United States General Accounting Office

GAO

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

May 1990

MEDICAL DEVICES

Underreporting of Serious Problems With a Home Apnea Monitor

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GAO/PEMD-90-17

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United States
General Accounting Office
Washington, D.C. 20548

Program Evaluation and
Methodology Division

B-237533

May 31, 1990

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

Dear Mr. Chairman:

In February 1989, we reported to the Subcommittee that our review of the implementation of the medical device reporting regulation had found evidence that some medical device manufacturers may have been over-reporting problems with devices, while others either were not reporting at all or were underreporting.[1] In its comments on the report, the Food and Drug Administration (FDA) said that our conclusion that the industry was underreporting was "questionable" and that FDA's medical device reporting regulation compliance inspection strategy was sufficient to identify compliance problems. Since the release of our report, we have received additional information from several sources that suggests that problems are underreported and that underreporting is not always identified through FDA's inspection program.[2]

On September 18, 1989, you asked us to investigate a citizen's report to the General Accounting Office (GAO) of numerous unreported deaths of patients associated with the Aequitron Medical, Inc., Model 8200 home apnea monitor and to include our investigation in our ongoing review of FDA's postmarketing surveillance of medical devices for the Subcommittee. With the concurrence of the Subcommittee staff, we undertook a case study based on three specific questions: (1) How many complaints involving the death of patients have been associated with the Model 8200 apnea monitor? (2) Did the device manufacturer comply with FDA's existing problem-reporting regulations and procedures? (3) When FDA received information from the device manufacturer or other sources that Model 8200 had been associated with numerous deaths, what actions did FDA take in response to that information? This letter presents our findings, conclusions, and recommendations.

[1]See U.S. General Accounting Office, Medical Devices: FDA's Implementation of the Medical Device Reporting Regulation, GAO/PEMD-89-10 (Washington, D.C.: February 1989), p. 3.

[2]The sources included citizen reports, device industry publications, consultation with members of our expert review panel, and review of individual recalls in connection with our earlier report entitled Medical Device Recalls: Examination of Selected Cases, GAO/PEMD-90-6 (Washington, D.C.: October 1989).

overall efficacy of the FDA medical device reporting regulation compliance program and, in particular, the finding that a number of FDA inspections had discovered instances in which reportable serious injuries and deaths had been recorded in a manufacturer's files but not reported to the agency.

This study of an apnea monitor is consistent with our earlier finding of differences in the interpretation of medical device reporting requirements.[5] In this case, a manufacturer's interpretation of the requirements has resulted in the underreporting of serious problems associated with its device. It also illustrates a weakness in the compliance inspection process. Although the manufacturer had been the subject of several inspections, it was nearly 4 years after the medical device reporting regulation went into effect before FDA's inspection program identified and attempted to resolve the underreporting.

Background

Medical devices include almost everything, other than drugs, that health-care professionals use to diagnose, treat, or prevent illness, improve human functioning, and support and sustain life.[6] More than 1,700 different types of medical devices are available in the United States today. They represent an industry of more than $14 billion a year. FDA is authorized to regulate medical devices during all phases of their development, testing, production, distribution, and use.

FDA has identified the apnea monitor as a "critical device." Critical devices are intended for surgical implant into the body or to support or sustain life. Their failure to perform when used properly in accordance with instructions provided in the labeling can be reasonably expected to result in a significant injury to the user.

[5]Medical Devices, p. 4.

[6]Section 201(h) of the Federal Food, Drug, and Cosmetic 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, that is (1) recognized in the official National Formulary or the U.S. Pharmacopeia or any supplement to them, (2) intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, in 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 amendments 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.

Aequitron Medical, Inc., Model 8200 home apnea monitor. The table contained 82 complaints with four categories of information for each complaint.[9] (The table is reproduced in appendix I.)

Our investigation of the origin and contents of the HID file determined it to be a list of complaints derived from the device manufacturer's "hazard, injury, or death" GMP record. The list contained complaints that the device manufacturer had received about its Model 8200 apnea monitor dated between January 1983 and January 1989.[10]

Our analysis of the HID file showed that it listed 68 complaints in which the word "death" was included in the category of reasons for the device's return to the manufacturer. Further research found that a similar list drawn from the manufacturer's general complaint record contained 2 additional complaints in which the word "death" was included. There were therefore a total of 70 complaints in which the allegation of a patient's death was included in the complaint description.[11] The remaining 14 complaints in the HID file were complaints that included allegations of either hazards to safety or injuries. (See table 1. The remainder of the table is discussed below.)

Table 1: Complaints and Medical Device Reporting Regulation Reports on Aequitron Medical, Inc., Model 8200 Apnea Monitor

	Complaints in Aequitron's files			Medical device reporting regulation reports to FDA		
	In "H/I/Death File"	In "general" file	Total	Before FDA's May 1988 inspection	After FDA's May 1988 inspection	Total
Deaths	68	2	**70**	5	2	**7**
Nondeaths	14	66	**80**	78	193	**271**
Total	**82**	**68**	**150**	**83**	**195[a]**	**278**

[a]150 of these reports were submitted in response to FDA compliance actions.

[9]The four data categories for each complaint were serial number, date, reason for return, and analysis. It is important to note that with regard to the "analysis" category, the general limitations of the technology employed in apnea monitors or the specific limitations of the design of a particular model may cause a monitor to fail to detect apnea events in some circumstances. Such an occurrence is known as a "false negative." If this happens, later testing of the monitor would not necessarily reveal that a component had malfunctioned, and the device could be found to be "within specifications."

[10]Model 8200 was introduced into the market in June 1982. According to the manufacturer, approximately 30,000 of the monitors were distributed between 1982 and 1987, but it is not possible to estimate the number in actual use or their frequency of use.

[11]The manufacturer confirmed that these were complaints alleging a death had been associated with the use of the device.

record, FDA found that 10 unreported complaints should have been reported, including 4 that alleged the death of patients.[13]

It is important to note that not all incidents in which a device is associated with the death of a patient must necessarily be reported to FDA under the medical device reporting regulation. The regulation requires reporting of incidents to FDA only if the information in the possession of the manufacturer "reasonably suggests" that a device may have caused or contributed to a death or a serious injury. If a health care professional states that this has happened, then the manufacturer is required to file a medical device report.[14] But in the case of a report from a layperson, if an immediate investigation by the manufacturer reveals that a patient was not connected to an apnea monitor at the time of death, or that the monitor's alarm sounded and the caregiver was alerted even though the patient could not be revived, then a report might not be required. FDA has characterized the circumstances in which home apnea monitors are used and the limitations of the technology they employ as sometimes making it difficult to determine whether a problem is reportable under the medical device reporting regulation.

Question 3: FDA's Actions

When FDA received information from the device manufacturer or other sources that Model 8200 had been associated with numerous deaths, what actions did FDA take in response to that information? One of the principal tools of FDA's postmarketing surveillance of medical devices is biennial inspections for compliance with the GMP regulation. In addition, FDA conducts "for cause" inspections when they are warranted by complaints or other evidence of problems with devices.[15] FDA assesses device manufacturers' compliance with the medical device reporting regulation by executing a special medical device reporting inspection program as

[13]A more detailed discussion of this review is contained in the following section of this report on FDA's actions.

[14]The "per se" reporting rule states that whenever a health care professional advises a manufacturer that one of its devices may have caused or contributed to a serious injury or death, the manufacturer is "per se" in receipt of information that "reasonably suggests" that a device may have caused or contributed to a serious injury or death, and it therefore must report the event. It does not, however, imply that reports from persons other than health care professionals are not reportable.

[15]A principal rationale for "for cause" inspections is information developed by FDA analysts who monitor and compare reports submitted through FDA's voluntary problem-reporting program, device recalls, and the medical device reporting system.

"per se" provision of the medical device reporting regulation and company policy, Aequitron did not submit these types of reports.

In our earlier study of the implementation of the medical device reporting regulation, we reported that the evidence suggested an undetermined amount of overreporting by some device manufacturers and that others were either not reporting or underreporting.[18] The most frequently identified dimension of noncompliance noted by FDA inspectors was failure to establish adequate procedures for handling complaints to determine their reportability (20 percent of all such citations for the first series of medical device reporting regulation compliance inspections and 53 percent for the second series).[19] We also encountered variations in the interpretation of reporting requirements among the FDA officials and staff we interviewed.

As a result of the October 1988 notice-of-adverse-findings letter and negotiations between FDA officials and the apnea monitor manufacturer, the manufacturer agreed to review its complaint records and revise its medical device reporting policy. Subsequently, Aequitron submitted medical device reports on 6 of the 10 incidents listed in the notice-of-adverse-findings letter, including 2 of the complaints in the HID file involving deaths. These 2 reports of death were submitted 1 year and 9 months, respectively, after the events they described. The manufacturer also submitted 144 reports of malfunctions involving confirmed alarm failures.[20] Aequitron thus submitted at least 150 medical device reports in response to FDA compliance actions. (See table 1.)

Aequitron also submitted a revised medical device reporting policy to FDA, and FDA notified the manufacturer that its revised policy was adequate. We found certain aspects of the revised reporting policy to be inconsistent with the medical device reporting regulation. Specifically, we believe that it is improper to condition the reporting criteria on the confirmation or observation of a malfunction. (Our complete analysis is contained in appendix III.)

[18]See Medical Devices, p. 61.

[19]See Medical Devices, p. 59.

[20]Apnea monitor alarms meet FDA's definition of a "critical device component"—that is, any component of a critical device whose failure to perform can be reasonably expected to cause the failure of a critical device or to affect its safety or effectiveness

FDA did not provide evidence that its inspection procedures included any systematic evaluation of trends in the frequency, type, or severity of complaints involving the failure of alarms that were made to the manufacturer or reported under the medical device reporting regulation. There were also no comparisons of overall complaint rates of alarm failures of Aequitron's Model 8200 to those of other monitors. The inclusion of these procedures in the inspection program could have served to more quickly identify both problems of underreporting and potentially serious device problems.

Conclusions, Recommendations, and Agency Comments

Conclusions

We conclude that the evidence from the current case of an apnea monitor is consistent with our earlier finding that there are differences in the interpretation of medical device reporting requirements among device manufacturers and between manufacturers and FDA.[23] In this case, the manufacturer's interpretation resulted in an undetermined amount of underreporting of serious problems with a device.

We found that FDA's review of a sample of Aequitron's records determined that some complaints alleging that the device was associated with hazards to safety, injuries, or death had not been reported to the agency because of the manufacturer's interpretation of the medical device reporting requirements.

As a result of FDA's intervention in this case and the device manufacturer's review of its own records, 144 additional medical device reports of malfunctions were submitted. We believe that malfunction reports should be considered as seriously as reports of serious injury or the death of a patient, especially as a preventive measure. Malfunction reports 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 injury or even death.

[23]See Medical Devices, p. 62.

and consider developing specific guidance for the manufacturers of any devices, such as apnea monitors, for which determining reportability is thought to present special difficulties.

Agency Comments and Our Response

The Department of Health and Human Services (HHS) agreed with our recommendations and reported that FDA had taken actions consistent with them. FDA conducted a comprehensive good manufacturing practices and medical device reporting regulation inspection of Aequitron and is currently reviewing the results to determine what regulatory action is warranted. The agency is also considering the development of device-specific guidance on medical device reporting and has established a study group to analyze the medical device reporting regulation and program, identify problems, and recommend solutions.

HHS's general comments indicated a concern that this case study is not an accurate representation of the way the medical device reporting regulation is implemented by most device manufacturers and that its findings cannot be generalized to the program as a whole. We agree that the case does not by itself support generalizations about the implementation of the medical device reporting regulation. The general statements in the report about the implementation of the medical device reporting regulation and its associated compliance inspection program are based on our earlier, general study of these issues. The case does, however, illustrate the principal findings of that report regarding compliance with the medical device reporting regulation. HHS's comments, along with our detailed responses, are reproduced in appendix IV.

HHS also provided technical comments on the report. We reviewed them and made changes in the report as appropriate. In one technical comment worth noting, HHS agreed with our opinion in appendix III, acknowledging that FDA's Center for Devices and Radiological Health made an error in allowing Aequitron to condition its reporting of complaints on the confirmation or observation of a malfunction. HHS stated that the firm was notified of the correct interpretation at the time of the inspection referred to above.

Objective, Scope, and Methodology

This review was a follow-up to our earlier general overview of FDA's implementation of the medical devices reporting regulation. The objective of this study was to conduct a case study of medical device problem reporting and FDA actions related to the Aequitron Medical, Inc., Model

Abbreviations

FDA	Food and Drug Administration
GAO	General Accounting Office
GMP	Good Manufacturing Practices
HHS	Department of Health and Human Services
HID	Hazard, Injury, Death

Number	Serial number	Date	Reason/return	Analysis
40	110139	12/86	Checkout only-death	Device in-spec
41	204165	12/86	Checkout death-no-alarm	Device in-spec
42	108272	1/87	Checkout only-death	Device in-spec
43	204768	1/87	Checkout only-death	Device in-spec
44	54319	1/87	Checkout only-death	Device in-spec
45	101216	4/87	Checkout only-death	Device in-spec
46	110870	4/87	Checkout death-no alarm	Device in-spec
47	108197	4/87	Checkout only-death	Device in-spec
48	105515	6/87	Checkout only-death	Device in-spec
49	63510	6/87	Checkout only-death	Device in-spec
50	54121	8/87	Checkout only-death	Device in-spec
51	106034	6/87	No 10 sec. apnea alarm	Device in-spec
52	202394	10/87	Checkout only-death	Device in-spec
53	60184	10/87	Checkout death-no apnea alarm	Device in-spec
54	66740	12/87	Checkout only-death	Device in-spec
55	110447	12/87	Checkout only-death	Device in-spec
56	63934	1/88	Checkout-death-no alarm	Device fully functional
57	111579	7/88	Checkout death	No other details avail
58	104348	8/88	Checkout only-death	Device in-spec
59	103552	1/88	Checkout only-death	Device in-spec
60	50657	1/88	Checkout only-death	Device in-spec
61	204894	1/88	Checkout only-death	Device in spec
62	104635	1/88	Checkout only-death	Device in-spec
63	52877	2/88	Checkout only-death	Device in-spec
64	201228	3/88	Checkout only-death	Device fully functional
65	66086	3/88	Checkout death-no audible alarm	Device in-spec
66	62873	3/88	Checkout only-death	Device in-spec
67	50903	3/88	Checkout only-death	Device in-spec
68	54569	3/88	Checkout death-no alarm	Device fully functional
69	250197	4/88	Checkout only-death	Device in-spec
70	205002	1/88	Checkout only-no apnea alarm	Device in-spec
71	108359	1/88	Checkout only-no brady alarm	Device fully functional
72	250215	6/88	Checkout only-death	Device in-spec
73	202134	6/88	Checkout death-no alarm	Device in-spec
74	205881	8/87	Checkout only-death	Device gave constant al
75	110094	6/88	Checkout only-death	Device not received
76	201785	5/88	Checkout only-no alarm	Device not received
77	66250	11/88	Checkout only-death	Device in-spec
78	201785	11/88	No apnea alarm-pt Ok	Device in-spec
79	51130	1/89	Checkout only-death-not in use	Device in-spec
80	109126	11/88	Checkout no audible alarm	Device in-spec

(continued)

Chronology of Contacts Between FDA and Aequitron

This chronology has been adapted from one supplied to us by FDA's Center for Devices and Radiological Health during our data collection. We did not use every entry we were given but selected items from the original chronology that were germane to the subject of this report.

August 18, 1984	FDA conducted a GMP inspection of the manufacturer, covering the manufacturing of Model 8200. No significant deviations were noted.
December 19, 1984	FDA conducted a limited inspection of the manufacturer in response to a complaint of the failure of Model 8200 to sound its alarm and a device distributor's complaint of overheating wires in the monitor. After 10,000 units were distributed, the manufacturer received 91 units returned with burned wires as well as 17 returned with problems relating to the alarm. FDA inspected the device distributor to follow up on a complaint about a Model 8200 monitor that delayed in sounding its alarm, although the light came on. Follow-up revealed that Model 8200 was designed with a 6-second delay. The distributor had approval from the manufacturer to eliminate the delay by replacing the switch if the customer so requested. During this inspection, the distributor identified a problem with "burn out" or "melting" wires with 6 of approximately 300-350 units. The manufacturer had repeatedly attributed the problem with the burned wires to user intervention and not design. However, an independent engineering firm hired by the distributor believed the problem was design-related. The distributor was not aware of any serious injuries or deaths relating to "burn out," and the manufacturer disputed the findings of the engineering firm.
December 28, 1984	FDA conducted a limited inspection of the device distributor to collect recall data on 30 Model 8200 monitors that the distributor had replaced in home visits and to collect a failed unit for laboratory analysis.
January 4, 1985	An FDA district office submitted a recall recommendation to FDA's Center for Devices and Radiological Health for the 30 Model 8200 monitors that the device distributor had replaced. The recommendation noted that there was much confusion regarding the "burn out" problem and specifically requested a technical evaluation concerning the validity of the

	that the action constituted a "Safety Alert" and that FDA testing confirmed the information presented by the manufacturer. The manufacturer agreed to submit a 510(k) application to add a circuit breaker to the device to resolve the "burn out" problem.
June 25, 1985	The manufacturer sent a letter to the distributors informing them about the "burn out" problem.
July 25, 1985	FDA classified the manufacturer's June 25 letter as a "Safety Alert."
August 7, 1985	In its Weekly Enforcement Report, FDA published information on the manufacturer's "Safety Alert."
December 26, 1985	The manufacturer sent a letter to FDA that requested a "Certificate of Export" for five models of monitors of various kinds, including Aequitron's Model 8200.
February 3, 1986	FDA sent a letter to the manufacturer approving the export of four of the monitors but denying the manufacturer's December 26 request to export Model 8200.
February 11, 1986	Responding to FDA's denial of a request for export, the manufacturer claimed it was in compliance and requested that the export of Model 8200 be approved.
March 4, 1986	FDA approved the export of Model 8200.
January 27, 1987	FDA conducted a GMP inspection and reviewed all injury and death complaints received by the manufacturer since 1985. FDA's inspector questioned whether two of the complaints on the Model 8200 monitor should have been reported under the medical device reporting regulation.[1]

[1]This inspection was not included in the chronology provide by FDA but was documented in a separate inspection report

	adverse-findings letter be issued for the manufacturer's failure to submit 10 medical device reporting regulation reports for Model 8200.
May 20, 1988	FDA conducted an inspection in response to an anonymous letter alleging that six Model 9216 apnea monitors, intended for hospital use, had caught fire. The inspection confirmed that the failure resulted from a transistor that had been used in a circuit application outside its electrical specifications.
June 6, 1988	The manufacturer wrote to inform FDA that it had instituted a field replacement program and a labeling change for all the Model 9216 hospital apnea monitors.
June 15, 1988	FDA visited the manufacturer and collected recall data.
July 18, 1988	FDA classified the manufacturer's field replacement and labeling change for Model 9216 as a Class II recall.
October 18, 1988	In response to the deficiencies in medical device reporting found in the May 1988 inspection, FDA issued a notice-of-adverse-findings letter to the manufacturer. FDA also conducted an inspection of the manufacturer in response to five complaints received by FDA on Model 8200.[2]
December 28, 1988	The manufacturer responded to the October 1988 notice-of-adverse-findings letter, stating that it would change its reporting policies and practices.
June 22, 1989	FDA notified the manufacturer by letter that it appeared to have adequately addressed the concerns listed in October 1988 notice-of-adverse-findings letter and that a review of the manufacturer's revised medical device reporting regulation policy found that the reporting guidelines appeared to be adequate.

[2]This inspection was not included in the chronology provided by FDA but was documented in a separate inspection report.

a manufacturer receives or becomes aware of information from a layperson that its device may have caused or contributed to serious injury or death, the medical device reporting regulation requires the manufacturer to determine whether the information "reasonably suggests" a link between the operation of the device and the injury or death. Information from a layperson reasonably suggests the link if a reasonable person would reach that conclusion. Thus, if a reasonable person would conclude that the device may have caused or contributed to serious injury or death, a report must be made.

The regulation does not require, expressly or by implication, that a malfunction need occur or be suspected in order for a reasonable person to conclude that the device is implicated in serious injury or death. A reasonable person may conclude that the device may in some way have caused or contributed to serious injury or death, thus necessitating a report by the manufacturer, even when serious injury or death is attributable to user error, poor maintenance, or the use of the device beyond its useful life.

FDA's rationale for this approach is explained in guidance accompanying the publication of the final regulation in the Federal Register:

"One comment asserts that a death or serious injury should not be required to be reported unless it is associated with or related to a device malfunction.

"FDA disagrees with the comment. A device that performs to its specifications or otherwise performs as intended does not 'malfunction' as defined in the final rule. However, because of flaws in its labeling or because of user error . . . , such a device could cause or contribute to a serious injury or death.

. . . . .

"In this context, the phrase 'contribute to' means to play a part in the serious injury or death." (49 Fed. Reg. 36,330 (1984); see also 49 Fed. Reg. 36,338 (1984))

FDA believes that it needs to be notified of deaths resulting from user error and problem labeling because these could indicate the need for educational programs, user notification, voluntary recalls, or corrective labeling to prevent future deaths or serious injuries. (49 Fed. Reg. 36,331-332, 36,339 (1984))

a report to FDA would be required if the information given to the company suggests to a reasonable person that a recurrence of a malfunction would likely cause or contribute to a future serious injury or death. In the second, the per se rule would require a report. As explained above, neither confirmation nor observation of a malfunction is required before a company may be required to report to FDA.

COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES ON THE GENERAL ACCOUNTING OFFICE (GAO) DRAFT REPORT ENTITLED "MEDICAL DEVICES: UNDERREPORTING OF SERIOUS PROBLEMS WITH A HOME APNEA MONITOR," MARCH 9, 1990

Although we agree that implementation of the Medical Devices Reporting (MDR) Regulations has been slower than we would like and the regulations are subject to interpretation, we disagree with the following conclusions of the draft report.

1. Although the report states that the study design precludes generalization to the medical devices industry, it proceeds to make statements such as "...there are persistent differences in the interpretation of the medical device reporting requirements,..." and "...we have received additional information from several sources which suggested that problem underreporting does occur and that it is not adequately identified through FDA's inspection program." We believe these and similar generalizations without apparent foundation should be deleted or sufficient data should be presented to substantiate the allegations and allow the Food and Drug Administration (FDA) to evaluate their validity in the context of the overall MDR program and competing priorities.

   We believe that the case study of apnea monitors is not an accurate representation of how MDR is implemented by most firms and the report is skewed, setting forth a worst-case scenario rather than a balanced presentation of MDR implementation. The report characterizes implementation of MDR as "flawed" based upon this one case. Yet, FDA has received thousands of reports from other firms that have led to regulatory actions such as recalls, seizures, and injunctions, as well as safety alerts, bulletins and even withdrawals of premarket applications (PMA) and premarket notifications (510(k)). MDR is primarily intended to elicit reporting from health care professionals who generally are in a position to observe product performance first hand and be able to appropriately assess the reportability of an event. Unlike most other devices, however, apnea monitors are prescription devices used in home care settings where health care professionals are unlikely to observe use failures and problems first-hand. Many reports are, therefore, made by nonprofessionals. Evaluation of data on apnea monitors both by the manufacturer and FDA is, therefore, more complicated than for most other devices.

2. The report faults FDA inspection strategy for failing to identify serious problems and for failing to recognize that the firm was misinterpreting the regulations, thus resulting in underreporting.

incorrectly created a presumption against reporting unless an event was confirmed. However, the preamble to the MDR regulation indicates that while mere allegation is insufficient, confirmation is unnecessary. Aequitron's criteria were also worded so as to make the time frames work against reporting. In fact, the presumption should be to report unless testing shows, within the time frames, that there is no reasonable suggestion there has been a malfunction.

GAO also correctly notes that the Aequitron criteria suggest that a health care professional must observe a malfunction before he/she reports it (unless tests confirm the malfunction). However, the rule that an event is per se reportable is invoked when the health care professional reports the malfunction even if he/she has not observed it.

It should also be noted that in its response to FDA's Inspectional Observations (Form FDA-483) given to the firm at the conclusion of a full GMP inspection from September 1989 through November 1989, Aequitron changed its policy. Aequitron stated:

> "At this point, Aequitron wishes to advise FDA that the company has elected voluntarily to report all incidents of death or serious injury that the company becomes aware of as MDR events to FDA whether justified or not. ... This action was taken by Aequitron voluntarily to avoid any debate pertaining to an appropriate construction and interpretation of the MDR regulation."

This action by Aequitron was precipitated by FDA's Minneapolis District's discovery of Aequitron's error in interpretation of the MDR as stated in their reporting criteria. As a result of Aequitron's change in policy, the firm has been submitting significantly more MDR reports than had previously been the case. FDA will continue its normal postmarket surveillance efforts of reviewing every MDR report that is submitted and determining reporting rates. If a significant fluctuation from the normal reporting occurs, FDA will follow up to determine the cause. By following these procedures FDA will be able to immediately determine if the firm deviates from the course of action it had committed to follow.

Finally, it should be noted that in the Fiscal Year 1991 budget proposal the Administration has requested an increase of eight full time equivalents and $600,000 for the MDR program.

Our comments on the recommendations are as follows.

The following are GAO's comments on the HHS April 27, 1990, letter.

HHS provided three types of comments on our report—general comments, comments on our recommendations, and technical comments. Our responses to the first two are contained in this appendix. We have responded to the technical comments by revising the body of the report as appropriate.

Comments on Recommendations

HHS agreed with our recommendation that a comprehensive good manufacturing practices and medical device reporting regulation compliance inspection of Aequitron Medical, Inc., giving special attention to all complaints listed in the HID file should be conducted. A full GMP inspection, including a determination of medical device reporting regulation compliance of Aequitron was conducted in December 1989, after we completed our fieldwork. The agency is currently evaluating the results of this inspection to determine what, if any, regulatory action is warranted.

HHS also concurred with our recommendation to review its medical device reporting regulation and its guidance to device manufacturers on problem reporting for clarity and effectiveness and to consider developing specific guidance for the manufacturers of devices such as apnea monitors for which determining reportability is thought to present special difficulties. HHS stated that FDA has established a medical device reporting regulation study group to analyze the medical device reporting program and regulation, identify problems, and recommend solutions. HHS expects that this study group will complete its work later this fiscal year.

General Comments

We agree that our case study does not by itself indicate how the medical device reporting regulation is implemented by most firms. We have stated in the report that this case illustrates some of the concerns that we identified in our earlier study of the implementation of the medical device reporting regulation.[1] This earlier report was based on the more than 50,000 medical device problem reports received during the first 3 years of the regulation's implementation, as well as the results of compliance inspections on 575 manufacturing establishments. It also reviewed FDA's report-processing and data-handling procedures and included analyses of regulatory actions and other initiatives FDA took on

[1]See U.S. General Accounting Office, Medical Devices: FDA's Implementation of the Medical Device Reporting Regulation, GAO/PEMD-89-10 (Washington, D.C.: February 1989), p. 4.

first years of the program's operations. The point here is that manufacturers are obliged by regulation to review problem reports and make judgments about whether the events described warrant a report to FDA.

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Medical Devices: FDA's Forecasts of Problem Reports and FTEs Under H.R. 4640, GAO/PEMD-88-30. Washington, D.C.: July 1988.

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"Medical Devices: The Public Health at Risk," statement of the Comptroller General, GAO/T-PEMD-90-2. Washington, D.C.: November 1989.

"Medical Devices: Underreporting of Problems, Backlogged Systems, and Weak Statutory Support," statement of Eleanor Chelimsky, GAO/T-PEMD-90-3. Washington, D.C.: November 1989.

Major Contributors to This Report

Program Evaluation and Methodology Division	Gerald L. Dillingham, Assistant Director L. Joseph Sonnefeld, Evaluator Elaine L. Vaurio, Evaluator
Office of the General Counsel	Julian P. Klazkin, Attorney

the basis of medical device problem reports. It is our earlier report that forms the basis for general statements about the implementation of the regulation and its associated compliance inspection program. The present report's conclusion is only that the evidence in the Aequitron case was consistent with the findings of our earlier work.

In addition, we did not find support in the text or preamble of the medical device reporting regulation or in associated guidance for HHS's statement that the medical device reporting regulation is primarily intended to elicit reporting from health care professionals. The regulation is focused on the reporting responsibilities of device manufacturers who learn of potentially serious problems associated with the use of their product, regardless of the source of information. In the report, we have acknowledged that the determination that a complaint is reportable may be more difficult for home apnea monitors than for some other devices, in part because many reports of problems with home monitors are received from laypersons as opposed to health care professionals.

The report does not fault FDA's inspection strategy, although we agree that it would have been desirable to conduct the first Aequitron compliance inspection earlier than 2 years after the promulgation of the regulation. We agree that the inspection scheduling strategy appears reasonable. It is only the effectiveness of the inspection program in establishing and resolving the problem with the firm's reporting criteria, despite the more-frequent-than-normal inspections, that the report calls into question.

The remainder of HHS's general comments review the manufacturer's compliance history and FDA's actions in more detail but are not inconsistent with our report. HHS does give a quotation from Aequitron's response to the "Inspectional Observations" given to the firm at the conclusion of the GMP and medical device reporting regulation compliance inspection conducted between September and November 1989. In this response, Aequitron stated that it planned to submit reports on all incidents involving serious injury or deaths that the company becomes aware of. This response was not available to us during the period of our data collection, but we are concerned that this reporting policy may not represent a satisfactory general solution to the interpretation of medical device reporting regulation requirements in the case of home apnea monitors. Rather, it could tend to contribute to the problem of "overreporting" identified during our earlier review. This problem appeared to affect FDA's ability to handle the volume of reports submitted during the

GAO Recommendation

We recommend that FDA take the following actions to improve the effectiveness of medical device problem reporting and to ensure the overall safety and effectiveness of medical devices.

1. Conduct a comprehensive good manufacturing practices (GMP) and medical device reporting regulation compliance inspection of Aequitron Medical Incorporated, giving special attention to all complaints listed in the HID file.

HHS Comment

In December 1989 FDA completed a full GMP inspection that included the MDR compliance status of Aequitron Medical Incorporated. The results of the inspection are currently under review in FDA. We, therefore, do not believe another such inspection is warranted at this time.

GAO Recommendation

2. Review its medical device reporting regulation and its guidance to device manufacturers on problem reporting for clarity and effectiveness; and consider developing specific guidance for the manufacturers of any devices, such as apnea monitors, for which determining reportability is thought to present special difficulties.

HHS Comments

We concur. FDA has established an MDR study group to analyze the MDR program and regulation, identify problems and recommend solutions. This group has been working on the MDR and plans to have its study completed later this fiscal year. The concept of developing specific guidance for certain industries, devices, etc., has been discussed by the CDRH and is part of this study group's objectives. In addition, a new guidance document for device firms has been drafted and is currently under review in FDA. It should be noted, however, that the MDR regulation covers some 1,700 categories of devices and 30,000 - 40,000 individual devices. It would be virtually impossible for FDA to craft language that would inform a firm about every event that the Agency would want reported for each device and/or every generic category.

(Additional technical comments were provided and have been incorporated, where appropriate, throughout the report.)

FDA agrees with GAO that it took longer than we would have liked to reach full implementation of the MDR regulation. The first of these inspections of Aequitron did not occur until 1987, at which time all complaints in the "H/I/Death File" (HID) file were evaluated for compliance. The inspectional program appears to have been successful in uncovering violations.

Moreover, under normal circumstances, FDA would have inspected Aequitron biennially. However, because of problems with the firm, FDA has visited the firm at least ten times in the last 6 years. A great deal of regulatory activity occurred with this firm as a result of those inspections including recalls, safety alerts, etc. It was during one of these inspections that the MDR problems were discovered and appropriate recall action initiated. It should also be noted that the Aequitron MDR policy in effect at the time of the 1987 inspection appears to more closely follow the MDR regulation as written than does the firm's later policy found during the May 1988 inspection. The firm was issued a Notice of Adverse Findings (NAF) as a result of the May 1988 inspection. Subsequent inspections have shown that the firm's HID complaint file was not always complete during previous inspections.

We believe that in this case FDA's inspectional program was reasonable. We did adopt an enhanced program on October 1, 1988. Districts are now directed to conduct an MDR inspection during the course of every other "good manufacturing practices" (GMP) inspection unless certain situations exist, in which case, "for cause" inspections are to be made as needed.

Also, the time required for FDA to identify the underreporting problem is not, in our opinion, a reflection of failure of the inspection strategy. As previously noted, this firm was inspected at least twice as often as would be expected during the time period of GAO's study. As problems were identified, regulatory actions were initiated that resulted in the submission of additional reports to FDA and the modification of the firm's MDR reporting criteria. See above.

The GAO report correctly observes that Aequitron's stated reporting criteria were overly liberal. As noted in FDA's Center for Devices and Radiological Health (CDRH) guidance document "Medical Device Reporting Questions and Answers," a report from a layperson, in contrast to a report from a health care professional, can be analyzed to decide whether it reasonably suggests that the event occurred (p. 19). Aequitron

Comments From the Department of Health and Human Services

Note: GAO comments supplementing those in the report text appear at the end of this appendix.

DEPARTMENT OF HEALTH & HUMAN SERVICES — Office of Inspector General

Washington, D.C. 20201

APR 27 1990

Ms. Eleanor Chelimsky
Assistant Comptroller General
United States General
Accounting Office
Washington, D.C. 20548

Dear Ms. Chelimsky:

Enclosed are the Department's comments on your draft report, "Medical Devices: Underreporting of Serious Problems with a Home Apnea Monitor." The comments represent the tentative position of the Department and are subject to reevaluation when the final version of this report is received.

The Department appreciates the opportunity to comment on this draft report before its publication.

Sincerely yours,

Bryan Mitchell
for Richard P. Kusserow
Inspector General

Enclosure

Second, when a report of a malfunction is received, confirmation of its existence by the manufacturer is not a precondition for the manufacturer's obligation to report. FDA explains in its published guidance why the regulations do not permit the manufacturer to refrain from reporting merely because it is unable to confirm a malfunction:

"FDA believes that it is not speculative, inefficient, ineffective, or uneconomical for the agency to require the submission of information about reportable events before such events have been confirmed by the manufacturer or importer. . . . It would be irresponsible for FDA to wait for confirmation of a reportable event by a manufacturer or importer before requiring reporting of any information about such event." (49 Fed. Reg. 36,330 (September 14, 1984)

Thus, although confirmation of a device malfunction may help a manufacturer determine whether its device actually caused or contributed to serious injury or death, lack of confirmation does not mean that a report is not required.

Aequitron's reporting criterion requiring that a health care professional observe a malfunction before it will report (unless a test by Aequitron confirms the malfunction) is also inconsistent with the medical device reporting regulation. When a health care professional notifies a company that one of its devices may have caused or contributed to serious injury or death, the company must file a report with FDA. No "reasonable person" analysis need be performed because, under the regulation, information from a health care professional reasonably suggests "per se" the required link, thereby triggering the reporting requirement. (49 Fed. Reg. 36,336 (1984)) The company has no discretion in this circumstance, even if it cannot confirm a device malfunction or can attribute the serious injury or death to user error, poor maintenance, or use of the device beyond its useful life. Nothing in the regulation requires that a health care professional must have observed a malfunction before the professional's report will be accepted as per se reasonably suggesting that the device may have caused or contributed to a serious injury or death.

Finally, Aequitron's reporting criteria are also inconsistent with the regulation in situations in which the company is made aware of a malfunction that did not result in serious injury or death but that may cause or contribute to a future one. Aequitron's criteria suggest that a report to FDA is not required if (1) the company cannot confirm a malfunction reported to it by a layperson or (2) the company is notified by a health care professional who did not observe the malfunction. In the first case,

Our Analysis of Aequitron's Medical Device Reporting Criteria

The Aequitron reporting criteria set out the conditions under which it must report to FDA when it receives information that one of its devices has malfunctioned. It appears that Aequitron's policy is not to report to FDA when someone other than a health care professional notifies the company that one of its devices has malfunctioned and may have caused or contributed to serious injury or death, unless the company is able to confirm a malfunction within a specified time. Additionally, if an initial report of a malfunction associated with serious injury or death comes from a health care professional, Aequitron's criteria appear to require either that the professional must have observed the malfunction or that the malfunction be confirmed before the company reports to FDA. Reports of malfunctions not resulting in serious injuries or death, but with the possibility of causing either in the future, are handled in similar fashion. FDA indicated in a letter to Aequitron that its reporting criteria appeared to be adequate. We believe these policies are inconsistent with FDA's medical device reporting regulation (21 C.F.R. 803) in several respects.

Under the medical device reporting regulation, a manufacturer must file a report with FDA whenever it receives information from a person other than a health care professional from which a reasonable person would conclude (that is, information that reasonably suggests) or a statement from a health care professional concluding that a device (1) may have caused or contributed to a serious injury or death or (2) has malfunctioned and a recurrence of the malfunction would be likely to cause or contribute to serious injury or death. (21 C.F.R. 803.3(f), 803.24(a))

According to Aequitron's reporting criteria, Aequitron will not report under the following circumstances (among others):

"The reported malfunction was not observed by a health care professional and the reported malfunction cannot be confirmed by testing of the device by adequately trained personnel within reporting time frames as established by the regulation. . . "

Thus, Aequitron's criteria seem to contemplate that, in order for a report to be required, there must have been a report of a malfunction, and the malfunction must either have been confirmed by Aequitron or have been observed by a health care professional. These criteria appear to be inconsistent with the regulation in several respects.

First, the requirement to report is not limited by the regulation to only situations in which a malfunction is reported to the manufacturer. When

February 12, 1988	The manufacturer requested an export certificate for a second home apnea monitor, Model 9200, plus three other devices.
March 9, 1988	The manufacturer submitted a medical device reporting regulation report indicating that Model 9200 failed to sound its alarm. According to the manufacturer, this was the first failure confirmed by the manufacturer's testing. Testing confirmed a 10-percent failure rate in the alarm component. The manufacturer had 24 reported failures of 4,800 units in distribution. The failures were related to a variation in voltage that would be likely to occur only when the monitor is running on its battery.
March 14, 1988	The manufacturer notified FDA of a recall of Model 9200, having issued a letter to dealers recommending the following: specified monitors should be used with only a particular model of battery charger and with AC power, the specified units should not be used on battery power only, and the monitor's audible alarm should be verified daily. The manufacturer advised that an interim solution would be made pending a permanent one. FDA visited the manufacturer to collect data on the recall.
April 4, 1988	FDA classified manufacturer's action as a Class I recall, based on a health hazard evaluation determining that the alarm problem presented a high risk. FDA sent a letter to the manufacturer advising that FDA was classifying the manufacturer's action as a Class I recall.
April 6, 1988	FDA disapproved the February 12 export request for Model 9200 but approved export of three other devices noted in its February 12, 1988, request.
April 15, 1988	Following FDA's March 14 inspection of the manufacturer, FDA sent a notice-of-adverse-findings letter to the manufacturer, noting deficiencies in inventory control.
May 11, 1988	FDA conducted a GMP inspection of the manufacturer, including a medical device reporting regulation compliance inspection. Six deficiencies were noted on the observation form; the manufacturer promised to correct all the deficiencies. The FDA district office recommended that a notice-of-

	recall, with an engineer to review the electronics test conclusion and a physician to evaluate the delayed-alarm feature.
January 8, 1985	FDA inspected the manufacturer to follow up on the recall recommendation for Model 8200. The inspection determined that the manufacturer believed that the device distributor had modified the 30 units without approval.
January 29, 1985	FDA conducted a limited inspection of the manufacturer in response to an assignment from the FDA Center for Devices and Radiological Health to collect mechanical and electrical drawings to assist in an analysis of the units and as follow-up to a medical device reporting regulation report on Model 8200. The manufacturer's analysis revealed the monitor to be performing within specifications. FDA's inspector recommended routine follow-up.
May 28, 1985	The manufacturer submitted 30 medical device reporting regulation reports on Model 8200. All were unrelated to the problem with burned wires. The manufacturer considered all 30 to be random failures. Most monitors were repaired and returned to the customers.
May 31, 1985	FDA hand delivered a letter to the manufacturer advising of the results of FDA's evaluation of the health hazard involved in the "burn out" problem with Model 8200. The letter indicated that the risk to users was high and that there was not enough evidence to show that the problem was limited to the 30 units modified by the distributor. The manufacturer indicated that it would prepare a list of options for dealing with the "burn out" problem and present them to FDA.
June 18, 1985	At a meeting between FDA and the manufacturer regarding the May 30 health hazard evaluation letter, the manufacturer reasserted that the wire "burn out" problem with Model 8200 occurs not during use but as the device is being set up. The manufacturer indicated that it was going to issue a letter to distributors and that it believed that the letter would constitute a "Safety Alert." FDA staff concurred with the manufacturer

Number	Serial number	Date	Reason/return	Analysis
81	206310	11/88	No alarm/no light-in hospital pt.Ok	Ic u4/cap c5
82	106327	1/89	Checkout only-death/alarmed	Device in-spec

H/I/Death File

Number	Serial number	Date	Reason/return	Analysis
1	50461	1/83	Checkout only-death	Device in-spec
2	51369	6/83	Checkout-death-no alarm noted	Device in-spec
3	51048	7/83	Checkout only-death	Device in-spec
4	52362	8/83	Checkout-death-brady alarm	Device in-spec
5	52435	9/83	Checkout-death-brady alarm	Device in-spec
6	53512	9/83	No apnea alarm-brady alarm (seizure)	Device in-spec
7	54078	11/83	Electrical burn (unfounded)	Device in-spec
8	53360	12/83	Checkout only-death	Device in-spec
9	54441	1/84	No audible alarm (unfounded)	Device in-spec
10	51224	2/84	Checkout only-death (unit not in use)	Not received
11	51994	7/84	Checkout only-death	Device in-spec
12	52944	8/84	Checkout-no apnea alarm	Device in-spec
13	52306	8/84	Checkout only-death	Device in-spec
14	60034	12/84	No apnea alarm (periodic breathing)	Device in-spec
15	53228	11/84	Checkout only-death	Device in-spec
16	xxxxx	12/84	Death	Device status unknown
17	63138	10/84	Death-no audible alarm	Device in-spec
18	64183	11/84	Death checkout only	Device in-spec
19	54711	12/84	Death-no alarm	Device in-spec
20	64512	12/84	Checkout only-death	Device in-spec
21	101467	1/85	Checkout only-death	Device in-spec
22	102224	5/85	Checkout only-death	Device in-spec
23	102842	8/85	Checkout only-death	Device in-spec
24	101457	8/85	Checkout only-death	Device in-spec
25	102748	8/85	No apnea alarm	Device in-spec
26	53881	10/85	Checkout-death-no alarm	Device in-spec
27	54775	10/85	Checkout only-death	Device in-spec
28	60496	12/85	Checkout-death-no alarm	Device in-spec
29	106149	12/85	Electrical burn-(unfounded)	Device in-spec
30	52701	1/86	Checkout only-death	Device in-spec
31	65221	1/86	Checkout only-death	Device in-spec
32	65942	2/86	Checkout only-death	Device in-spec
33	52950	6/86	Checkout-death-no alarm	Device in-spec
34	62944	6/86	Checkout-death (shock/burn)	Device status unknown
35	201411	7/86	Death	Device status unknown
36	101472	7/86	Checkout only-death	Device fully functional
37	54267	8/86	Checkout only-death	Device in-spec
38	66150	11/86	Checkout only-death	Device in-spec
39	109286	12/86	Checkout only-death	Device in-spec

(continued)

Contents

8200 home apnea monitor. Our fieldwork was conducted from September 1989 through December 1989.

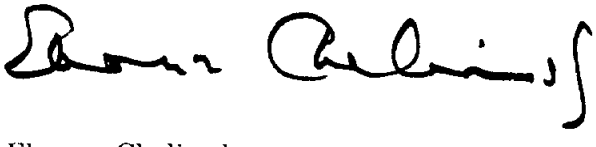
The information on which this report is based was obtained from multiple sources and required both qualitative and quantitative analysis. We conducted a selective review of the available technical literature, including apnea monitor engineering studies and the National Institutes of Health consensus report on the status of apnea monitors, in order to provide ourselves with background for identifying and understanding the relevant issues.[24]

We systematically reviewed FDA documents, including records of inspections and regulatory actions related to the device manufacturer, and correspondence between FDA and the device manufacturer. We also analyzed reports submitted to FDA under the medical device reporting regulation. To clarify, supplement, and confirm the documentary evidence, we conducted structured interviews with representatives of the device manufacturer, FDA officials in the Center for Device Radiological Health, district and regional offices, and other knowledgeable persons. Our review was conducted in accordance with generally accepted government auditing standards.

We will send copies to the Secretary of Health and Human Services, to the Director of the Center for Devices and Radiological Health, and upon request to others who are interested.

If you have any questions or would like additional information, please call me at (202) 275-1854 or Dr. Michael J. Wargo, Director of Program Evaluation in Physical Systems Areas, at (202) 275-3092. Other major contributors to this report are listed in appendix V.

Sincerely yours,



Eleanor Chelimsky
Assistant Comptroller General

[24]National Institutes of Health, Infantile Apnea and Home Monitoring (Bethesda, Md., October 1986).

Although FDA has provided all registered device manufacturers with some guidance on reporting requirements in the form of a "questions and answers" document, the example we have presented suggests a potentially serious problem in the manufacturer's interpretation of the requirements and formulation of a reporting policy based on that interpretation, rather than random or isolated failures to report.

Our study illustrates the serious consequences that shortcomings in the implementation of the medical devices reporting regulation and subsequent inspection program can have. In this case, FDA did not have information on a number of adverse experiences with the device in question when the agency made critical decisions with respect to recalls and other regulatory actions. FDA found that this manufacturer's interpretation of the reporting requirements differed from the agency's in ways that put it in noncompliance with the regulation. The compliance inspection program did not identify and resolve these differences for a substantial period of time after the regulation went into effect. During that time, FDA was unable to make valid comparisons of the monitor's problem rates or trends with those of other, similar monitors made by other manufacturers, thus compromising one of the most important uses for data from the medical devices regulation. It was beyond the scope of our study to conduct an in-depth review of the device manufacturer's problem reporting policies, but we did analyze certain aspects of the manufacturer's revised reporting policy.

The design of our study precludes generalizing to other devices or manufacturers. However, the findings, taken with the findings of our earlier report, raise a concern that the problem-reporting and inspection issues may pertain to a much broader segment of the device manufacturing industry and to the safety and effectiveness of medical devices in general. Therefore, we believe they are worth further attention by FDA.

Recommendations

We recommend that FDA take the following actions to improve the effectiveness of medical device problem reporting and to ensure the overall safety and effectiveness of medical devices.

1. Conduct a comprehensive good manufacturing practices and medical device reporting regulation compliance inspection of Aequitron Medical, Inc., giving special attention to all complaints listed in the HID file.

2. Review its medical device reporting regulation and its guidance to device manufacturers on problem reporting for clarity and effectiveness

The time required in this case for FDA to identify the underreporting problem raises questions about the effectiveness of the agency's inspection program and its capacity to identify potentially serious device problems through monitoring complaints. The inspection strategy is designed to include special emphasis on firms manufacturing the types of devices that have demonstrated reportable problems and scheduling more frequent medical device reporting regulation inspections for those manufacturers.

Nine of the complaints in the HID file involving alarm problems and the death of patients are dated before the manufacturer underwent its first GMP inspection. By the end of the manufacturer's third year of operations and before a second FDA inspection, it had received an additional 7 complaints of alarm problems and deaths. According to the device manufacturer, all the complaints that had been received with allegations of hazards, injuries, or deaths were placed in the appropriate GMP record. The first GMP inspection, in 1984, found "no significant deviations." During the second inspection in 1984, in response to a complaint of the monitor's failure to sound its alarm, FDA noted that the manufacturer had 17 monitors returned for problems with the alarm.

During this time, there were several inspections and other interactions between the manufacturer and FDA about a variety of problems associated with various models of apnea monitors. FDA reported that during an inspection in January 1987, it reviewed all complaints of hazards, injuries, and deaths received since 1985. It was not until a May 1988 inspection, 4 years after the first GMP inspection, that FDA dealt with the reportability of complaints about alarms. By that time, FDA had received a total of 83 medical device reporting regulation reports on the monitor.[21] (See table 1.) More than 88 percent of these involved allegations of an alarm failure, including the death of two patients.[22]

[21]Many of these reports did not originate in complaints to the manufacturer. Reports must be made under the medical device reporting regulation, not only in response to complaints but also whenever a manufacturer acquires information from any source that reasonably suggests that one of its devices may have caused or contributed to serious injury or death or has malfunctioned in such a way that, if the malfunction were to recur, it would be likely to cause or contribute to serious injury or death. Some of the other sources of such information include the manufacturers' own research, testing, or servicing of their devices as well as the medical and scientific literature.

[22]Of 278 reports submitted by September 1989, consisting of 271 malfunction reports and 7 reports of deaths, the manufacturer's tests confirmed that Model 8200 had malfunctioned in 271 of the complaints. However, Aequitron's tests did not confirm that the device had malfunctioned in any of the 7 complaints in which the death of a patient occurred

part of its GMP inspections. The results of these inspections can lead to additional actions by the agency.[16]

We found that between August 1984 and June 1989, FDA had various contacts with Aequitron, including at least eight formal inspections. Three were GMP inspections, and two of these included the medical device reporting component. Five were "for cause," including three that were initiated in response to complaints FDA had received. One was a follow-up to a medical device report on Model 8200, and one was a follow-up to an FDA district office's recommendation to recall Model 8200. (A selective chronology of contacts between FDA and Aequitron Medical, Inc., is given in appendix II.)

During a May 1988 GMP inspection, FDA examined the manufacturer's complaint records and identified 10 unreported complaints that FDA inspectors believed met the medical device reporting regulation's definitions of reportable events. Four of these complaints contained allegations of the death of patients. As a result of this May 1988 inspection, a notice-of-adverse-findings letter indicating "noncompliance" with the medical device reporting regulation was issued to the manufacturer in October 1988.[17]

According to FDA's inspection report, Aequitron's complaint records were reviewed for the previous 15 months (January 1987 through April 1988). However, the earliest of the unreported complaints in the HID file that FDA cited in its notice-of-adverse-findings letter was dated only 6 months prior to the inspection, in October 1987.

Representatives of the manufacturer stated that FDA's finding of "noncompliance" resulted from a difference in the interpretation of the medical device reporting requirements. According to the manufacturer, many of the unreported complaints had not been made by health care professionals and could not be confirmed by the company within the required reporting time. Therefore, in accordance with its interpretation of the

[16]According to FDA, the inspection strategy adopted by the agency will result in a medical device reporting regulation compliance inspection for every firm manufacturing medium-risk (class II) and high-risk (class III) devices at least once every 4 years and incorporating manufacturers of low-risk (class I) devices less frequently

[17]A notice-of-adverse-findings letter may be sent to a manufacturer when an inspection reveals that a manufacturer or individual is in violation of the laws and 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 manufacturer or individual).

Question 2: Compliance

Did the device manufacturer comply with FDA's existing problem-reporting regulations and procedures? FDA's primary source of information about problems associated with the use of medical devices consists of the manufacturer's reports generated by the requirements of the medical device reporting regulation (21 C.F.R. 803). This regulation requires that device manufacturers telephone an initial report to FDA on serious injuries and deaths within 5 calendar days, and it requires that this be followed by a more complete written report within 15 working days. Reportable malfunctions that do not involve serious injury or death must be reported within 15 working days of the manufacturer's receiving the device-problem information. One important source of information that leads to medical device reports is complaints to the manufacturer, which can be made by health care professionals or other users of devices.[12]

We compared the 70 complaints that contained the word "death" with FDA's record of medical device reports and found that 14 complaints were dated before the medical device reporting regulation was promulgated. The significance of this is that before the regulation was promulgated, the device manufacturers' obligations were fulfilled by maintaining general complaint records and making them available to FDA during GMP inspections. We found 56 complaints associated with deaths whose listed dates fell after the medical device reporting regulation was implemented. Only 4 reports in FDA's medical device reporting data base as of September 1989 could be matched with the 56 complaints as having been reported to FDA in accordance with the provisions of the regulation. One additional medical device report on a death associated with Model 8200 was reported to FDA during this time but could not be identified with a specific complaint on the HID file, because the manufacturer had not submitted a serial number with the medical device report. Thus, at least 51 of the 56 complaints of death had not been reported before FDA began to take compliance actions.

The information in the HID file alone was not sufficient for us to make a definitive judgment about the reportability of the complaints or to establish causal connections between the device and the safety hazard, injury, or death. The examination of the manufacturer's complete record for each complaint, which would be necessary for such assessment, was beyond the scope of our review. In a partial review of the complaint

[12]According to the GMP regulation, a complaint is a written or oral expression of dissatisfaction regarding the identity, quality, durability, reliability, safety, effectiveness, or performance of a device

Apnea is a prolonged lack of respiration that can result in low blood oxygen levels, which can lead in turn to brain damage and death. The condition can be induced by a variety of underlying medical disorders. However, premature and low birthweight infants are particularly prone to apnea.

Apnea monitors are electronic devices intended to detect episodes of apnea. In a typical device, when either breathing or heart rate falls below set levels or when the device's electrical leads are improperly attached to a patient, both audible alarms and flashing lights are triggered. Specialized models of apnea monitors are designed for hospital and home use. To avoid lengthy hospital stays, home apnea monitors have been increasingly used in recent years.

Findings

Question 1: Complaints of Death

How many complaints of the deaths of patients have been associated with the Aequitron Medical, Inc., Model 8200 home apnea monitor? We received information through our fraud hotline that there was evidence of serious nonreporting or underreporting of problems associated with Model 8200.[7] We were also told that many of the unreported complaints involved the deaths of the patients.

FDA's good manufacturing practices regulation requires that manufacturers maintain two types of records regarding the complaints they receive from users about their products.[8] The first is a general record of all users' complaints. The second is a record exclusively devoted to complaints alleging that hazards to safety, injuries, or deaths are associated with a medical device.

Evidence subsequently provided to us included a table labeled "H/I/Death File" (HID file) and identified as users' complaints related to the

[7]This information was simultaneously provided to the staff of the Subcommittee on Health and the Environment of the House Committee on Energy and Commerce.

[8]Section 520(f) of the 1938 Federal Food, Drug, and Cosmetic Act, added by the Medical Device Amendments of 1976, authorizes FDA to promulgate regulations that specify practices in the manufacture, packaging, storage, and installation of devices. The good manufacturing practices established by the GMP regulation include controls over manufacturing, specifications, processing procedures, device components, packaging, labeling, manufacturing equipment, and records.

Results in Brief

With regard to the first question in the paragraph above, we found that Aequitron had received at least 70 complaints that the deaths of patients were associated with the use of the Model 8200 monitor.[3] With regard to the second question, we found that the manufacturer had maintained the required record of complaints but had not fully complied with the reporting requirements of the medical device reporting regulation.[4] A partial review of the manufacturer's complaint record by FDA found that 10 unreported complaints should have been reported, including 4 that involved the death of patients. We could verify that only 6 of the complaints of deaths dated after the implementation of the medical device reporting regulation were reported to FDA. Two of these complaints of death were reported only after FDA compliance actions, nearly 1 year after the events.

With regard to the third question, we found that when FDA received information about the association of the monitor with deaths, it investigated whether a sample of complaints should have been reported to FDA. Following the investigation, FDA cited the device manufacturer for noncompliance with the medical device reporting regulation and, in concert with the manufacturer, reviewed the manufacturer's problem-reporting policy. FDA then reviewed and approved a revised problem-reporting policy submitted by the manufacturer. These actions resulted in the submission of more than 150 additional reports to FDA.

Our case study methodology precludes generalizing from these findings and conclusions to other devices and manufacturers. Instead, the study's function is to illustrate some of the critical concerns that we identified in our earlier generalized work on the implementation of the medical device reporting regulation. Included there were concerns about the

[3]We found that an Aequitron document entitled "H/I/Death File" (or "Hazard, Injury, Death (HID) File") contained information abstracted from the special section of the record of complaints reserved for hazards to safety, injuries, and deaths that a device manufacturer is required to maintain under the good manufacturing practices (GMP) regulation (21 C.F.R. 820.198). The HID file listed 82 complaints, 68 of which referred to deaths. Two additional complaints of death of were contained in a similar list drawn from the "general" portion of Aequitron's GMP record of complaints. (See appendix I.) According to the manufacturer, the HID file contains complaints alleging that serious injuries or deaths were associated with the device, but some of the complaints do not allege that a malfunction of the monitor occurred. We did not independently investigate each complaint on the list to determine the circumstances of the events; causal connections between the device and the safety hazard, injury, or death; or the actual occurrence of the events listed.

[4]The medical device reporting regulation, effective December 13, 1984, requires that device manufacturers report to FDA whenever they become aware of information that reasonably suggests that one of their devices may have caused or contributed to a serious injury or death or has malfunctioned in such a way that, if the malfunction were to recur, the device would be likely to cause or contribute to a death or serious injury or death. See Medical Devices for a detailed discussion of the medical device reporting regulation