was not attributable to the device. There were also 27 reports on devices which were not regulated by the Center.

Analysis of Problem Report Dispositions

The final step in the analysis and processing of MDR reports is the determination of the report disposition. Table 4.1 indicates that of the 52,863 reports FDA received between 1985 and 1987, 32,130, or 61 percent, were closed with one of the standard report dispositions. According to the data tape we obtained from the Center, 20,733, or 39 percent of all the reports, were open and pending disposition. There were 8,533 reports, or 48 percent, open in 1985; 4,437, or 24 percent, in 1986; and 7,763, or 47 percent, in 1987. FDA officials indicated that it would not be unusual to have a substantial number of the 1987 reports open while investigations were still being conducted and that a large number of early reports had in fact been closed, although their disposition codes had not yet been entered into the data base.[2] These officials indicated that an effort was under way to review and enter data from these reports.

[2]Interviews with analysts conducted by an FDA contractor indicated that a change in the closeout procedure intended to allow the entry of reports which had been closed on paper but not in the data base resulted in two closeout procedures being available for a time in 1986. Although a supervisor stated that all analysts had been informed, the contractor's report indicated that some may have felt that there was a lack of communication concerning the procedures.

Table 4.1: Final Disposition of Closed MDR Reports, 1985-1987

Disposition	Number	Percent
Historical reference	19,954	62[c]
Recalls[a]		
Class I	6,118	19
Class II	481	1
Class III	111	0
Insufficient information to process	2,522	8
Voluntary action by manufacturer[a]	2,346	7
Report not verified	342	1
No discernible problem	245	1
Forward to other FDA center	6	0
Forward outside FDA	1	0
Information letter to manufacturer	1	0
Notice of adverse findings (NAF) letter	1	0
Seizure, injunction, prosecution	1	0
Total closed MDR reports	**32,130[b]**	**99[c]**

[a]These are the numbers of problem reports closed because of an earlier recall or other voluntary action by a manufacturer. A single recall or other action may result in the closing of many problem reports associated with a specific medical device. See the Glossary for definitions of the three recall classes.

[b]This category represents 61 percent of the 52,863 reports received between 1985 and 1987.

[c]Percentages do not add to 100 because of rounding.

Table 4.1 shows that of the 32,130 MDR reports that were closed with one of the standard report dispositions, 19,954, or 62 percent, were assigned to the category of "historical reference." MDR program managers and analysts told us that this category is a sort of residual or default category that is used when one of the other dispositions does not apply and the report may be referred to some time in the future. The final disposition for 2,522, or 8 percent of all reports, was a conclusion that there was "insufficient information" available to make a determination.

The data tape we analyzed contained very few instances of traditional FDA regulatory actions that could be linked directly to the MDR data. Only one notice of adverse findings (NAF) letter is recorded in the MDR data base. A Center official told us, however, that 75 other NAF letters had been sent to manufacturers, but that these had not been entered into the data base.[3] We found records of two other reports involving traditional

[3]A notice of adverse findings letter may be sent to a firm when an inspection reveals that a firm or individual is in violation of the law or regulations, or when there is information that an existing condition or practice may lead to a violation if left uncorrected (although the agency has concluded that the nature of the violation does not require immediate action against the firm or individual).

regulatory actions, one of which had been closed with a disposition indicating that there had been a seizure of devices. The other had been closed with a disposition indicating that an information letter had been sent to the manufacturer. In neither of these cases were we able to confirm the action's connection with the MDR system. There were no injunctions or prosecutions listed in the data base as having been associated with MDR reports.[4]

Center officials told us that the number of distinct regulatory actions based on MDR reports could not be obtained from the MDR data base. They indicated that separate records of regulatory actions, including recalls, are maintained by FDA, but that these actions are not always clearly linked to MDR reports. The final disposition of each closed MDR report, however, provides an indirect indicator of the regulatory actions FDA has taken on the basis of medical device reporting (MDR) regulation data.[5] This is only an indirect indicator since any number of reports may be closed by a single action. For example, FDA may have received any number of problem reports associated with a particular device, after which the device manufacturer may initiate a recall. An analyst may then, as a result of that single recall, close all of the open reports and any subsequent MDR reports that identify the same problem with that device.

Relationship Between Severity of Problem and Report Disposition

One indication of whether the actions taken by FDA in response to MDR reports are appropriate for the nature of the reports is given by the relationship between report type (death, injury, or malfunction) and the kind of disposition the report received at close-out. Although the distributions of dispositions for reports closed during the years 1985-1987 are not identical for the three report types, there is no clear indication that the more serious adverse events—deaths and serious injuries—are being closed with more stringent regulatory actions (such as regulatory letters or product seizures) than device malfunctions that do not result in the death or serious injury of the patient. The main source of the difference in the disposition distributions appears to be that 25 percent of all injury reports were closed by class I recalls, while the class I recall disposition was used in only 3 percent of reports involving deaths and 2

[4]An injunction is a legal order which FDA may obtain through the courts to prevent distribution of violative products or to correct the conditions in the establishment where the violation occurred. Injunctions are sought when "imminent health hazards" have been identified.

[5]Some intermediate steps are taken by analysts, such as requests for additional information and field assignments to FDA inspectors. These are considered actions based on MDR data by FDA. However, these actions are not reflected in the report disposition data.

percent of those concerning malfunctions. Our interviews with the analysts who are responsible for cardiovascular devices indicated that the disproportionate number of class I recalls associated with injury reports is primarily a reflection of pacemaker explants due to manufacturer's recall.

Case Histories of MDR Data Use

Center officials indicated that actions which are generally viewed as traditional regulatory actions (such as NAF or regulatory letters, product seizures, or injunctions) do not represent the entire spectrum of uses for MDR data. These officials said that regulatory actions are short-term, immediate, or interim solutions to device problems. They are generally "reactive," and the ideal goal is to develop broad-based, long-term solutions to medical device problems. The Center has recently begun to document the use of MDR data in ways other than through FDA's direct regulatory intervention, and in fact provided us with 19 retrospective case histories involving 12 separate devices.[1]

Our review of the case histories showed that for at least some there was a temporal sequence of events suggesting that the MDR data has been instrumental in a number of medical device problem-solving activities. For example, several of the case histories indicated that, on the basis of MDR reports, the Center initiated field inspections of manufacturing facilities; commissioned scientific studies; or consulted with the device firm. Following these activities, the device firms or FDA issued a safety alert to hospitals and other health care professionals; made labeling changes; issued a device recall; or revised or upgraded a safety alert or a recall that was already underway. Although we believe that it is difficult to attribute causality to a program on the basis of such information alone, Center officials stated in each case that these corrective activities were initiated as a direct result of MDR reports.

The MDR program managers indicated that the Center expects to increase its focus on long-term and broad-based solutions utilizing the educational and scientific resources of FDA rather than exercise its regulatory authority in more traditional ways. For example, in 1987 the Center's Office of Training and Assistance awarded a contract to a private company to study the human engineering aspects of blood glucose monitors. According to FDA, this initiative was taken in response to the more than

[1]This information was received after our data collection and analysis were completed. It was not contained in the MDR data base, and we were unable to verify the information with any other sources. The devices covered by the case studies included defibrillators, glucose monitors, apnea monitors, dialysis systems, replacement heart valves, magnetic resonance imagers, and gastric bubbles.

1,800 reports of erroneous blood glucose self-monitoring test results received since the implementation of the MDR rule. For many of these cases, Center analysts had concluded that the cause of the problem was inadequate user training or failure to follow labeled instructions, with the complexity of procedures and design contributing to user errors. The human factors study was intended to evaluate glucose monitors' design and labeling, and the tasks they require of users. Professional organizations and manufacturers are being informed of the results so that modifications can be made in the design and labeling of glucose monitors. There are also plans to cooperate with diabetes professional groups and manufacturers to develop user education strategies and instructional materials.

The Use of MDR Data in Device Prioritization

FDA is now testing a method for choosing devices to be the subject of intensive scrutiny by the Center.[7] The method includes both a prioritization system that was developed in 1985 and the problem definition study, a type of device-specific research report that was widely used by FDA up to 1982. Basically, the prioritization system uses a simple linear mathematical model to calculate a parameter called the device priority score.[8]

To calculate each device's priority score, the model uses six evaluation factors common to all devices, with each factor weighted to reflect its societal importance.[9] A group of experts drawn both from the Center and outside assessed a number of risk-abatement factors that may have been associated with a particular device. Their findings and evaluation were then combined with other pertinent information in a data base. FDA officials said that this system is a significant improvement over previous efforts because the scoring is uniform and reproducible, devices can be compared across classes and all specialties, the data base can easily be analyzed to see how Center priorities change as their views of the relative importance of the evaluation factors change, and the system can easily incorporate the MDR data.

[7]See Harvey Rudolph, et al., "High-Priority Devices: How Are They Chosen?", Medical Device & Diagnostic Industry, 9:6 (1987), 64-68.

[8]According to FDA officials, these priority scores are not intended to be an index dictating the order in which each device will be addressed by FDA action programs. Rather, they are flags that raise agency sensitivities, alerting them to potential or actual problems, and then prioritizing these concerns for future action.

[9]The evaluation factors and weights are as follows: (1) frequency of mortality, 0.38; (2) frequency of serious injury, 0.30; (3) frequency of less-serious injury, 0.12; (4) frequency of use, 0.08; (5) health benefit, 0.08; and (6) device effectiveness, 0.04.

The device prioritization model described above was used to select 100 devices as candidates for problem-definition studies. After a screening procedure, FDA selected 16 "high-priority-device candidates" for the study, including those that had been the subjects of one or more MDR death reports, 100 or more MDR injury reports, or 100 or more MDR malfunction reports. Four of the most frequently reported devices in our current MDR implementation study—implantable pacemaker and leads, inflatable or gel-filled breast protheses, and intravascular administration set—were also among these 16 candidates.

Conclusions

The focus of this chapter was a description of how FDA analyzes and uses the information it obtains under the MDR reporting requirements. We found that over one-third of all the reports that were received by the Center for Devices and Radiological Health between 1985 and 1987 had not yet been completely processed at the time of our review.

Approximately half of the problem reports that were closed were assigned to one of three causal categories: the device itself, its use, or physiological and procedural factors. The device itself was held to be the cause of the event for 77 percent of these reports. The remaining half of the reports were closed without any attribution of causal factors, but 89 percent of these were given evaluation designations that indicated that FDA would monitor the frequency and severity of the problem to determine if any follow-up or other action was called for.

The MDR data base documents very little use of the MDR data by FDA. The final dispositions of more than 60 percent of reports closed as historical references indicate that no action by FDA or the manufacturer was taken or judged to be appropriate at the time. A small proportion of the reports were closed with recalls or voluntary actions on the part of the manufacturers.

There is insufficient information in the data base to determine whether the manner in which device reports are closed is logical and consistent with the risk to public safety associated with the reports—that is, whether the more serious problems are being closed with more stringent actions. The more serious regulatory actions—such as NAF letters, seizures, and injunctions—are represented too infrequently among MDR report dispositions to permit valid statistical tests of the association between report type and report disposition.

FDA's use of MDR data in analyzing and taking corrective actions on device problems has not been sufficiently documented in the MDR data base. However, narrative information supplied by the Center does indicate that MDR data may have played an important role in the resolution of a number of device problems—leading to recalls, design and labeling changes by firms, issuance of safety alerts by FDA, and at least one educational program for device users.

MDR Coverage and Compliance

An analysis of the number and types of MDR reports received by FDA is an essential element in evaluating the implementation of the MDR regulation. Equally important are the issues of coverage and compliance—that is, first, the degree to which these MDR problem reports represent the population of medical device firms that might be expected to report and, second, the degree to which those firms in possession of information about MDR events transmit that information to FDA and maintain the appropriate records and procedures.

Reporting Coverage Under the MDR Regulation

A total of 652 different medical device firms submitted at least one MDR report to FDA between January 1, 1985, and December 31, 1987. There was an upward trend in the number of different firms submitting MDR reports between 1985 and 1987. There were 377 firms reporting in 1985, 408 in 1986, and 421 in 1987.

One year after the implementation of the MDR regulation, FDA's internal implementation study reported that a high percentage of the MDR reports were being submitted by a relatively few firms. The report stated that 12 of the most frequently reporting firms had contributed 70 percent of the MDR reports during the first year. The remaining 30 percent of reports were distributed among the more than 350 other reporting medical device firms. This pattern of concentration among firms reporting may in part reflect the concentration of the industry. According to one estimate, 15 percent of medical device firms account for 90 percent of all sales.[1] FDA officials indicated, however, that at least some of the reporting concentration may be an indication of systematic overreporting by some firms and underreporting by others.[2] Firms were thought to be either uncertain about reporting requirements or concerned about the product liability implications of the MDR regulation. FDA expected that the reporting concentration apparent in the first year's data would

[1] R. C. Grant, Evaluation of the First Year of Experience with the Medical Device Reporting Regulation, technical report (Washington, D. C.: Center for Devices and Radiological Health, FDA, January 1986).

[2] We did not attempt to assess, independently of FDA's efforts, whether manufacturers and importers exhibited the appropriate reporting rates or were in general compliance with the MDR regulation. Neither FDA nor we were able to obtain the data necessary (for example, market share statistics or number of units sold) to make systematic comparisons of individual firms that are similarly situated in the marketplace. In any case, the findings from such an analysis would not be a definitive assessment of compliance and would be subject to various interpretations. For example, differences in reporting rates among manufacturers and importers may be interpreted as a reflection of their different interpretations of the reporting requirements, different internal compliance policies, real differences in the numbers of events reported to the companies, or some measure of compliance. A direct comparison of manufacturers' and importers' records would still be necessary to confirm apparent differences in compliance.

decrease as more firms came to understand the MDR system and the reporting requirements.

Our data show that the pattern of concentration among firms reporting that was apparent after the first year of implementation has persisted. In 1987, the 12 most frequently reporting firms accounted for nearly 60 percent of all reports. The membership of the group of 12 most frequent reporters has changed slightly over the last 3 years, and some of those firms that have remained in the top dozen have shifted positions. However, 9 of the 12 original most frequently reporting firms have remained the same. These firms can be characterized generally as manufacturers and importers of implanted devices, life-support devices, and anesthesia equipment.

One logical method for assessing the degree of MDR coverage would be a comparison between the number of existing firms and the number of firms filing MDR reports in a given year. However, FDA indicated that over a given year some "unknown" number of firms cease doing business or otherwise become "inactive," and new firms may of course start up, but only establishments re-register each year. As a result, FDA does not have an up-to-date count of the number of device firms in existence.

FDA, the Emergency Care Research Institute (ECRI), and other experts, however, have attempted to derive estimates of the number of existing firms from sources such as the registration and listing data required under section 510 of the Food, Drug and Cosmetic (FD&C) Act and then estimate the number of these firms that could be expected to submit MDR reports.

Section 510 of the FD&C Act requires that device firms annually register their "establishments" and list their devices with FDA. An establishment is defined by FDA as a site for the manufacture, relabeling, etc., of finished medical devices. A single firm may have many establishments in which it conducts its operations. For example, several of the largest firms have more than 50 establishments. However, the best available information indicates that in the majority of cases the firm is synonymous with the establishment. The number of MDR reports submitted by a firm should represent the sum of reports received at its related establishments. FDA's latest available registration and listings records contain over 12,000 establishments.

FDA's estimate of the number of firms expected to report under the MDR regulation was contained in the Center's analysis of the first year of MDR

implementation and reporting. FDA's estimate was founded on an initial base of 8,000 registered establishments. The potential number of reporting firms was reduced by the calculation that about 15 percent of the total, or 1,200 establishments, make only class I devices, which would seldom be associated with MDR events. The assumption was then made that the number of firms was about 75 percent of the number of establishments. A factor of 0.75 multiplied by the estimated 6,800 active establishments manufacturing class II and III devices produced a potential reporting population of 5,100 firms. FDA then concluded that of the estimated 5,100 potential reporters, "only a small portion, perhaps one-third," might be expected to report in any given year.[3]

A second estimate can be derived from a study that combined FDA registration and listings, employment data, and corporate credit information into a unique data base to estimate the number of potential reporters.[4] Analysis of these data also indicated that the number of firms was about 75 percent of the number of establishments. The study predicted, however, that there would be about 9,000 "active" establishments by the end of 1985. If the 75 percent figure is valid, these 9,000 establishments would have represented 6,750 firms or potential reporters.

A third estimate was derived from an analysis done by ECRI at the end of the second year of MDR regulation implementation. The study referred to 12,000 device establishments registered with FDA and pointed out that many of these represented multiple locations of a single firm or small, local firms, such as denture or eyeglass manufacturers or makers of customized orthopedic appliances. ECRI therefore suggested that the more than 3,000 firms listed in its Health Devices Sourcebook probably represented a more realistic number of potential reporters.

Our analysis shows that the largest number of firms reporting in any one year was 421 in 1987. This represents 8 percent of FDA's estimate of 5,100 firms that could be associated with an MDR event (that is, the potential reporters) and 25 percent of the one-third, or 1,700 firms, "expected" to report in any one year. The 652 actual reporters that we found in the data base for the years 1985-1987 represent only 22 percent of ECRI's estimate of 3,000 potential reporters under the MDR system and only 10 percent of the 6750 potential reporters identified in the Gieser study.

[3]The arbitrary nature of this estimate was acknowledged by the analyst.

[4]N.C. Geiser, "The Evolving Medical Device Industry: 1976 to 1984," Medical Device and Diagnostic Industry, 8:11 (1986), 50-54.

FDA officials indicated that the total number of firms found in their 1985 implementation study was evidence of some level of underreporting. Although there was a significant increase in the number of firms submitting MDR reports from 1985 through 1987, the actual number of reporting firms was considerably less than predicted by any available estimate. We believe that the only valid way of determining whether the actual number of firms reporting under the MDR regulation represents adequate coverage by the MDR system of the population of manufacturers is through up-to-date knowledge of the relationship between establishments and their parent firms and an assessment of individual establishments' compliance with the MDR reporting requirements.

FDA's Compliance Program

FDA's principal means of assessing compliance—compliance inspection—is information collected and analyzed on establishments rather than firms. If an establishment is determined to be in compliance with the MDR regulation, it does not necessarily mean that all establishments associated with a particular firm or parent company itself are in compliance.

In 1984, using its registration and listings records, FDA notified all registered establishments about the new medical device reporting rule, and provided them with a pamphlet containing a copy of the regulation and an overview of the reporting requirements. A protocol for assessing whether establishments comply with the rule was pilot-tested in January of 1985, and a formal MDR compliance program was implemented in the fall of 1986.

According to FDA's MDR compliance program instructions, the MDR inspections were to be conducted in conjunction with the agency's biennial good manufacturing practices inspections, and other types of inspections (such as those for importers and "for cause") are assigned by the Center.[5] Initially, the inspections were conducted by field investigators from FDA's district offices and their findings submitted to the district offices and the Center for review and recommendations for regulatory actions. After the compliance program had been evaluated by the Center and policy guidelines developed, the Center had planned to delegate responsibility for regulatory and administrative follow-up entirely to the district offices.

[5]A principal source of "for cause" inspections is information developed by analysts who monitor and compare reports submitted through the voluntary problem-reporting program, device recalls, and the MDR system.

The selection of companies for participation in the first wave of inspections was based in part on patterns of reporting evident in the MDR system and the problem-reporting program (PRP) data bases. The selection criteria included the Center staff's intuitive knowledge of a particular firm's size and product line. The primary focus of the inspections was to identify "non-reporters" and firms that appeared to be reporting markedly less often than device firms of similar size and product line.[6]

On September 25, 1986, approximately 2 years after the regulation became effective, FDA issued written instructions to its investigators on how to conduct MDR inspections. A six-page, 23-item questionnaire, or checklist, was produced by the office of compliance to assist in evaluating the information derived from the inspection. Prior to conducting an MDR inspection in an establishment, the FDA investigator is required to obtain copies from the Center of all the MDR reports submitted by the establishment in the past twelve months. These reports enable the investigator to see whether there are any discrepancies between the reports and the information in the manufacturer or importer's file previously submitted to FDA. If an establishment has not submitted any reports, investigators may look at the MDR reports of manufacturers and importers of similar devices to ascertain the number and types of events that might have been reportable.

The MDR inspection begins with a request for a company's written procedures for handling MDR events.[7] Inquiries are also made as to whether any labeling changes have been made—for example, whether a company has changed its labeling to include the failure rate for a particular component of a device—as a result of its MDR responsibilities.

The second step in the inspection is the identification of all MDR reports submitted to FDA. The investigator audits a minimum of 20 randomly selected reports; if there are less than 20, all that are available are audited. For each MDR report selected, the investigator asks to see all records that the MDR regulation requires manufacturers to keep.

The third step in the MDR inspection is a review of the establishment's good manufacturing practices complaint file. This review consists of inspecting a maximum of 100 complaints involving death, serious injury,

[6]According to FDA officials, the sample of establishments was intentionally biased and not intended as a base for statistically valid generalization to the population of establishments.

[7]Although FDA requires firms to establish MDR procedures, the MDR regulation does not require firms to have written MDR procedures; thus, failure to have such a document is not a violation.

or malfunction to determine whether the establishment's complaint file contains information that should have been reported to FDA under the MDR regulation, but was not. If an establishment services or repairs the devices it manufactures, the investigator also reviews a random sample of 20 service or repair records to determine whether any information contained in these records constitutes a reportable event under the MDR regulation.

The investigator is required to report suspected violations directly to the Center's division of product surveillance, which then determines whether a violation has occurred. If one has occurred, the Center notifies the manufacturer or importer directly with an informal letter or a notice of adverse findings (NAF) letter. The more formal notice of adverse findings is usually sent in cases where the violations could lead to official actions if not corrected. Persons or corporations found in violation of the MDR regulation are subject to civil injunctions or criminal prosecution. To date, there have been no civil or criminal enforcement proceedings for MDR regulation violations.

Implementation of MDR Compliance Inspections

The first round of compliance inspections was scheduled to run for 2 years. Before the end of our data collection period, 993 inspections had been recorded in a Center information system as having been completed. FDA provided us with data from 572 of the "establishment inspection reports" that had been closed by March 24, 1988. These included 291 of 422 inspections conducted under the original procedures and 289 of 571 inspections conducted with a revised questionnaire and new procedures. The selection of establishments for the first round of inspections was not random or intended to produce a representative sample of the population of manufacturers on characteristics such as the type of device manufactured or the size of the establishment. Instead, establishments were selected in two ways: (1) as a cost-saving measure, MDR inspections were conducted as add-ons to good manufacturing practices inspections already scheduled; (2) establishments were selected if, in the judgment of managers and staff from the responsible divisions within the office of compliance, there was reason to suspect that a manufacturer or importer was underreporting or not reporting when it should. FDA officials told us that these judgments were based on patterns of MDR reporting and knowledge of segments of industry, including (but not restricted to) problem reporting by competitors. The resulting sample thus was intended to be biased in that it was likely to include more of those device firms in noncompliance with the MDR regulation than would be the case in a representative sample.

When we interviewed FDA officials to obtain their assessments of the MDR inspections to date, they identified a number of problem areas in the implementation of the compliance inspections and in the results obtained. Their first area of concern centered on the training and authority given the investigators. In the very early stages of implementing the inspections, Center officials reported a lack of understanding of the outlined inspection procedures on the part of the inspectors. Field inspectors did not understand how the survey information would be used. Operating as they have traditionally done in GMP inspections, the field inspectors preferred to follow any "leads" developed in documenting violations at the site. A compliance official stated that part of the problem was that investigators conducting MDR inspections did not have the authority to discuss possible violations with the firm during the MDR inspection. He added that this was in marked contrast with their authority in good manufacturing practices inspections. After this type of inspection, and before leaving the establishment, inspectors fill out a form detailing observed problems, which they then leave with the inspected establishment. This list of observations subsequently is reviewed by field management for possible regulatory action. In contrast, inspectors tended to see their MDR program role as merely one of "collecting data for headquarters."[8]

A second problem with the MDR inspections stemmed from the data collection procedures originally followed, by which inspectors were not required to fill out a questionnaire or data collection form directly. Instead, analysts at the Center attempted to fill out the questionnaire on the basis of establishment inspection reports, in narrative form, submitted by the inspectors. When it became clear that these reports often did not contain enough information to permit the questionnaires to be filled out, all FDA district offices were given the questionnaires to guide the collection of the detailed information required during each inspection. Although inspectors' conclusions about establishments' compliance were then obtained by FDA, it was not always possible to ascertain how these conclusions were reached, so copies of documents obtained during inspections had to be requested.

Near the end of the first year of implementation, a revised version of the questionnaire form and program guidance was provided to the

[8]In commenting on a draft of this report, FDA stated that the program had recently undergone significant changes and that inspectors were now discussing possible MDR violations with the management of device firms at the conclusion of the inspections.

investigators. The revised questionnaire requests more detailed information about the establishments' MDR procedures, and about other matters such as their understanding of the "per se" reporting rule.[9] Center officials told us that they planned to delegate greater responsibility and authority to the district offices, and they began to do so in June 1988. This procedural change and the new questionnaire form were expected to produce better and more complete compliance data.

Results of the MDR Compliance Inspections

FDA officials indicated that the problems with the implementation of the MDR compliance program make the preliminary results difficult to interpret simply as measures of compliance with the MDR regulation. The main problem with the compliance data collected thus far is that in at least 120 cases, or 41 percent of the first series of inspections, and in 184, or 64 percent of those inspections conducted under the revised procedures, either the compliance program inspection had clearly not been performed as written in the guidance manual or there was a sufficiently serious question about whether it had been followed for the Center analysts to flag the conclusions and place the results in a separate subcategory. The result is that in the judgment of Center officials, there are many cases in which the information obtained was insufficient to determine whether the establishment was in compliance with the MDR requirements. Some conclusions about compliance were nonetheless drawn by the Center from these data, and some actions were taken by FDA in response to the findings. More detailed findings on the individual compliance items are also available for the second series of inspections and for at least some comparable items from the first series of inspections.

Conclusions reached by FDA on the first 291 MDR compliance inspections closed under the original procedures and 289 closed under the revised procedures are shown in tables 5.1 and 5.2. The inspection conclusions are statements about whether objectionable conditions were found during the inspection. They also record instances in which no inspection was conducted on site because, for example, the firm had gone out of business or was no longer making a product covered by the MDR regulation. The districts' decisions are actions that the FDA district offices take after considering (1) the conditions found during the inspection, (2) the

[9]Whenever a health-care professional advises a manufacturer that one of its devices may have caused or contributed to an event reportable under the MDR regulation, the manufacturer is "per se" in receipt of information that "reasonably suggests" that a device may have caused or contributed to a death or serious injury, and it therefore must report the event.

events that occurred following the findings (such as an immediate voluntary correction by the manufacturer or importer), and (3) agency policy and guidance.

Table 5.1: Inspectors' Conclusions for 575 Closed MDR Compliance Inspections

Conclusion	No. of inspections	Percent
No action indicated	410	71
Correction indicated	155	27
Referred to the Center for conclusion	9	2
Not an official establishment	1	0
Total	**575[a]**	**100**

[a]Although FDA provided data from 580 closed inspections, only 575 inspectors' conclusions were included.

Source: Division of Product Surveillance, Office of Compliance, the Center

Table 5.2: District Office-Center Review Conclusions for 572 Closed MDR Compliance Inspections

Decision	No. of inspections	Percent
No action indicated (concur with inspector)	308	54
No action indicated	170	30
Voluntary actions promised by manufacturers		
Routine reinspection	40	7
Accelerated reinspection	6	11
Voluntary actions taken by manufacturers	4	11
No inspection made	44	8
Total	**572[a]**	**100**

[a]Although FDA provided data for 575 inspectors' conclusions, there were only 572 corresponding district office-Center reviews.

[b]Percentages do not add to 100 because of rounding.

Source: Division of Product Surveillance, Office of Compliance, the Center

One indicator of the early problems with the implementation of MDR inspections is the fact that when FDA district offices and the Center reviewed the inspectors' reports, their conclusions often differed from those of the inspectors. For example, the district office-Center review concurred in only 54 percent of the cases with an inspector's conclusion that no further action was indicated. There is, however, some indication that agreement between the inspectors' conclusions and the results of the review is increasing. In the second series of inspections, the proportion of agreement between district office-Center review and the inspectors' conclusions of "no action indicated" increased to 63 percent.

Some findings from the second series of compliance inspections are shown in table 5.3. Ninety-seven, or 34 percent, of the establishments

whose inspections had been closed under the revised procedures indicated that they were not aware of the MDR rule.[10] Of the establishments that were aware of the rule, 50, or 26 percent, had not developed written procedures for handling MDR reports. The great majority of these establishments, 156, or 82 percent, had not submitted any MDR reports to FDA. In addition, 107, or 37 percent of the 289 inspected establishments, indicated that they had received no complaints about the medical devices they manufacture or import.

Table 5.3: Summary of MDR Compliance Inspection Findings[a]

	Yes		No		
Finding	No. of inspections	Percent	No. of inspections	Percent	Not applicable
Manufacturer aware of MDR regulation	192	66%	97	34%	
Have MDR procedures	142	74	50	26	
Have submitted MDR reports	34	18	156	82	
Familiar with "per se" rule[b]	153	80	39	20	
Aware dates met (timely MDR submission)	33	50	33	50	151
Text discrepancies[c]	3	4	69	96	120
Unreported corrective actions	4	5	76	95	
Severity and frequency data maintained	136	47	153	53	
Compliance acceptable	207	74[d]	74	26[d]	

[a]The table data are for 289 inspections in the second series of EIRs that had been closed as of March 24, 1988. Frequencies seldom add to 289 because inspections did not yield complete data on every item in the compliance questionnaire.

[b]See the glossary for a definition of the "per se" rule.

[c]Discrepancies between the narrative text of the MDR report filed with FDA and the text of the report received by the manufacturer.

[d]Because the inspected establishments were not a representative sample of registered establishments, these percentages cannot be generalized to the population of device firms.

Source: Division of Product Surveillance, Office of Compliance, the Center

The most frequently identified dimension of noncompliance noted by inspectors was failure to establish adequate procedures for handling

[10]FDA officials suggested that part of this "lack of awareness" on the part of firms might be attributable to new business starts and changes of ownership since the rule notification was issued in 1984.

complaints to determine their reportability (20 percent of all such citations for the first and 53 percent for the second series of inspections). Twenty-eight unreported deaths or serious injuries were uncovered in the first series of inspections, while only one was reported in an establishment's records during the second series, possibly indicating either that the selection procedure had successfully identified a larger proportion of noncomplying establishments for the first inspections than for the second or, conversely, that compliance is in fact improving.

Some immediate action (beyond a "friendly letter" notifying device firms of findings) was decided on for a fairly small number of establishments. These actions are presented in table 5.4. The most frequently recommended actions were notice of adverse findings (NAF) letters. Officials indicated that these letters were mainly employed in cases of failure to report a death or serious injury. In addition, inspectors identified four cases in which they recommended a device recall and one case in which a regulatory letter was recommended.

Table 5.4: Further Actions Taken on the Basis of MDR Compliance Inspections

Action taken	First series	Second series
Follow-up inspection	2	1
Request for additional information	1	1
Regulatory letter	1	0
Notice of adverse findings letter	12	2
Recommend recall	2	2
Other	6	3
Total	**24**	**9**

Source: Division of Product Surveillance, Office of Compliance, the Center

Inspectors found that a substantial number of reports of death and serious injury that device establishments claimed to have submitted to FDA were not listed on the printouts provided to field investigators prior to their inspections. They reported cases of unreported deaths or serious injuries for 153, or 80 percent, of those establishments in the second series of compliance inspections that were aware of the MDR regulation. Compliance officials said that in part this discrepancy could be the result of delays in entering reports into the data base, as well as of failures of communication between manufacturers and FDA.

Overall, judgments concerning the acceptability of compliance were made by inspectors in only 94 of the 291 closed inspections from the first series. Seventy-seven percent of the 94 inspected establishments

were judged to be in an acceptable state of compliance. This is slightly greater than the 74 percent acceptability figure for establishments inspected under the revised procedures (which were viewed with greater confidence). (See table 5.3.)

In assessing the results of inspections conducted thus far, FDA officials said they believed that, for the most part, larger device firms—those with regulatory departments—were attempting to comply with the regulation. The majority of device firms that had only vague ideas about the existence of the MDR regulation were reportedly small manufacturers of "innocuous" devices. FDA officials told us that their belief about the nature of the establishments that were not aware of the MDR regulation was largely intuitive and based on professional judgment without empirical support. A detailed analysis and report of the results of the first round of compliance inspections was to be conducted by Center analysts. However, it was not yet completed during the period of our review.

Conclusions

We have reviewed the available evidence concerning the proportion of device firms that have submitted problem reports under the provisions of the MDR regulation and FDA's efforts to ensure that firms are in compliance with the regulation.

Because FDA does not maintain an up-to-date file of device firms, the number of potential MDR reporters must be estimated. Estimates of the population of potential reporters vary, depend on assumptions that are difficult to evaluate, and sometimes appear arbitrary. Nevertheless, using even the most conservative of the estimates, it is clear that only a small proportion of the potential reporters have filed MDR reports during any of the first three years of the system's operation. At most only about one-quarter of the number expected by the Center have reported during any year. Evidence suggests that some device firms are "overreporting" and that others are either not reporting at all or are underreporting. Twelve device firms account for more than 60 percent of the reports for each of the years 1985-1987. Because data on device sales, market share, and device use—as well as on the true incidence of device problems—are also lacking, it is at present impossible to say how many more firms "ought" to be reporting, or what their appropriate reporting levels would be.

FDA has instituted a program of inspections in an effort to assess manufacturers' compliance with MDR reporting requirements by comparing

reports received with manufacturer complaint and service records. The compliance program has encountered difficulties in implementation, but preliminary results indicated that the majority (74 percent) of the establishments inspected were judged to be complying acceptably with MDR requirements. However, many manufacturers, especially those with smaller establishments, were found to have been unaware of the existence of the MDR requirements. The inspections also uncovered records of a number of deaths and serious injuries in firms' files that had not been reported to FDA.

Because early MDR inspections did not produce complete data, and because the establishments inspected were not selected to be a representative sample of the population of device manufacturers, preliminary compliance program results cannot be generalized to manufacturers' compliance as a whole. The result is that it is not at present possible to generate a reliable and unbiased quantitative estimate of the proportion of device firms that are in compliance with the MDR regulation, and thus FDA does not at present have a basis for determining whether the number of firms reporting under the MDR system represents an appropriate coverage of the population of device firms.

Conclusions, Recommendations, Agency Comments, and Our Response

The focus of our review was on the development, implementation, and the first three calendar years of operations of the MDR problem reporting system. We pursued four study objectives: (1) describe the level of information generated by the MDR regulation, (2) review the principal organizational structures and procedures of FDA's processing system for reports filed under the MDR regulation, (3) describe the analysis and use of the MDR data, and (4) describe the degree to which medical device firms are in compliance with the MDR reporting requirements.

Conclusions

Information Flow

Our review of the flow of information generated by the reporting requirements under the MDR regulation revealed that FDA annually receives about 18,000 medical device problem reports. These reports are in addition to the 2,500 reports FDA receives annually through the problem-reporting program (PRP). Reporting is concentrated among a relatively few medical specialties and devices within those specialties. Of the approximately 1,800 generic device types regulated by FDA, 10 devices accounted for about 63 percent of all reports submitted. Several of the devices that were identified in our study as being among the most frequently reported had been identified by FDA as problem devices even before the MDR data were available.

Overall, the cardiovascular medical specialty, with nearly 50 percent of all reports, had far more reports than any other specialty. The pacemaker, with 27 percent of all reports, was the device with the largest number of reports in the MDR data base from 1985 to 1987. It is logical that pacemakers, pacing leads, other implants, and ventilators account for a large proportion of problem reports because their failure, unlike that of most other device types, requires surgical intervention or places the patient at serious risk.

Underlying the 7 percent decline in overall reporting between 1985 and 1987 are variations in reporting activity for a few devices. One possible explanation of why problem-report statistics may be skewed for a given time period and specific device is that FDA has granted some firms alternative reporting requirement that permit reporting in monthly, quarterly, or yearly "batches." For example, in June 1987, one manufacturer submitted over 200 malfunction reports related to intra-aortic balloons.

Thus, in the month, quarter, or year that these manufacturers submit these reports to FDA, the totals would tend to be skewed.

It is not possible to make a definitive assessment of the proportion of the actual device-problem occurrences these reports represent. However, compared to the information FDA receives through PRP, the MDR regulation has clearly increased the number and types of medical device problems that FDA has information about. In addition, since MDR requirements apply only to the problems that a device firm has knowledge of, many potential sources of problem reports are excluded from reporting. For example, our earlier report found that hospitals were reporting to outside organizations about 46 percent of the problems that occur in hospitals.[1]

It was beyond the scope of this study to assess possible changes in the reporting behavior of hospitals or the screening effect of transmitting reports through device firms. However, as we concluded in our 1988 report, the enactment of legislation that would require hospitals to report to FDA would further increase the number of problems reported to FDA.

Organizational Structure and Procedures

FDA contracted with U.S. Pharmacopeia (USP) to receive and enter MDR reports of deaths and serious injuries into an automated data base. Under this contract, reports of device malfunctions are reported directly to FDA, analyzed, and subsequently forwarded to USP for computer entry.

The analysis and disposition of problem reports are primarily carried out by a team of 12 analysts in the Center's office of compliance. We found that the volume and types of the reports submitted and the complex nature of the Center's workflow were the principle factors contributing to a constant report processing backlog, and in some instances resulting in inefficiencies in analyzing and taking action on problem reports. For example, we found that close to one-third of the reports that FDA has received under the MDR system have not been fully processed to closure, including more than 10,000 malfunction reports. Many of the reports were submitted more than 2 years ago. Additionally, there were examples of critical information that had not been entered into the MDR data base in a timely fashion, including both

[1]See Medical Devices: FDA's Forecasts of Problem Reports and FTEs Under H.R. 4640 (GAO/PEMD-88-30, July 1988).

reports of deaths and serious injuries and records of actions that FDA had taken in response to problem reports.

This situation is made worse by the lack of formal written procedures for report analysis and reliance on informal training for analysts in the use of the computer and available Center data bases. In the final analysis, it is clear that analysts must make public-health decisions on less than the best available information.

We found several internal problems with the automated data processing facilities (such as limitations on the accessibility of the data base, lack of an automated thesaurus, delay in establishing statistical trend analysis capability, and unexpected results from data requests) which could affect the validity of device problem analysis and FDA's responses to problem reports. Additionally, although there are several data bases at the Center that relate to postmarketing surveillance (PMS), they are not integrated, easily accessible, or complete enough for adequate problem-report analysis.

Although FDA first proposed a mandatory adverse-experience reporting system more than 7 years ago, we found little evidence of overall system development and planning to efficiently handle the increased volume and types of reports that were expected to be generated by the MDR regulation. The current system functions basically as an individual device problem-reporting and tracking system, and is not able to provide quantitative analysis of problem-reporting patterns.

Analysis and Use

Individual problem report analysis consists primarily of a causal evaluation and report disposition. Over one-third of all the reports that were received by the Center between 1985 and 1987 had not been closed with causal evaluations or report dispositions. The cause of the device problem was tentatively identified in half the reports evaluated. In 77 percent of these reports for which a cause was indicated, the device itself, rather than user error or other factors, was found to be the cause.

The MDR data base documents very little use of the MDR data by FDA. The final disposition of more than 60 percent of reports indicated that they were closed as historical references, which means that no action by FDA or the firm was taken or judged to be appropriate at the time. The data tape we analyzed contained very few instances of traditional FDA regulatory actions that could be linked directly to the MDR data. One report

was associated with a product seizure, and one with an NAF letter. However, narrative information supplied by the Center does indicate that MDR data may have played an important role in the resolution of a number of device problems, leading to recalls, design and labeling changes by firms, issuance of safety alerts by FDA, and one educational program for device users.

Coverage and Compliance

Reporting is concentrated among a relatively small number of device firms. However, FDA could not provide us with a total number of firms that are subject to the reporting requirements of the MDR regulation; therefore, any assessment of the degree of the device firms' compliance with the MDR requirement is at best a guess. Our analysis, which compared the actual number of firms that have made an MDR report to the smallest of several estimates of the number of potential reporters, indicates some unspecified degree of underreporting or noncompliance.

The first round of establishment inspections designed to assess compliance is currently under way. Although many of the early inspections were not properly implemented and did not provide complete information, FDA concluded that the majority of firms were in compliance. We agree that a well-executed program of inspections is the best approach to assessing manufacturers' compliance. However, the procedure FDA used to select the sample of firms for inspection, the implementation of the inspections, and the preliminary results do not permit generalization to the population of potential MDR reporters.

Recommendations

This study and two recent assessments of the PMS system—by an FDA study group and an outside contractor—have all identified problems that severely limit the use and usefulness of the MDR data and the overall effectiveness of FDA postmarketing surveillance efforts. Recommendations aimed at the development of a centralized, integrated, and comprehensive PMS system were made in both of the previous assessments.

The implementation of the recommendations made in these previous reports may improve the quality and usefulness of the MDR data base and the overall operating efficiency of the PMS system. In addition, an adequate implementation of the MDR regulation should couple these system improvements with an expansion of Center efforts to determine the population of device firms subject to the MDR reporting requirements, the development and consistent implementation of a sound methodology

to assess the degree of compliance, and documentation of the uses made of MDR data.

Specifically, we recommend that the Secretary of Health and Human Services

- require all firms that manufacture or import medical devices to submit an annual statement indicating either that they filed no MDR reports during the calendar year because they did not receive or otherwise become aware of information concerning MDR-reportable events, or that they filed a specific number of reports on each type of reportable event and that the firm received or became aware of information concerning only these events;
- ensure that FDA completes a methodologically sound program of MDR compliance inspections that would permit valid generalization of the results to the population of device manufacturers and importers (that is, select establishments for inspection on a sound statistical basis);
- encourage FDA to continue to strengthen their documentation of the use of MDR data in taking corrective actions on device problems, especially by ensuring that such actions are recorded in the MDR data base.

Agency Comments and Our Response

HHS found GAO's draft report to be a fair and generally factual discussion of the MDR program, and concurs with our recommendation that FDA improve documentation of MDR data use in correcting device problems, especially by recording corrective actions in the MDR data base. The HHS comments (located in appendix III) also describe a number of initiatives addressing this and other issues raised by our findings that either were undertaken after we completed our data collection or were planned for the near future. These include the establishment of a historical index of significant MDR issues and an MDR issue tracking system, review of the recall and MDR data bases to ensure proper cross-referencing and coding of corrective actions, development of new procedures for tracking and acting on MDR reports, change of procedures for processing malfunction reports to increase efficiency, and delegation of responsibility for regulatory and administrative follow-up of MDR compliance inspections to the FDA district offices.

HHS does not concur with our recommendation that the agency require device manufacturers to submit an annual statement affirming that the number of reports submitted cover all reportable events of which the company has learned during the preceding year. The agency feels that

such a requirement would be unduly burdensome for both manufacturers and the agency and would provide no additional public health benefit. HHS also states that its strategy for scheduling MDR compliance inspections makes it unnecessary to sample establishments in such a way that the results of inspections on the sample are validly generalizable to the population of manufacturers, because current plans will result in the inspection of all class II and III firms at least once every 4 years (including the placing of special emphasis on firms manufacturing types of devices that have been the subject of MDR reports and the scheduling of more frequent inspections for specific device types as needed). HHS's current plans also call for less frequent inspections of manufacturers of class I devices.

We were unable to review those Center initiatives described in the HHS comments that were intended to improve the operation of the MDR system, because they were all either begun after we had ceased data collection or were still in the planning stages.

GAO believes that the submission of a single annual letter—which for the majority of firms would merely assert that they had nothing to report and for others only that the stated number of reports submitted covered all MDR reportable events of which the firm became aware—would not constitute an undue burden. It could be processed as part of the annual re-registration of establishments and would provide data that could confirm or correct FDA's conclusion that the limited number of firms reporting under MDR is what is to be expected (given the number of firms who manufacture only class I devices). Most importantly, the annual letters would resolve the problem of the lack of awareness on the part of many manufacturers that they must provide early warning of any reportable problems with their devices (even if these devices are thought to be innocuous).[2]

GAO believes that the proposed annual statement would not only serve as a compliance instrument but also would provide FDA and outside analysts and decision makers with valuable information about the implementation of the MDR regulation. First, it would provide an annually updated listing of device firms, which are the reporting entities under the MDR regulation. Although FDA maintains an annually updated listing

[2]In developing the 1983 reproposal of the MDR rule, FDA considered exempting class I or class I and class II device manufacturers, but rejected the idea because such manufacturers would be likely to have few reports to make even without an exemption. FDA also argued that "if a device has caused or contributed to a death or serious injury or has malfunctioned and recurrence of the malfunction is likely to cause or contribute to a death or serious injury, its level of classification is irrelevant."

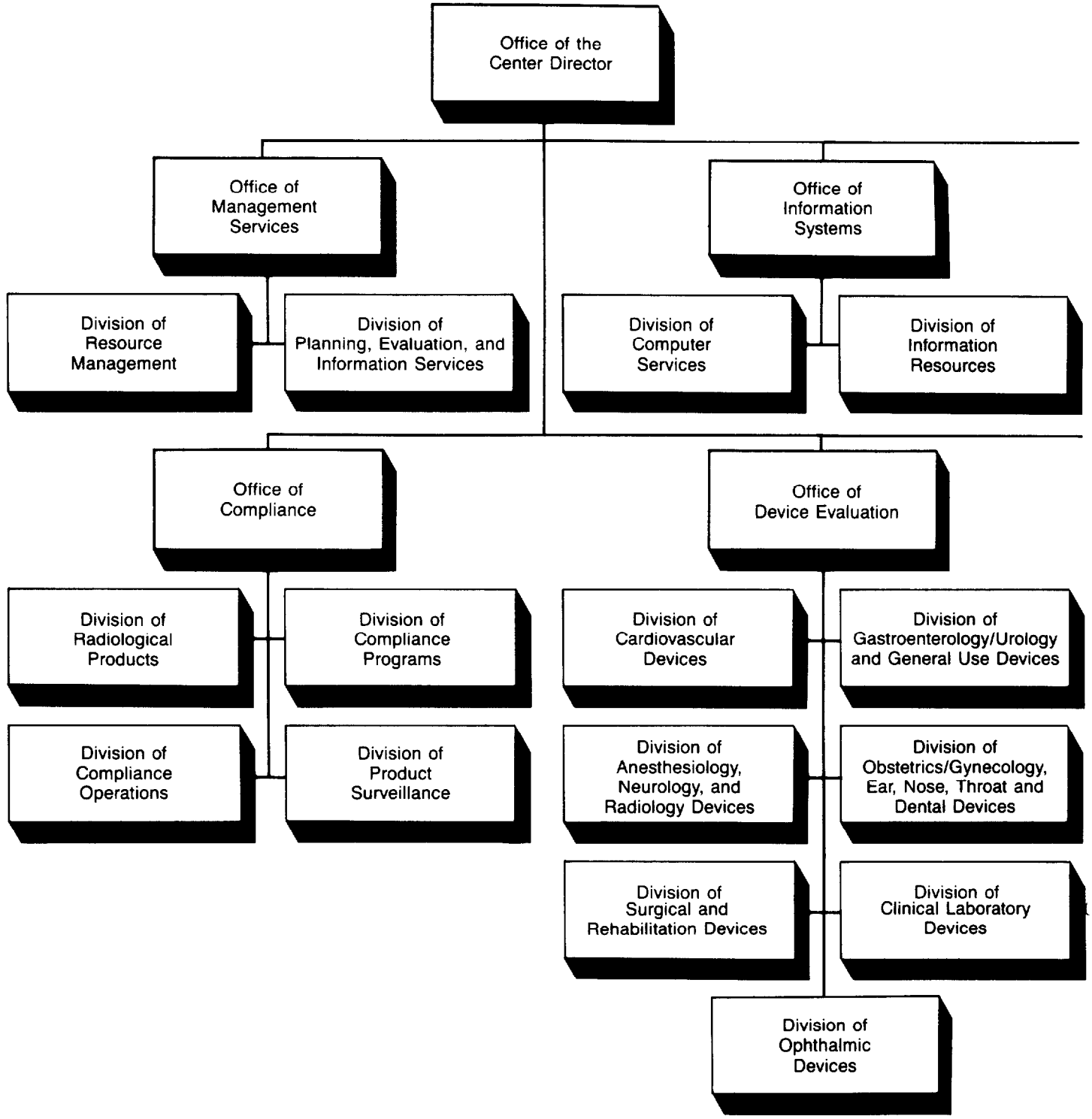
of device establishments, the structure of the industry makes it necessary to estimate the number of firms in existence from the number of establishments registered (using an accepted rule of thumb such as ".75 x the number of establishments registered = number of firms"). Second, requiring such statements will provide an annual basis for interpreting the number of firms who have reported during the year. At present, nonreporters who believe they have not received information about MDR-reportable events cannot be distinguished from those firms that have not heard about or understood their reporting requirements under MDR or are otherwise in noncompliance (with the exception of firms that have been inspected during the course of that year). Third, such statements will provide an indication of the effectiveness of FDA's program to educate the industry regarding MDR requirements (by distinguishing those firms that do not believe that they have received information about MDR-reportable events from those that remain unaware of MDR in spite of the education program, and that thus will presumably fail to file the statement). The statements will also allow FDA to check the number of each type of reportable event a firm claims to have submitted during a particular year against the reports in the MDR data base, and to investigate discrepancies that suggest some reports may have been "lost" or delayed in the processing system.

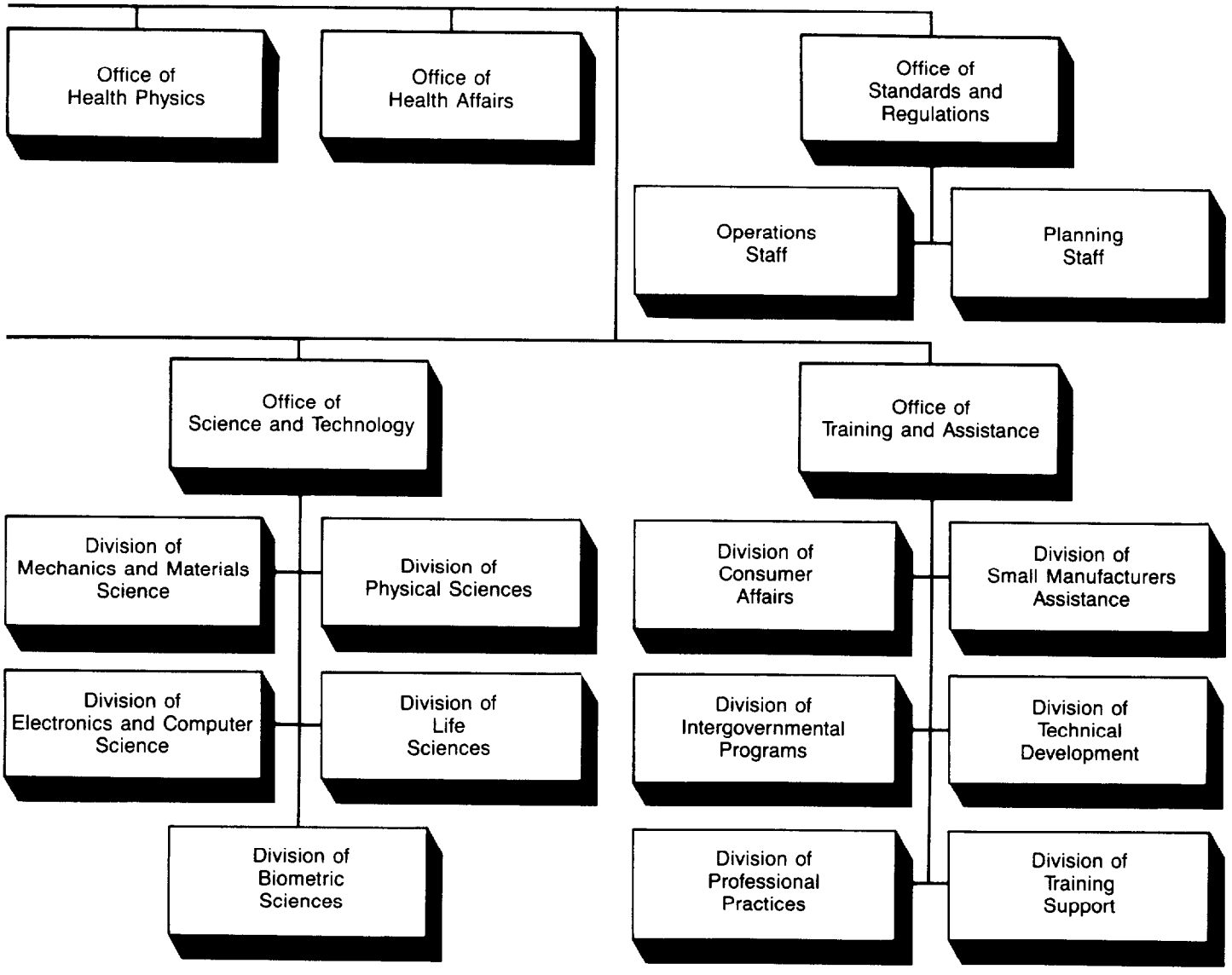
GAO's view of FDA's preferred judgmental selection process for scheduling MDR compliance inspections (leading to a census of establishments within four years) is that such a procedure may be justified at the beginning of the program (when the primary goal of compliance inspections is to educate manufacturers and induce compliance with reporting requirements). However, when the chief program goal becomes the production of unbiased estimates of the industry's state of compliance, the consequence of adopting this procedure will be to render the goal unachievable—that is, statistics produced before the completion of the census cannot be validly generalized to the population of device firms. In addition, many of the early inspection results may be out of date by the time the census is complete.

In contrast, a random sample can be stratified to ensure that important types of manufacturers are included, and those establishments targeted by a judgmental selection can always be added to the list produced by random sampling if they have not been selected in the random draw. GAO therefore continues to believe that its recommended action is warranted. If the agency continues to use its present judgmental procedures, GAO believes that, at minimum, the limitations of any interim summaries

of MDR compliance-inspection results must be pointed out. (HHS also provided other comments to which we have responded by revising the text of the report as appropriate.)

Center for Devices and Radiological Health Organizational Chart





Source: the Center, Resource Manual (Rockville, Md.: FDA, October 1986).

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Comments From the Department of Health and Human Services Comments From the Department of Health and Human Services

COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES ON THE GENERAL ACCOUNTING OFFICE DRAFT REPORT "MEDICAL DEVICES: FDA'S IMPLEMENTATION OF THE MEDICAL DEVICE REPORTING REGULATION," October 1988

We have reviewed the draft report and find it to be a fair and generally factual discussion of the program.

GAO Recommendation

We recommend that the Secretary of Health and Human Services:

--Consider requiring that all registered device establishments who do not submit MDR reports during a given year submit at a minimum a statement indicating that they did not receive or become aware of MDR reportable events involving their devices during the preceding year.

Department Comment

We do not concur. To require firms to submit the statements described by GAO would place an unnecessary burden on them, as well as on the limited resources of FDA. The Medical Devices Reporting (MDR) regulation limits reporting to only very serious or potentially serious events and does not anticipate reporting by every medical device firm. For instance, firms that manufacture only Class I devices would seldom, if ever, have a reportable event occur. We, therefore, believe GAO's conclusion of underreporting by the industry is questionable. FDA's projection of expected reports was relatively low based upon its knowledge of devices that have the potential to generate reportable events. We would expect a limited number of firms to be making reports, which has been the agency's experience to date. Further, the extra resources required to process the statements described by GAO would provide no additional public health protection.

To assure that device manufacturers do understand and follow the regulations, FDA has undertaken an extensive program to educate the industry regarding MDR requirements. This program includes conducting regulatory workshops issuing technical publications, responding to numerous telephone inquiries, and sending a list of MDR questions and answers to all registered firms to provide them with guidance regarding compliance with and interpretation of the regulations. Firms that are inspected and found to be out of compliance with MDR requirements are also informed of the requirements and specifically directed to take corrective action.

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GAO Recommendation

--Ensure that FDA completes a methodologically sound program of MDR compliance inspections on a set of establishments sampled in such a way as to permit valid generalization of the results to the population of device manufacturers and importers.

Department Comment

We do not concur. The MDR inspection strategy adopted by FDA will result in an MDR compliance inspection of every firm manufacturing Class II and Class III devices at least once every 4 years. FDA's practice is to carry out MDR inspections in conjunction with Good Manufacturing Practices inspections, which allows the Agency to do MDR inspections at a minimal cost. FDA's strategy also includes placing special emphasis on firms manufacturing the types of devices that have already experienced reportable events, scheduling more frequent MDR inspections for specific device types as the need arises, and incorporating manufacturers of Class I devices on a less frequent basis. We believe this strategy precludes the need for the recommended sampling program.

GAO Recommendation

--Encourage FDA to continue to strengthen their documentation of the use of MDR data in taking corrective actions on device problems, especially by ensuring that such actions are recorded in the MDR data base.

Department Comment

We concur. A number of activities are underway to strengthen documentation in various areas. A historical index of significant MDR issues has been compiled, and all individual MDR reports that are involved with each issue are referenced. An Issue Tracking System that rapidly identifies MDR issues and ensures that they are evaluated, resolved, and documented has been established. The Recall and MDR data bases have been reviewed to ensure proper cross referencing and coding of MDR and Recall data that involve corrective actions. FDA is also improving procedures to ensure that corrective actions associated with MDR are promptly entered into the data base. These improvements will require redesign of the report processing, internal systems, and computer programs. These enhancements will be undertaken as funds and staff are available.

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Glossary

Anesthesia Gas Machine	A device used to administer to a patient, continuously or intermittently, a general inhalation anesthetic and to maintain a patient's breathing. The device may include a gas flowmeter, vaporizer, ventilator, breathing circuit with bag, and emergency air supply.
Apnea Monitor	A device intended to measure or monitor a patient's respiratory rate. The device may provide an audible or visible alarm when the respiratory rate is outside predetermined limits.
Class I Device	One of the three regulatory classes set up by the Medical Device Amendments of 1976. Class I, general controls, contains devices for which general controls authorized by the act are sufficient to provide a reasonable assurance of safety and effectiveness. Manufacturers of class I devices must, among other things, register their establishments, list their devices with FDA, notify FDA 90 days before marketing a device, and conform to good manufacuring practices.
Class II Device	A regulatory class of devices for which general controls are insufficient to provide a reasonable assurance of safety and effectiveness and for which scientific information is sufficient to establish performance standards to provide such assurances. the general controls provisions for class I devices under the the Medical Device Amendments of 1976 also apply to class II devices.
Class III Device	A regulatory class of devices for which general controls are insufficient to ensure safety and effectiveness, for which scientific information does not exist to establish performance standards, and in which the devices support life, prevent health impairment, or present a potentially unreasonable risk of illness or injury. The general controls provisions for class I devices under the Medical Device Amendments of 1976 also apply to class III devices.
Class I Recall	A situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death.

Class II Recall	A situation in which the use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences, or when the probability of serious adverse health consequences is remote.
Class III Recall	A situation in which the use of, or exposure to, a violative product is not likely to cause adverse health consequences.
Contact Lens	A device intended to be worn directly against the cornea of the eye to correct a defect of vision. (Contrast with Intraocular Lens.)
Defibrillator (Including Paddles)	A device used for defibrillating (restoring normal heart rhythm) to the atria or ventricles of the heart or for eliminating other cardiac arrhythmias through delivery of an electrical shock. The device may either synchronize the shock with the proper phase of the electrocardiogram or may operate asynchronously. The device delivers the electrical shock through paddles placed either directly across the heart or on the surface of the body.
Dialysis System and Accessories	An artificial kidney system for the treatment of patients with kidney failure or toxemic conditions. It consists of a peritoneal access device, an administration set for peritoneal dialysis, a source of dialysate, and in some cases, a water purification mechanism. The system may also regulate and monitor the dialysate temperature, volume, and delivery rate, together with the time course of each cycle of filling, dwell time, and draining of the peritoneal cavity. A disposable administration set for peritoneal dialysis consists of tubing, an optional reservoir bag, and appropriate connectors. It may include a peritoneal dialysate filter to trap and remove contaminating particles.
Diagnostic Intravascular Catheter	A device used to record pressures within the heart, to sample blood, and to introduce substances into the heart and vessels. Included in this generic device type are right-heart catheters, left-heart catheters, and angiographic catheters.
Explant	To transfer from the body. The surgical removal of an implanted device such as a pacemaker or heart valve.

Glucose Monitor	A device used to measure blood glucose quantitatively, using hexokinase or another in vitro diagnostic reagent. Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders, including diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia, and pancreatic islet-cell carcinoma.
Heart Valve (Replacement)	A device intended to perform the function of any of the heart's natural valves. This device type includes valves constructed of prosthetic materials, biologic valves (for example, porcine valves), and valves constructed of a combination of prosthetic and biologic materials.
Hexokinase (Glucose Test System)	Hexokinase is an in vitro diagnostic reagent used in a glucose test system intended to measure quantitatively glucose in blood. (See Glucose Monitor.)
Infusion Pump	A device used to pump fluids into a patient in a controlled manner. It may use a piston pump and may be powered either electrically or mechanically. The device may also operate by using a constant force to propel the fluid through a narrow tube that determines the flow rate. The device may include the means to detect a fault condition—such as air in, or blockage of, the infusion line—and to activate an alarm.
Intra-Aortic Balloon and Control System	An inflatable balloon that is placed in the aorta to improve cardiovascular functioning during certain life-threatening emergencies, and a control system for regulating the inflation and deflation of the balloon. The control system, which monitors and is synchronized with the electrocardiogram, provides a means for setting the inflation and deflation of the balloon according to the cardiac cycle.
Intraocular Lens	An implanted device made of a material such as glass or plastic and intended to replace the natural lens of an eye. (Contrast with Contact Lens.)
Intravascular (I.V.) Administration Set	A set of devices used to transfer fluids from a container to a patient's vascular system through a needle or catheter inserted into a vein. It may include the needle or catheter, tubing, a flow regulator, a drip chamber,

	an infusion line filter, an I.V. set stopcock, fluid delivery tubing, connectors between parts of the set, a side tube with a cap to serve as an injection site, and a hollow spike to penetrate and connect the tubing to an I.V. bag or other infusion fluid container.
Intrauterine Device (IUD) And Introducer	A contraceptive device placed high in the uterus, with a string extending from the device into the vagina. This generic device type includes the introducer but does not include contraceptive IUDs that function by drug activity, which are subject to the new-drug provisions of the Federal Food and Cosmetic Act.
Pacemaker	A device with a power supply and electronic circuits that produce a periodic electrical pulse to stimulate the heart. It is used as a substitute for the heart's intrinsic pacing system to correct both intermittent and continuous cardiac rhythm disorders.
Pacemaker Electrode	Also called a "pacemaker lead." A device that consists of flexible, insulated electrical conductors with one end connected to an implantable pacemaker pulse generator and the other end applied to the heart. It is used to transmit a pacing electrical stimulus from the pulse generator to the heart and from the heart to the pulse generator.
Per Se Rule	Requires a device manufacturer to report to FDA whenever a health care professional provides the manufacturer with information indicating that a death, serious injury, or malfunction (that would be likely to cause or contribute to a death or serious injury if it were to recur) has occurred and, in addition, the health care professional has used the words "death," "serious injury," "malfunction," or equivalent language. In such instances, the manufacturer is "per se" in receipt of information that "reasonably suggests" that a device may have caused or contributed to a death or serious injury, or has malfunctioned as previously described, and therefore the manufacturer must report the event under the MDR regulation.
Respiratory Gas Humidifier	A device that adds moisture to, and sometimes warms, the breathing gases administered to a patient.

Unscented Menstrual Tampon	A plug made of cellulosic or synthetic material that is inserted into the vagina and used to absorb menstrual or other vaginal discharge. This generic device type does not include menstrual tampons treated with scent (fragrance materials) or those with added antimicrobial agents or other drugs.
Ventilator	Also called a respirator. A device intended to mechanically control or assist patient breathing by delivering a predetermined percentage of oxygen in a breathing mixture. Adult, pediatric, and neonatal ventilators are included in this generic device type.

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