

Ensuring the Safety of Marketed Medical Devices

CDRH's Medical Device Postmarket Safety Program

January 18, 2006

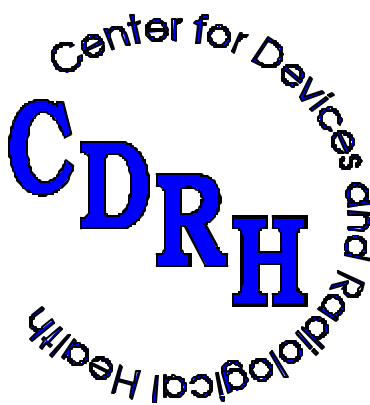


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Ensuring the Safety of Marketed Medical Devices: CDRH's Medical Device Postmarket Safety Program

Introduction

The goal of medical device regulation is to promote and protect the public health through oversight of the safety and effectiveness of medical devices available to the U.S. public. Medical devices are diverse in design and function and require varying levels of oversight based upon their complexity and risk profiles. Using the FDA process model for risk management of medical products as a guide (see Appendix A, Agency Perspective of the FDA Core Work Processes), CDRH uses its premarket review and evaluation programs to ensure safety and effectiveness of new, high risk, and complex devices, and its postmarket surveillance and assessment methods, scientific research, regulatory enforcement tools, and educational programs, to maintain optimal safety and effectiveness of medical devices following approval for use. It is the interaction of these CDRH programs that is intended to ensure a continuum of safety and public health as medical devices move from design concept, to accepted use in health care delivery and ultimate replacement as new versions of improved devices and novel technologies are developed. Information and assessment findings from the postmarket safety programs often drive improvements seen in new device applications. Further, the postmarket programs also support the premarket approval process through the development of guidance documents and standards that are applied to the next generation of medical devices seeking approvals.

Based upon the work of a CDRH internal postmarket safety workgroup, this report presents a discussion of the CDRH medical device postmarket safety framework and the approaches used to monitor and address adverse events and risks associated with the use of medical devices that are currently available in the market. It does not include a discussion of CDRH's radiological health programs, such as MQSA, because they have their own system of facility inspection and oversight that differs from the process for medical devices. The document also does not provide an in depth discussion of the premarket review process. Reference is made, however, to the connection between the CDRH medical device premarket review process and the postmarket safety programs.

Key goals of CDRH's postmarket programs are to:

- 1) Access comprehensive, accurate and timely statistical, epidemiological, and surveillance data that measures the safety and effectiveness of marketed medical devices and that alerts responsible parties to signals of potential risk
- 2) Establish partnerships and alliances with public and private enterprises throughout the medical device community to ensure ongoing communication and leveraging of resources
- 3) Maintain an on-site enforcement inspection and assessment presence throughout the medical device manufacturing community that reinforces quality standards,

- identifies and addresses problems before they impact the public health, and recognizes best practices that could benefit medical device stakeholders.
- 4) Communicate every significant medical device risk in a timely and appropriate manner to the audience that needs to know in language that is clear and meaningful
 - 5) Build postmarket learning into premarket device assessment
 - 6) Identify and communicate examples of excellence and best practice demonstrated by industry in the regulatory process
 - 7) Build and manage information and knowledge systems that support our regulatory and public health responsibilities, and
 - 8) Develop continuously improving human resources who will be skilled and knowledgeable with future medical device issues and priorities.

This document outlines the problem identification, assessment, and resolution processes utilized by the Center. Based on the discussions of surveillance activities, science based information, enforcement actions, information/education tools, and best practices within the organization; the report provides a foundation for program improvement with a focus on prioritizing efforts and maximizing available resources.

Challenges to Ensuring Postmarket Medical Device Safety and Effectiveness

The desire to rapidly bring new medical device technologies to the market must be balanced with a comprehensive postmarket risk management strategy that takes into account the unique characteristics of the variety of medical devices used in the delivery of health care. Premarket studies are generally conducted by highly skilled clinicians treating specially selected patient populations. However, as device technology moves from clinical trial to community practice, there is a need to take a broader view of the skill level of the user of the device, the patient, and the environment in which the device is used. Surveillance and other post market strategies must be able to focus on new technologies as they emerge onto the market while constantly monitoring the diverse use of mature technologies already in use at various levels of the health care delivery system. While CDRH relies on the clinical data submitted by manufacturers for the review and approval process for higher risk medical devices, a large number of medical devices are classified as lower risk, and are either “exempt” from clinical testing, or are shown to be “equivalent to” devices initially approved by evaluation of clinical data. Regardless of the method of review and approval, CDRH’s surveillance systems play a critical role in identification of problems associated with the use of medical devices once they are available to the public.

In addition, off-label use of medical devices is commonplace and demands a thoughtful assessment that acknowledges both the potential risks to the patient as well as the added benefits to medical treatments.

While there are a large number of adverse events attributed to use error in the Medical Device Reporting (MDR) database, there are tremendous challenges to understanding the

cause of the adverse events. This includes basic information on the use interface of the device, labeling, and instructions for use. Experience has also shown that human factors and use-related error issues are often key factors in adverse outcomes and related morbidity and mortality,^{1, 2, 3, 4, 5, 6, 7, 8, 9, 10} and should be given ongoing attention from the industry and the Agency.

Whether used in the in the home of a patient, in the hospital, laboratory, or office of a private practitioner, the Center's ability to understand the risks of adverse events related to the use of medical devices is limited by both the lack of informative, validated adverse event reports and quality epidemiologic information. Congressional reports have estimated that perhaps as few as 1 in 100 medical device adverse events are actually reported. Later research has suggested that device-related adverse events are at least as common as drug-related events in the hospital (see Appendix B, Epidemiologic Aspects of Postmarket Medical Device Safety, Estimates of the Frequency of Adverse Medical Device Events), that in-hospital device use and device-related problems are poorly documented (see Appendix B, Epidemiologic Aspects of Postmarket Medical Device Safety, Lack of Documentation in Healthcare Records of Device Use and Device-Related Problems), and that the underreporting rate is even worse than had been thought (see Appendix B, Epidemiologic Aspects of Postmarket Medical Device Safety, Underreporting of Adverse Medical Device Events).

Diversity in use and experience with devices adds a special challenge to public health efforts and to risk communication efforts aimed at pushing targeted safety information to both the user community and potential patients. The medical device industry in 1995-97 consisted of about 3,000 product lines and 84,000 individual products. The US industry in 1997 was comprised of approximately 6,000 medical and diagnostic companies, about 80% that employed 50 or fewer people. However, these small companies accounted for only 10% of sales, whereas the largest 2% accounted for 45% of sales. The industry

¹ Amoores J, Ingram P. Learning from adverse incidents involving medical devices. *Nurs Stand.* Apr 2-8 2003; 17(29):41-46.

² Gosbee J. Introduction to the human factors engineering series. *Jt Comm J Qual Saf.* Apr 2004;30(4):215-219.

³ Gosbee J. Human factors engineering and patient safety. *Qual Saf Health Care.* Dec 2002;11(4):352-354.

⁴ Gosbee J, Gardner-Bonneau D. The human factor. Systems work better when designed for the people who use them. *Healthc Inform.* Feb 1998;15(2):141-142, 144.

⁵ Lin L, Vicente KJ, Doyle DJ. Patient safety, potential adverse drug events, and medical device design: a human factors engineering approach. *J Biomed Inform.* Aug 2001;34(4):274-284.

⁶ Render ML. Research and redesign are safer than warnings and rules. *Crit Care Med.* Apr 2004;32(4):1074-1075.

⁷ Welch DL. Human factors in the health care facility. *Biomed Instrum Technol.* May-Jun 1998;32(3):311-316.

⁸ Reid MH, Sawyer D. The human factors implications of peritoneal dialysis: cyclor overfill incident reports. *Int J Trauma Nurs.* Apr-Jun 1999;5(2):68-71.

⁹ Fairbanks RJ, Caplan S. Poor interface design and lack of usability testing facilitate medical error. *Jt Comm J Qual Saf.* Oct 2004;30(10):579-584.

¹⁰ Kaye R, Crowley J. Medical device use-safety: incorporating human factors engineering into risk management; identifying, understanding, and addressing use-related hazards. Guidance for Industry and FDA Premarket and Design Control Reviewers. [Http://www.fda.gov/cdrh/humfac/1497.pdf](http://www.fda.gov/cdrh/humfac/1497.pdf). July 18, 2000.

continues to grow. Recent information indicates that there are now approximately 15,000 manufacturers of medical devices. The majority of these manufacturers however, are still small businesses. The preponderance of small manufacturers continues to pose unique challenges in device regulation. Mass production is quite different from small scale processes often used to manufacture devices, and many of the numerous small firms have limited experience because they make just one or only a few products. These small firms may lack the experience to anticipate, recognize, or address manufacturing problems that may pose safety concerns. Acquisition of small firms by larger firms is frequent and presents a challenge in identification of the device manufacturer.

In 2004, the FDA issued a rule regarding barcoding of medical products, including blood and biological products and human drug products, but not medical devices. The major reason that medical devices were not included is because of the challenge of developing a unique identifying system for the diverse universe of medical devices and their many variations. This lack of specificity to identify which devices and models are involved in adverse events, likewise, complicates CDRH's ability to initiate postmarket regulatory activities.

Another unique challenge is the monitoring of *in vitro* diagnostic products (IVD's). Approximately 10 billion laboratory tests are performed per year with up to 80% of medical decision-making now guided by the use of laboratory tests.¹¹ Laboratory test performance occurs in the laboratory, by health care providers, as well as both at the site of the delivery of clinical care, and by home users. The performance errors for IVD's are difficult to identify and understand and may become confused with clinical signals. In addition, the diagnostic performance of an IVD may be affected by conditions surrounding the setting in which it is used.

Oversight of medical device safety is also challenged by the shift of health care delivery to outpatient clinics and the home environment. As a result, patients are spending fewer days in a hospital and are now expected to continue their care or recovery at home. Devices previously designed only for professional use are being used by lay users who are not given the depth of training to recognize device-related problems, and who do not know the process for reporting adverse events.

CDRH Postmarket Safety Framework

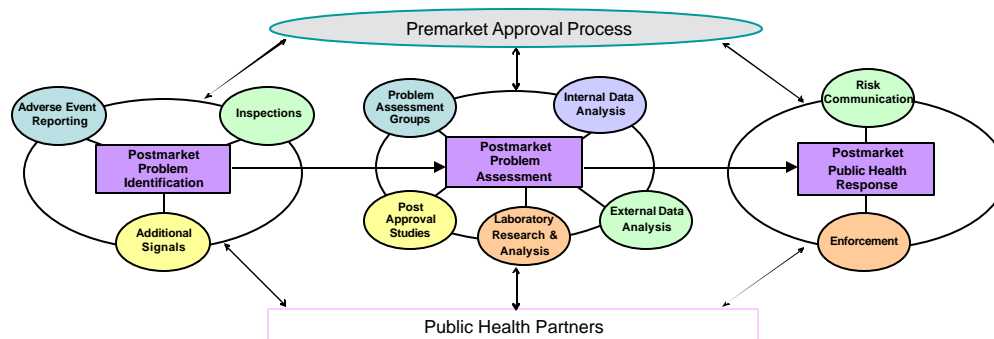
The CDRH Postmarket Safety framework is a network of programs and tools that are focused toward minimizing harm associated with the use of marketed medical devices and improving future generations of medical devices. This framework is modeled after the FDA process for risk management-minimizing harm as shown in Appendix A. Similar to the FDA model, the CDRH postmarket program is directly linked to the

¹¹ IVD manufacturers, labs should be subject to same standards – Advamed. *The Gray Sheet: Medical Devices, Diagnostics & Instrumentation* 2004;30(35):5.

premarket approval process through its sharing of adverse event data, development of guidances and standards, and scientific technology assessment information.

This safety framework is composed of quality systems and inspections, surveillance systems that monitor adverse events and device defects, and assessment and evaluation of potential post market safety issues. Additional tools include 1) mechanisms to inform and educate manufacturers, health care practitioners, and the public, and 2) regulatory processes designed to resolve safety problems and minimize their reoccurrence.

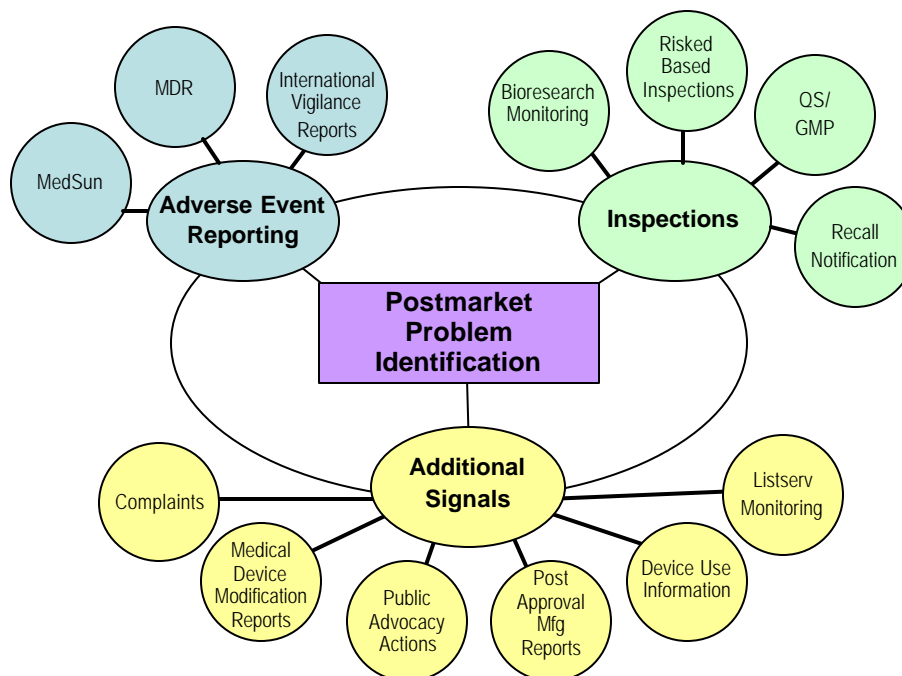
The CDRH postmarket safety framework, shown in the following model, operates through the tools in three integrated areas. They are Postmarket Problem Identification, Postmarket Problem Assessment, and Postmarket Public Health Response. The CDRH processes are linked to the CDRH pre-market programs and are supported by CDRH's internal programs (after-action reviews, and education and training), and the Center's external public health partners.



The report presents the CDRH framework by describing the tools in each of the three process areas. A discussion section for each area is also included that identifies limitations and potential areas for improvement, and provides a basis for suggested recommendations for both short term changes and long term improvement.

Postmarket Problem Identification

The following model depicts several key tools used in the CDRH postmarket problem identification process. Postmarket problem identification tools are used to identify unanticipated public health hazards and to enhance the quantity and quality of information about potential medical device risks in the marketplace.



The problem identification tools include those that are primarily used for surveillance (Adverse Event Reporting and Additional Signals), as well as reports and data that are generated from our industry inspection and recall programs. CDRH's education and training programs help to inform patients, health care practitioners, and industry about the required and voluntary processes for reporting adverse events. At the same time, the resulting information from adverse events enhances the identification of signals through improving the quality of information in adverse event reports and improving the quality of information collected during inspections.

Adverse Event Reporting

The submission of adverse event reports is essential for CDRH to be able to identify existing and potential risk factors of medical devices. Reports submitted by manufacturers and health care practitioners are used to assess the underlying cause and seriousness of an adverse event. The data from these reports are used by staff to conduct health hazard evaluations and product assessments, and as a basis for compliance actions

and recall classifications. It is also used for trend analysis such as detecting safety profile discrepancies across various manufacturers within a product class.

Information on the actual use of devices in the clinical and global community, including the identification of problems due to use-related error, facilitates rapid investigation of emerging health issues. CDRH uses the data to focus on prevention of problems through educational outreach and feedback to healthcare practitioners and medical device manufacturers.

Medical Device Reporting (MDR)

CDRH monitors postmarket device-related adverse events (AEs) through both voluntary and mandatory reporting, to detect potential public health safety issues. Voluntary reporting to the FDA began in 1973 and presently continues under MEDWatch,¹² a program created in 1993 to encourage voluntary reporting by all interested parties.

In 1984 CDRH implemented mandatory reporting as part of the Medical Device Reporting Regulation [21CFR803]. Under this regulation, manufacturers and importers are currently required to submit reports of device-related deaths, serious injuries, and malfunctions. Serious injuries are defined as life-threatening events, events that result in permanent impairment of a body function or permanent damage to a body structure, and events that require medical or surgical intervention to preclude permanent impairment or damage. Malfunctions are defined as the “failure of a device to meet its performance specifications or otherwise not perform as intended”. The term “device-related” means that “the event was or may have been attributable to a medical device, or that a device was, or may have been, a factor in an event including those occurring as a result of device failure, malfunction, improper or inadequate design, poor manufacture, inadequate labeling, or use-related error”. Use-related error is often linked to poor design or inadequate labeling. As needed, guidance is issued to reporting entities to more clearly define the reporting requirements for specific events, such as failures of implanted medical devices.

The enactment of the Safe Medical Device Act (SMDA) in 1990 and Medical Device Amendments of 1992 made a significant impact on the mandatory aspect of the CDRH Postmarket program. SMDA initiated mandatory universal reporting of adverse events by device user facilities. Since SMDA, reports from industry and user facilities are collected in a data base that currently houses over 1.8 million reports. Approximately 95% of these reports are from industry, with the remaining from health care facilities and providers. The number of reports submitted has continued to increase with approximately 180,000 reports submitted and 160,000 entered in 2004. See chart in Appendix C, MAUDE Reports.

¹² Kessler DA, Kennedy DL. MedWatch: FDA’s new medical products reporting program. *J Clin Eng.* 1993; 18(6):489-92.

Medical Device Surveillance Network

MedSun is CDRH's response to a section of the Food and Drug Administration Modernization Act (FDAMA), which required FDA to move from a mandatory program to surveillance reporting by a subset of clinical facilities. The program's principal objective is to increase both the quantity and quality of user facility reporting by recruiting a cadre of well-trained and motivated facilities, and to establish a collaborative effort to better understand medical device use in the clinical environment. Since 2002, CDRH has collected data about medical device use problems from a convenience¹³ sample of hospitals and nursing homes. By mid-2005, MedSun expanded to approximately 350 health care institutions (mostly hospitals) nationwide.

In addition to enhancing the detection of emerging device problems, the network acts as a two-way communication channel between the FDA and the clinical community and serves as a setting for applied clinical research on device issues. To succeed, the effort must train staff in the recognition and reporting of adverse events, assure reporting confidentiality, minimize the burdens of participation, and provide timely feedback on safety information. To achieve its mission, CDRH MedSun staff have initiated a variety of efforts within the network, including monthly newsletters (highlighting device reports, CDRH actions, and other notable safety initiatives by other agencies), clinical engineering audio-conferences, device safety exchanges (highlighting best safety practices and safety solutions), and surveys on high-profile safety concerns.

International Vigilance Reports

The reach of adverse event surveillance became global under the auspices of the Global Harmonization Task Force (GHTF) established in 1992. The GHTF was established to respond to the increasing need for international harmonization in the regulation of medical devices. The GHTF is a voluntary international consortium of public health officials, responsible for administering national medical device regulatory systems and representatives from regulated industry. The task force acts as a vehicle for convergence in regulatory practices related to ensuring the safety, effectiveness and quality of medical devices and promoting technological innovation, as well as facilitating international trade. This is principally accomplished through publication and dissemination of harmonized guidance documents on basic regulatory practices.

¹³ A convenience sample is a sample where the patients are selected, in part or in whole, at the convenience of the researcher. The researcher makes no attempt, or only a limited attempt, to insure that this sample is an accurate representation of some larger group or population. In contrast, a random sample is one where the researcher insures (usually through the use of random numbers applied to a list of the entire population) that each member of that population has an equal probability of being selected.

One of the five GHTF study groups (Study Group 2) is charged with reviewing current adverse event reporting, postmarket surveillance and other forms of vigilance for medical devices. The group is analyzing the different reporting requirements in an effort to harmonize data collection and reporting systems. A process for the global exchange of vigilance reports between National Competent Authorities (NCAs) has been established. Standardized reports about potentially high-risk issues for which action is to be taken, are submitted electronically to a shared list-server. General and specific criteria for categorizing issues as high risk have been established and include the equivalent of US Class I and high level Class II recalls, all public health notifications, and special public health concerns (e.g., high index of preventability or particularly vulnerable populations). Currently, the program exchanges approximately 150 reports per year.

Inspections

A core post-market tool for risk identification is the inspection of establishments (manufacturing sites, clinical study sites, etc.). An establishment inspection is a careful, critical, official examination of a facility to determine its compliance with laws administered by CDRH. Potential safety problems are identified through routine postmarket inspections. Inspections may be used to investigate signals of potential public health problems or to obtain evidence to support legal action related to violations of federal laws and regulations. Inspections may be directed to obtain specific information on new technologies, good practices, or to gather data for establishing standards or regulations.

Inspections provide information on the current state of the medical device industry. The kind and type of inspection is defined by a compliance program or an assignment. A “Comprehensive Inspection” covers everything in the firm subject to CDRH jurisdiction. A “Directed Inspection” covers specific areas to the depth described in the program or assignment. “For cause” inspections are issued to determine the extent of reported problems as well as provide documentation to support voluntary and compelled corrective actions.

Inspections are also a problem prevention tool. When an inspector identifies problems, a firm often makes corrections “on the spot”, thereby preventing a potential health hazard. When trends are identified by inspectors, or through an analysis of field inspection data, educational material is prepared and presented to the industry. Education includes the development of guidance documents, presentations at industry seminars and workshops, as well as face to face meetings with industry.

Quality System/Good Manufacturing Practice (QS/GMP) Inspections

CDRH inspects firms to ensure that systems are in place which enable the device industry to identify systemic quality system deviations. Early identification of potential problems prevents or mitigates health hazards. Good Manufacturing Practice inspections help keep the industry in compliance with federal regulations. CDRH has an obligation under 510(h) of the Federal Food Drug and Cosmetic Act to

inspect medical device manufacturers once every two years. The medical device QS/GMP regulation (21 CFR 820) became effective on June 1, 1997. The Quality System Inspection Technique (QSIT) is a procedure for performing GMP subsystem inspections that can help determine a firm's state of control compliance. The method is helpful in focusing on specific problems and evaluating the firm's follow-up or corrective actions relating to those problems.¹⁴

A QSIT inspection includes a review of the firm's Corrective and Preventive Actions (CAPA) subsystem. The purpose of the CAPA subsystem is to collect and analyze information, identify and investigate product and quality problems, and take appropriate and effective action to prevent recurrence. The CAPA subsystem includes a review of Medical Device Reports (MDR), Reports of Corrections and Removals (CAR), and Medical Device Tracking. Compliance with the Medical Device Tracking regulation ensures that manufacturers and importers can expeditiously locate and remove devices from the market and/or notify patients when significant device problems are identified. The QS/GMP inspections are a key element in insuring that postmarket problems are identified and corrective actions are implemented.

Risk-Based Inspection Strategy

The Center has moved to a risk-based strategy for field inspections. The new process incorporates a definition of risk that is consistent with the ISO 14971:2000 definition. The process incorporates risk-based analytical results from various CDRH monitoring and surveillance programs into the decision making process. Because the device area represents a diversity of products, the expanded process allows for the incorporation of multiple risk-based models including the clinical model, product model, patient model, and technological model.

A Risk-Based approach mitigates potential hazards by focusing limited resources on devices with the greatest risk. Due to the increasing number of medical device firms and limited Field resources, FDA is unable to cover inspections for the entire medical device industry within the two year mandate required under 510(h) of the Federal Food Drug and Cosmetic Act. Under the 1979 Good Manufacturer Procedure (GMP) regulation, investigators followed a "bottom-up" inspectional approach which successfully identified many violative manufacturers. In 1997, the Quality System (QS)/GMP regulation design control requirements increased inspectional time by approximately 50%. CDRH therefore changed the inspection work planning approach to a risk-based inspection strategy. In 2002, CDRH improved the Risk-Based Work Plan (RBWP) process by utilizing information from other postmarket tools noted in this document. All CDRH offices participate in the prioritization process.

¹⁴ A quality system is composed of subsystems. QSIT assesses the following four subsystems: 1. Management Controls, 2. Design Controls, 3. Production and Process Controls, and 4. Corrective and Preventive Actions (CAPA).

At the conclusion of a statutory inspection, an Inspector details the findings of the inspection via an FDA 483 form and an Establishment Inspection Report (EIR). Assignments and “for cause” inspection results are reported according to the format specified under an inspectional guidance section of the assignment.

Bioresearch Monitoring (BIMO) Inspection

Bioresearch Monitoring inspections/investigations ensure data integrity. The purpose of a BIMO inspection is to establish reasonable assurance of the safety and effectiveness of regulated medical devices before and after they reach the market. The BIMO program is a comprehensive program of on-site inspections and data audits designed to monitor all aspects of the conduct and reporting of FDA regulated research. BIMO inspections investigate alleged research misconduct, address human safety protection and data integrity issues, and assure compliance with Good Laboratory Practices (GLP). Under the BIMO program, FDA inspects clinical investigators, non-clinical laboratories, device sponsors and monitors, and Institutional Review Boards. As part of CDRH’s effort to link the premarket approval process with postmarket monitoring, consideration is being given to utilize the BIMO inspection process to collect information that would enable the Center to monitor the status of Condition of Approval studies.

Recall Notification

Per 21 CFR 806, recall activities involving medical devices include “corrections and removals”.¹⁵ Under Section 519(f) (1) of the Act, manufacturers and importers must report information required by the “corrections and removals” regulation to CDRH. If the correction or removal does not present a risk to health, the firm may not be required to file a report. Firms are encouraged to voluntarily report a correction or removal that is not required by section 806 as part of CDRH’s voluntary recall policy (21 CFR 7).

Recall reports, or recalls identified during inspections, are often CDRH’s first notification of a potential medical device risk. Even though recalls are usually voluntary, Section 519(f) of the Act was amended in the 1990 SMDA to ensure that the industry reports recalls to the CDRH. Manufacturers are responsible under device regulations for monitoring their manufacturing process and complaint reports. When a device recall is necessary, the firm notifies the FDA District Office and CDRH’s Office of Compliance. FDA District Offices notify CDRH about a potential recall within 24 hours of the initial notification of a problem. The firm has 10 days to submit the required report. Once the firm’s report is received, CDRH evaluates the

¹⁵ A “correction” covers a number of activities, including the repair, modification, adjustment, relabeling, destruction, inspection, or patient monitoring of a device, even without physical removal from its point of use. A “removal” also covers a number of activities, including the physical removal of a device from its point of use to some other location for repair, modification, adjustment, relabeling, destruction or inspection.

information. Information provided by the firm includes the nature of the defect, assessment of risk, and relevant complaint and MDR reports.

Additional Signals

In addition to information from inspections and adverse event reports, there are several additional sources of information used in identifying medical device problems and potential risks. They include post-approval manufacturer reports, reports of modifications to marketed medical devices, monitoring of professional listserv's, complaints, and public advocacy actions.

Post-approval Manufacturer Reports

A condition of approval for a Premarket Application (PMA) is a requirement to submit post approval reports to the CDRH. Reports have traditionally been submitted at intervals of 1 year from the date of approval of the original PMA and annually thereafter, although the Center may order information to be submitted on an “anytime” schedule.¹⁶

Changes that affect safety and effectiveness must be submitted to the Agency for review and approval in the form of PMA supplements or 30-day Notices prior to including them in the annual report. It is the responsibility of the applicant to determine whether changes made to the device or manufacturing processes may impact safety and effectiveness and therefore require a PMA supplement or 30-day Notice and FDA’s approval prior to implementation of the changes. If the applicant believes there is no impact, the applicant may implement changes without obtaining Agency approval and report these changes in the PMA annual report.

In addition to providing information regarding design, labeling, and manufacturing changes made to the device, the PMA applicant is also required to indicate in the annual report whether they are either:

- a. Unaware of any unpublished reports about their device or similar devices, or
- Aware of on-going studies about their device or similar device and include the reports/articles of clinical and/or non-clinical studies or from the literature in

¹⁶ The annual report must contain the following information required under 21 CFR 814.84:

- a. a list and description of changes to the device or manufacturing processes that affect the safety and effectiveness of the device (21 CFR 814.39(a));
- b. a list and description of changes to the device that do not affect the device’s safety and effectiveness (21 CFR 814.39(b));
- c. copies of unpublished reports of data from any clinical investigations or non clinical laboratory studies involving the device or related devices and known to or that reasonably should be known to the applicant; and
- d. copies of reports in the scientific literature concerning the device and known to or that reasonably should be known to the applicant.

the annual reports. In addition, the applicant should include a discussion on how the data included in these reports/articles may or may not have impact on the known safety and effectiveness profile of the device. If the applicants determine that changes to the device or labeling are necessary after reviewing the data in these reports, they should inform CDRH of their plan and if necessary, provide the Center with the proper PMA supplement. Likewise, if the Center staff decides that changes are necessary, the Center will convey its recommendation to the applicant.

The information contained in a PMA annual report enables the Center to monitor changes to the marketed device or on-going studies about the device on an annual basis. If necessary, CDRH can require an applicant to make appropriate changes to ensure that the device remains safe and effective.

Listserv Monitoring

CDRH also receives information about potential hazards and ethical issues through monitoring information available on professional listserv postings on the Internet. This method of gathering information provides immediate feedback about problems from actual users of devices and can also provide an early indication of a developing problem.

In November 2002, a work group was convened to monitor real world performance of in vitro diagnostic devices (IVDs) by utilizing professional web based listservs concerning laboratory issues. Over a dozen general laboratory listservs were identified. Subject specific issues included chemistry, microbiology, molecular diagnostics, and virology. The signals are triaged by a central coordinator and shared with both members of the compliance work force and members of the premarket review group that have experience working with IVDs. These signals are also presented at an internal monthly Patient Safety Meeting.

In the past two and a half years, about a dozen signals of interest have been identified and action has been taken to clarify several of these reported problems. In some cases, the information obtained was used to corroborate issues highlighted from other sources (MDRs, user complaints). In other cases, unique issues were identified. The monitoring of the Listserv for IVDs often provides information that is unavailable through our other reporting mechanisms.

Complaints and Public Advocacy

CDRH receives oral and written complaints from a variety of sources, including a firm's competitors, clinical investigators, whistleblowers, and patients. Information may come in as a consumer complaint or a trade complaint through one of FDA's 21 District Offices or through the CDRH consumer phone line. Information is submitted through official tracked correspondence, e-mails, letters, and phone calls. If the

nature of the complaint is serious, CDRH can issue a “for cause” or Bioresearch Monitoring (BIMO) inspection.

Device-Use Information

The interaction between users and medical devices results in many adverse patient outcomes annually. Approximately one third of all the MDRs that CDRH receives annually could be linked to use-related errors. It is crucial for CDRH to monitor and identify potential device use-related errors in order to reduce the number of unanticipated adverse events. As part of an ongoing effort to identify use-related errors with medical devices, CDRH staff routinely review published literature. Device use information is also collected from quality systems inspections. Participation in health hazard evaluations and in PMI action teams also enable CDRH staff to identify those adverse events associated with use-related errors.

Another method for identifying use-related errors is the implementation of an analysis, description, and educational tool (UPCARE) developed by CDRH staff. The UPCARE tool is designed to help those who report adverse events to CDRH and CDRH field staff, to describe and analyze medical device use-related problems. It is also intended to serve as a structured repository for additional information on use-related problems with medical devices. The content and structure of the UPCARE tool was developed from discussions with nurses from various specialty areas and biomedical engineers, and was further supported by information generated from analyses by CDRH staff of use-related problems with medical and non-medical devices.

Public Health Partners

Fortunately, CDRH does not act alone in public health protection. There are a number of efforts external to CDRH that are directly or indirectly involved in collecting and analyzing data relevant to estimating medical device use and risk and in communicating risk to target populations. The Department of Health and Human Services has also been interested in encouraging coordination of the various initiatives across the various HHS agencies. These initiatives have a common aim of doing their part to facilitate progress in public health within their individual statutory mandates. The following are some of CDRH’s public health surveillance partners.

Centers for Medicare And Medicaid Services (CMS)

Medicare Data

CDRH is currently collaborating with CMS and the Dartmouth Center for the Evaluative Clinical Sciences in a pilot study examining the potential utility of Medicare data (Parts A and B, and denominator file) for postmarket surveillance. Comparative short- and long-term morbidity and mortality of open surgical versus

endovascular stent-graft repair of abdominal aortic aneurysms will be examined, as will manufacture-specific outcomes and trends in use of either approach by region of country. The implications of this study for the postmarket surveillance of medical devices using claims data will be described. Pending the results of this pilot, and additional funding from CDRH, further efforts may be planned.

CMS-Mandated National Registries

CMS has recently issued national coverage decisions, calling for the collection of prospective data via national registries, on two high-profile devices: left ventricular assist devices (LVADs) and carotid stents. A third registry for implantable cardioverter defibrillators is currently under discussion. As part of the decision, Medicare will cover those patients who meet certain criteria and who are entered into the registry. For LVADs, NIH is the lead agency in overseeing data collection and analysis. For carotid stents, data may be collected under the auspices of a FDA post-approval study. FDA's access to the data and relationship with CMS/NIH data monitoring and analysis is as yet undetermined.

National Institutes of Health (NIH)

Dynamic Registry

The NIH has had a long-standing interest in percutaneous transluminal coronary angioplasty (PTCA) procedures, dating back to the 1980s. Since then, they have established four consecutive nation-wide registries, the most recent being the National Heart, Lung, and Blood Institute's "Dynamic Registry." The multi-center Dynamic Registry is the only formal registry of consecutive percutaneous coronary intervention (PCI)-treated cases that captures both in-hospital and long-term patient outcomes, while characterizing initial procedural strategy and outcome in great detail on the patient and lesion level. The Registry was extended through June 2007 to continue to collect data on prior "waves" of registry patients, including 4-year annual follow-up of 2000 Registry patients who undergo PCI with the first-generation of drug-eluting stents and 1-year follow-up of an equal number of patients who will undergo PCI at a time when subsequent generations of drug-eluting stents have penetrated clinical practice.

In the mid-1990s, with funding from the OWH, CDRH epidemiologists collaborated with investigators overseeing the Registry to investigate gender differences after coronary angioplasty with the Palmaz-Schatz stent. Both short- (30 day) and long-term (1 year) outcomes were investigated among equal numbers of men and women (about 500 each) from registry data collected from 1990-94. CDRH continues to review the literature produced by this important ongoing endeavor.

Agency for Healthcare Research and Quality

In recognition of the importance of medical devices to patient safety, AHRQ is supporting and collaborating with CDRH for three initiatives.

Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample (NIS)

The NIS is a stratified probability sample of more than 995 non-federal hospitals in 35 states participating in HCUP, and is designed to approximate a 20% national sample of hospital discharges. Demographic and hospital information, as well as ICD-9 CM codes for diagnoses and procedures, are used to estimate in-hospital morbidity and mortality rates associated with various procedures performed in non-federal hospitals in the U.S. CDRH has used these data to estimate patient characteristics and in-hospital mortality rates associated with aortic-valve replacement (both tissue and mechanical). AHRQ staff are collaborating with CDRH on projects to assess similar information pertinent to hip replacements. NIS data had also been used by CDRH to provide national estimates of numbers of hospital discharges related to Toxic Shock Syndrome, and further collaborative investigations of TSS are planned. NIS data are being used to understand the extent and economic consequences of adverse medical device events indicated by discharge claim codes, to develop a medical device-related patient safety indicator, and to estimate the amount of MDR underreporting for automatic implantable cardioverter defibrillators.

Health Information Technology Development: Global Medical Device Nomenclature

AHRQ is planning to help fund development of the Global Medical Device Nomenclature because a rational, complete system of identifying devices will be crucial to a complete and well-designed system of health information technology. Effective health information technology is one of the objectives of the Department Secretary.

Health Information Technology Development: Documentation of Device Use and Device-Related Problems

In collaboration with the University of Utah, CDRH documented the general lack of device use and device-related problems in hospital patient charts. In response, AHRQ funded a workshop to brainstorm strategies for addressing the problem. The importance of increasing this type of documentation is that all types of surveillance rely on basic documentation. The lack of documentation in the

patient records severely limits the development of effective systems of adverse medical device events.

Consumer Product Safety Commission (CPSC)

National Electronic Injury Surveillance System (NEISS)

CPSC's NEISS is a national probability sample of hospitals in the U.S. and its territories. Patient information is collected from each NEISS hospital for every emergency visit involving an injury associated with consumer products. From this sample, the total number of product-related injuries treated in hospital emergency rooms nationwide can be estimated. With CDRH funding, the first-ever national estimates of medical-device associated adverse events resulting in emergency room visits were established in 2000.⁴¹ With continued funding, more detailed record abstraction is underway with the aim of refining the public health burden posed by medical devices and of identifying potential public health interventions. NEISS has been praised and recommended for emulation by other federal agencies by the Institute of Medicine Committee on Injury Prevention and Control.¹⁷

Professional Society Registries

American College of Cardiology (ACC) National Cardiovascular Data Registry (NCDR)

In the late 1990s, ACC began to develop its NCDR. Currently, there are over 700 institutions nationwide who submit cardiac catheterization data to the registry. These data include over 140 core elements needed for measuring the clinical management and outcomes of patients undergoing diagnostic cardiac catheterizations and percutaneous coronary interventions.

CDRH was the first governmental entity to do collaborative research with ACC in use of their NCDR. Both hemostasis devices and drug-eluting stents have been the subjects of investigation. The largest observational studies of hemostasis device in general, and manufacturer-specific devices, have recently been completed in a collaborative effort between CDRH and ACC.^{18,19} Both studies

¹⁷ Bonnie RJ, Fulco CE, Liverman CT, eds. Reducing the burden of injury: advancing prevention and treatment. National Academy Press, Washington DC, 1999.

¹⁸ Tavis DR, Gallauresi BA, Lin B, Rich SE, Shaw RE, Weintraub WS, Brindis RG, Hewitt K. Risk of Local Adverse Events Following Cardiac Catheterization by Hemostasis Device Use and Gender. *Journal of Invasive Cardiology* 16(9):459-64, 2004.

¹⁹ Tavis DR, Dey S, Albrecht-Gallauresi B, Brindis R, Shaw RE, Weintraub WS, Mitchel K. Risk of Local Adverse Events Following Cardiac Catheterization by Hemostasis Device Use: Phase II. *J Invasive Cardiol* 2005; 17(12):644-50.

were funded by OWH. In addition, CDRH currently has a contract with ACC to access specific patient- and procedure-level information relevant to assessing prevalence of both on- and off-label use drug-eluting stents.

Society of Thoracic Surgeons (STS) National Adult Cardiac Surgery Database

The STS database was developed in 1990 as a multi-center clinical repository for quality improvement and clinical research. The database currently collects data from approximately two-thirds of all U.S. cardiothoracic hospitals (over 700) and contains detailed data on patient demographics, clinical profile, and acute outcomes on more than 2.1 million procedures. CDRH has collaborated with the Duke Clinical Research Institute (the data coordinating center) in use of STS data to assess use and outcomes of transmyocardial revascularization (TMR). This CDRH-funded project found: 1) a marked increase in use of TMR during its early years of U.S. marketing; 2) only 17% of procedures were based on labeled indications; and 3) operative mortality was significantly higher in those patients with recent myocardial infarction, unstable angina, and depressed ventricular function.²⁰ As important cardiovascular device issues surface, CDRH continues to examine whether the STS database can provide relevant data to help address our concerns.

ECRI

ECRI is a nonprofit health services research organization. ECRI's focus is health care technology, health care risk and quality management, and health care environmental management. It provides health care-related services to a wide variety of customers through its more than 30 databases, publications, information services, and technical assistance services.

ECRI's services alert readers to technology-related hazards; disseminate the results of medical product evaluations and technology assessments; provide expert advice on technology acquisitions, staffing, and management; report on hazardous materials management policy and practices; and supply authoritative information on risk control in health care facilities and clinical practice guidelines and standards.

For more than 30 years, ECRI has gathered and investigated reports of incidents involving medical devices (including capital equipment, reusable and disposable instruments, reagents, etc.). Information is gathered from health care providers, patients, and manufacturers around the world. As a result of ECRI's investigations, many manufacturers have recalled or modified their devices. ECRI publishes many of these reports as Hazard Reports and User Experience

²⁰ Peterson ED, Kaul P, Kaczmarek RG, Hammill BG, Armstrong PW, Bridges CR, Ferguson TB Jr; Society of Thoracic Surgeons. From controlled trials to clinical practice: monitoring transmyocardial revascularization use and outcomes. *J Am Coll Cardiol*. 2003 Nov 5;42(9):1611-6.

Network™ articles in [Health Devices](#) and as Hazard Bulletins, Urgent Bulletins, and Action Items in [Health Devices Alerts](#).

CDRH frequently makes use of ECRI's various databases to assess device safety issues. In addition, MedSun staff consult with ECRI on a variety of "real-time" incidents. ECRI staff provide written device assessments (many times including their own device testing) in response to these consult requests.

Utah Entities

CDRH has been collaborating with University of Utah to study the extent and nature of documentation of device use and related problems. The first study found that in a hospital with electronic medical charts, devising and using "flags" of adverse events in real time patient care, and using procedure codes in discharge claims, many more adverse medical device events were detected (24 to 53 times more) than were reported to the hospital incident report system.⁴² The second study was undertaken to get a better estimate of the true rate of adverse medical device events and compare the results by detection source. These results showed the inadequacy of relying on the incident reports (detected 3.9 events/1000 patient days) and the chart (detected 21 events/1000 patient days) in discovering device related problems, but also illustrated the intensity of effort (direct observation detected 839 events/1000 patient days) required to find the most problems.

The Salt Lake City Veterans Administration Medical Center has begun informal collaboration with the University of Utah and CDRH to study adverse medical device events and their detection.

The Department of Health for the State of Utah has begun negotiation to collaborate with CDRH to explore using its collection of statewide discharge claims data to study and monitor adverse medical device events as a public health tool.

Discussion - Postmarket Problem Identification

The Center's ability to identify potential risks associated with the use of marketed medical devices is highly dependent upon the robustness of information gathered from the tools described in this section of the document, and the process of signal and risk identification inherent in the daily work of the Center. Both suffer from a variety of challenges. These challenges include 1) the need for cross-Center communication and sharing of reports, research, and other signal information, 2) a lack of quality information and a method to efficiently process the information submitted, 3) education about reporting requirements, quality, and data needs, and 4) technology utilization for efficient device identification, data mining, and timely access.

The Center advocates a Total Product Life Cycle (TPLC) model as shown in Appendix D which includes a goal of improved communication across Offices. The development of an infrastructure to facilitate “analysis-centered” access to inspection, adverse event, pre-submission, post-submission, and complaint data will enhance CDRH’s ability to approve safe and effective devices as well as prevent or mitigate postmarket public health risks.

Documentation of device use and device-related problems is sporadic in our health care system (see Appendix B, Epidemiologic Aspects of Postmarket Medical Device Safety, Lack of Documentation in Healthcare Records of Device Use and Device-Related Problems) and is hindered by the lack of standardized device nomenclature and identifiers. Development of this technology and utilization by health care practitioners and facilities could contribute to timely electronic submissions of adverse event reports, provide the capability to quickly identify specific medical devices in use, and provide information to more fully understand the circumstances surrounding the use of medical devices in health care settings.

While the Center has many useful tools to collect information both from the users and from the manufacturers of medical devices, the information is collected for a variety of different reasons (i.e. adverse event reports, quality inspection information) and it is reported in a variety of formats (i.e. structured questions or narrative observations) at different times (i.e. as adverse events occur, annual reports, or as part of a recall). In addition, the information flows into the individual Center offices that are responsible for specific regulatory functions. The information may be adequate for a specific purpose, but not always viewed in the aggregate for the purpose of postmarket problem identification. One key to improved identification would be to compare or look at the data from the different databases and sources in the aggregate. The efficient use of database technology would lead to more productive methods to identify postmarket risks.

Mandatory reporting requirements enable CDRH to obtain safety data which is supplemented by voluntary reporting systems. These spontaneous reporting systems are important in the identification of unusual, unexpected and severe events but have limitations for addressing other surveillance challenges such as follow-up on long term implants. Some of the weaknesses of the adverse event collection mechanisms can be attributed to severe underreporting (see Appendix B, Epidemiologic Aspects of Postmarket Medical Device Safety, Underreporting of Adverse Medical Device Events), which, in part, is due to the passive nature of these systems (see Appendix E, Capability Analysis of Surveillance Programs Internal and External to CDRH with Respect to Surveillance Goals, Surveillance Methods: “Active” vs. “Passive”). The consequences of underreporting include an uncertainty about the frequency of adverse events and limited capability to compare reports across device manufacturers and device types. Because device use and device-related problems are not routinely documented in medical records, the only currently available tool for obtaining objective real time use data is medical device registries, which have potential for some products and specific concerns (see Appendix B, Epidemiologic Aspects of Postmarket Medical Device Safety), but are established for only a few specific devices.

Another limitation is that adverse event reports frequently lack pertinent information that is critical for understanding the event and the relationship of the event to the device. The Center's MedSun program is designed to improve the quality of reports by training better reporters through feedback and follow-up. The lack of knowledge about FDA's role and MDR's reporting requirements are factors which also contribute to under-reporting of adverse events.

In contrast to the fact that underreporting of medical device adverse events continues, the volume of reports being submitted to the MDR system currently exceeds the Center's ability to consistently enter or review the data in a routine manner. The Center has attempted to address this volume by using alternative reporting strategies for well known products and problems, and utilization of triaging signals to guide further investigation. Additional data mining and triage technologies may be helpful in management of the current volume and anticipated future increases in adverse event reporting.

MedSun has expanded the Center's surveillance scope by connecting directly to the device user, educating reporters and obtaining more complete information. The unique strength of more actively solicited reporting is its ability to provide CDRH with very rapid notification of adverse events that are high risk regardless of the frequency of recurrence. Electronic real time reporting reduces the delay even further between the time the event occurs and the time it is submitted. Implementing an electronic reporting system for MDR reports with quality checks built into an electronic submission system could reduce the likelihood of incomplete, poor quality, or non-validated reports that are difficult to decipher.

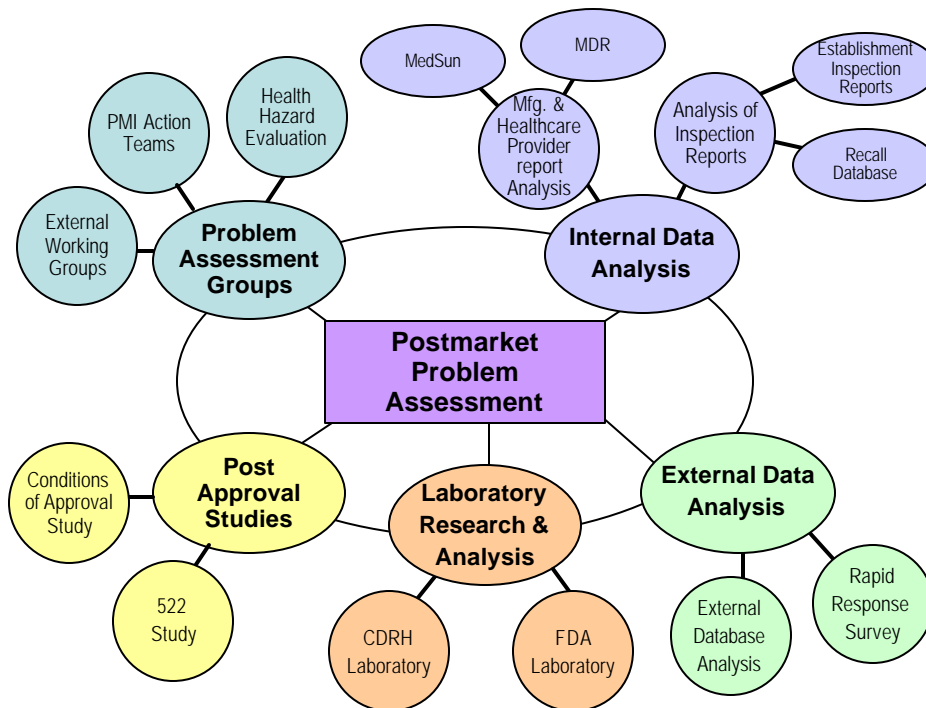
Information gathered from the Center's Quality Systems inspections is particularly helpful in the identification of risk associated with the use of medical devices. The primary purpose of the CDRH inspection process is to identify deviations from CDRH regulations which could result in a public health hazard. One key objective is to ensure that the industry has a Quality Systems Process in place and that it is effectively working to improve patient safety. Quality systems information, as well as information gathered from other specially requested inspections, however, is not routinely integrated into the Center's pool of information and data used to monitor postmarket risks for products. Full implementation of the calculation of risk depends on the availability of objective data about the extent of device-use and device-related problems, which may not be routinely available from facilities. Developing a method of utilizing device use information derived from quality systems inspections may help the Center to more fully realize and improve our current process for risk calculation.

Further, the quality of information generated from the inspection process is dependent upon the skills, knowledge, and ability of the inspector/investigator. It is therefore important that FDA continue to recruit, hire, and educate our Field staff regarding the information needed for adequate use as signals for device safety when analyzed with data or information from other sources.

The inspection process is also resource intensive for the field staff of FDA. With its current level of resources, the Center is not able to meet its current statutory obligation to inspect the total industry every two years. The risk-based concept focuses device inspection resources upon the part of the industry that is thought to present the greatest public health risks. An extension of this concept to supplement our inspection process with the use of third party inspections (for the part of the industry that is a lower priority under the risk-based concept) would improve our current process and provide needed information on a wider range of risks associated with the use of medical devices.

Postmarket Problem Assessment

The following model depicts the major tools used in the CDRH postmarket problem assessment process. Postmarket problem assessment tools are used to scientifically evaluate the factors related to the potential for risk and actual adverse events associated with the use of medical devices. This includes conducting additional data collection and analyses, identifying factors in device failure, assessing use interface issues, evaluating labeling information, and collecting and analyzing user experience information. Ideally, findings from the postmarket assessment process are directed back to the premarket process for consideration by reviewers. They also serve as the basis for postmarket public health response actions.



Adverse event analysis and epidemiological tools are the backbone of the Postmarket Assessment Process. Information collected from the various problem identification tools is analyzed by CDRH staff, as is additional information from post-approval studies, laboratory research studies, and external data sources.

The problem assessment tools utilized by the Center are divided into five major categories. They include internal data analysis, external data analysis, laboratory research and analysis, post approval studies and problem assessment groups. An additional level of tools within the categories is shown on the model above to further delineate the variety of data and information available to analysts for CDRH's postmarket problem assessments.

Internal Data Analysis

CDRH staff analyzes the data and other information reported to CDRH by the industry, consumers, and the health care community. Analysis of inspectional information includes data from routine inspections, directed assignments, and other information from recall recommendations. Data and information from the industry and the health care community is included in medical device reports, potential recall data, MedSun reports, published literature presenting case studies, clinical trials, and observational studies.

Manufacturer and Health Care Provider Report Analysis

Adverse event data is used to identify areas which require additional investigation, to determine the scope of the problem and to develop strategies for addressing public health issues.

Medical Device Reports (MDR)

The MDR system is a passive reporting system and as a result, reports are often incomplete or difficult to understand (see Appendix B, Epidemiologic Aspects of Postmarket Medical Device Safety, Incompleteness of Reports), As reports are entered into the database, they are first triaged to identify reports that may signal high risk issues such as pediatric deaths or exsanguinations. Analysts read and evaluate reports based on their knowledge of the product area. The reports are individually reviewed for rare or unexpected events and events occurring at a higher rate than expected. The data is assessed to identify problems uncorrected or unknown by the manufacturer and across device types. Summary reports capture well-characterized and well-known device events and amount to a quarterly submission by manufacturers of line-listed data. The data elements per event include the manufacturer, model-specific device, event and receipt dates, and patient and device problem codes. A system is being developed to perform automated numerator-only

trend analyses looking for month-to-month variation, monthly moving averages, and 12-month trends. About 60% of the reports are in summary format.

Report reviewers may request additional information from the manufacturer or other reporter and also consult other CDRH staff to learn the premarket path of the device, any compliance history, or consult with the human factors staff and laboratory scientists as needed.

The reports are reviewed from a variety of perspectives including the potential for failure, (e.g. poor design, manufacturing defect), use-related error (e.g. device mis-assembly, errors in installation, calibration, incorrect clinical use, maintenance, misreading instructions), packing error, support system failure, adverse environmental factors, underlying patient disease or co-morbid conditions, idiosyncratic patient reactions, maintenance error, and adverse device interaction.

Because many devices involve complex human interaction, CDRH is interested in usability testing and human factors analysis. Human factors analysis assesses how users interact with devices at every phase: how they install, calibrate, operate, maintain, and ultimately, dispose of medical devices. To identify and understand these factors, when device use issues arise, CDRH looks at all of the essential components of the device-use system including: device users - patients, family members, physicians, nurses, and professional caregivers; typical and atypical device use; device and patient characteristics; characteristics of the environments in which the device will be used; and the interaction between users, devices, and the environment in which the device is used.

When potential hazards are detected either from individual reports or from the aggregate review of several reports, a number of actions are taken, usually beginning with routine requests for additional information from the reporters or convening an internal meeting of experts. Frequently, such inquiries include a search for a more thorough understanding of the event, an attempt to acquire denominator data and a search of the regulatory history of the device and other adverse event reports. As additional information is obtained, additional actions may include recommending directed inspections of the manufacturer and alerting other regulatory bodies outside the U.S. to inquire if they have additional information on similar events.

The number of MDR reports has been steadily increasing ever since they were required (see Appendix C, Maude Reports). In 2004, 95% of the reports were from manufacturers, and only 2% were from individuals. In 1995, some manufacturers were granted permission to submit specified combinations of device modifications and adverse events in summary reports, which now constitute between 40-50% of the entire database of reports.

Medical Device Surveillance Network (MedSun)

Initial MedSun report review is conducted by the contractor's staff so that CDRH is provided with a more complete report, if possible. MedSun reports include a small number of deaths and serious injuries with the majority of reports designated as minor injuries, potential for harm, malfunctions and "close calls" (where no patient injury occurs). When CDRH is alerted to problems before patient injury occurs, we can be proactive in attempting to prevent another more serious occurrence of the same problem.

MedSun and other Center staff participate in a weekly triage that focuses on reports that appear to be high risk or of particular concern. This triage group consists of staff with various types of expertise, so that reports can be assessed from different view points. Additionally, it permits FDA to ask the contractor to contact the reporting site with additional questions, when necessary. The review team will note reports that are of particular interest and then interact with the FDA analysts assigned to review of all device adverse events. The team tracks whether or not regulatory action was taken on the reports and the outcome of those actions. Additionally, the MedSun team will often champion problems with device-use issues for which the solution is user education rather than regulatory action. Reports are also in the MAUDE database where they may be viewed by Center staff. A well written, well documented MedSun report often will initiate action on the part of the Center even though there may have been similar reports in the larger adverse event (MAUDE) database. Because MedSun reports come directly from the device users and often contain a detailed account of an adverse outcome, analysts are able to more fully define the problem and the seriousness of the event.

Analysis of Inspection Reports

Medical device information is collected as part of the Center's inspection process and tracking of manufacturer's recall activities. While the information and reports are submitted as part of tracking manufacturers' compliance with medical device regulations, the reports provide a rich source of device use and device related information. The information is assessed as part of the recall and compliance activity of the Center.

Recall Database Analysis

Recall data is used to assess a public health risk related to the use of specific medical devices that have been recalled by the manufacturer. The analysis of patterns of occurrence from recall databases identify broad problems which can be shared with pre-approval reviewers and the industry.

The recall process includes documentation contained in several types of reports, including a 24-Hour Alert, a Recall Recommendation, the Classification of the Recall, oversight of the firm's recall strategy, and the Termination of the Recall. The

Agency maintains the above information in an FDA Recall Enterprise System (RES). In addition, CDRH maintains two recall databases; a CDRH Recall Database, and a Recall Problem Database. Analysis of the information within the three databases is used to identify trends and develop strategies to prevent future medical device problems. The data is used as part of the risk-based inspection process to ensure appropriate inspection coverage of high risk devices. Recall data is also used for issue definition and development prior to initiating a health hazard evaluation, PMI action team review, or a problem workgroup.

Establishment Inspection Report (EIR) and Inspection Assignment Analysis

Compliance with CDRH regulations is important because it is a proactive way to prevent public health problems. Establishment Inspection Reports contain factual, objective observations with supporting documentation. FDA form 483 is used to list deviations (from Good Manufacturing Procedures and other FDA regulations) identified during inspections. These deviations need to be addressed to bring a facility or a procedure into compliance.

Information is gathered either from routine inspection visits or as part of a special Field assignment. Information gathered via routine FDA Field inspections is analyzed to determine the current state of the industry, identify trends, and provide support for informed decision making. The information is used to support scientific decisions, justify administrative and judicial regulatory actions, and determine program direction. Information gathered from special field assignments is analyzed to determine the extent of a problem or to determine if strategies are effective in solving or mitigating the public health hazards.

External Data Analysis

Information from internal data may be supplemented by accessing data from external sources to further define issues of medical device postmarket safety and effectiveness. The CDRH staff utilizes its epidemiologic and surveillance expertise to investigate medical device problems through analyses of external databases.

CDRH laboratory research and data analyses supplement the data collected for problem identification. The laboratory interdisciplinary scientific expertise provides an independent source of investigation that supplements epidemiological assessment of external data.

External Database Analysis

The epidemiology program makes use of a variety of databases and develops device-specific supplemental questions that are included in nation-wide surveys.²¹ In

²¹ For example, CDRH accesses the Health Care Utilization Project Nationwide Inpatient Sample administered by the Agency for Healthcare Research and Quality to evaluate in-hospital mortality

addition, the program explores new means of surveillance,²² explores methods of active surveillance,²³ develops and expands existing device registries,²⁴ reviews and assesses observational literature,²⁵ conducts applied research on device-related risks,²⁶ conducts research on the effectiveness of ongoing regulatory actions,²⁷ and explores data-mining methodology as a tool for signal detection. A description of many external databases routinely utilized by CDRH is provided in Appendix E (Capability Analysis of Surveillance Programs Internal and External to CDRH with Respect to Surveillance Goals).

Rapid Response Survey

When data sources fail to provide enough information to perform a risk/hazard analysis, CDRH implements a tool called “Rapid Response Surveys”. The variety of problems seen with medical products dictates that each survey effort will be unique in that each will involve a different type of product used by different health care professionals. This tool allows CDRH to quickly contact device users (health care professionals) to learn whether or not they have experienced a similar problem. From these “real time” surveys, CDRH may learn if a reported adverse outcome is an isolated incident or a signal of a potentially serious product problem.

Laboratory Research and Analysis

CDRH Laboratory

The CDRH laboratory performs laboratory evaluations and analyses in support of CDRH premarket and postmarket activities. Specifically, the laboratory develops and conducts

associated with heart valve replacement (Astor BC, Kaczmarek RG, Hefflin B, Daley WR: Mortality after aortic valve replacement: results from a nationally representative database. *Ann Thorac Surg* 2000; 70:1939-1945.). CDRH developed a supplement to the US National Mortality Followback Survey to assess characteristics of persons receiving pacemakers in their final year of life (Hefflin, BJ. Final-year-of life pacemaker recipients. *J Am Geriatr Soc.* 1998; 46(11):1396-400.).

²² E.g. through a nation-wide surveillance network of emergency departments operated by the US Consumer Products Safety Commission (CPSC): Hefflin, BJ, Gross TP, Schroeder TJ. Estimates of medical device-associated adverse events from emergency departments. *Am J Prev Med* 2004; **27**(3):246-253.

²³ In a large tertiary hospital: Samore, MH, Evans RS, Lassen A, Gould P, Lloyd J, Gardner RM, Abouzelof R, Taylor, C, Woodbury DA, Willy M, Bright RA. Surveillance of medical device-related hazards and adverse events in hospitalized patients. *JAMA* 2004; **291**:325-34.

²⁴ E.g. exploring device safety using the American College of Cardiology National Cardiovascular Data Registry: Tavis DR, Gallauresi BA, Lin B, Rich SE, Shaw RE, Weintraub WS, Brindis RG, Hewitt K. Risk of Local Adverse Events Following Cardiac Catheterization by Hemostasis Device Use and Gender. *Journal of Invasive Cardiology* 2004; 16(9):459-64.

²⁵ E.g. studies of cellular phones and their relation to brain cancer.

²⁶ E.g. breast implants and rupture rates: Brown SL, Middleton MS, Berg WA, Soo MS, Pennello G. Prevalence of rupture of silicone-gel breast implants revealed on MR imaging in a population of women in Birmingham, Alabama. *AJR* 2000; **175**:1057-1064.

²⁷ Kaczmarek RG, M.D. Beaulieu MD, Kessler LG, Medical device tracking: results of a case study of the implantable cardioverter defibrillator. *Am J Cardiol*, 2000; **85**(5): 588-92.

research and testing programs in physical, life, and engineering sciences related to medical devices and radiological health products. It develops data needed for current and future regulatory challenges, conducts research, manages, develops, and supports standards used for regulatory assessments, and anticipates the impact of technology on the safety, effectiveness, and use of regulated products.

The CDRH laboratory provides analytical support to postmarket regulatory activities in a variety of ways:

- Scientific and engineering reviews and analyses
- Laboratory investigations of product performance
- Participation in inspections of medical device establishments
- Forensic reviews and investigations
- Identification and assessment of device safety and performance issues
- Scientific and engineering expertise and analysis for health risk assessments
- Provision of training to the Center and industry

One of the major functions of the CDRH laboratory is to provide an independent source of data generated in its core laboratories. The basic strength of the lab is derived from the ability to generate laboratory data on the mechanistic understanding of the device performance or a test procedure. This enables the Center and device manufacturers to gain an improved understanding of issues related to safety and efficacy. The CDRH lab contributes to Center-wide teams on issues identification as well as science-based analysis of postmarket device performance.

The lab's reviews and investigations provide an independent assessment of claims concerning safety or effectiveness. The reviews assess the adequacy of medical device design, information from failure investigations, and the manufacturers' production or quality processes. These in-house reviews and analyses are augmented by expertise solicited from colleagues in academia, other government laboratories, or other industry sectors.

FDA Laboratory

FDA maintains a medical device laboratory at the Winchester Analytical and Engineering Center (WEAC) outside Boston, Massachusetts. WEAC is equipped to conduct certain routine testing protocols that have been established for specific classes of medical devices. WEAC conducts ad hoc investigations originating from the Field staff and maintains a limited research portfolio. WEAC and the staff from the CDRH laboratory actively cooperate to maintain collaborative and complementary programs and capabilities.

Post Approval Studies and Annual Reports

Post-approval studies include Conditions of Approval studies and 522 Studies. CDRH staff design these studies and work with Premarket Application (PMA) review teams, Post-Market Issue Teams, and other Center experts to assess the study results.

Conditions of Approval Study and Annual Reports

Approvals of premarket applications (PMAs) frequently require the sponsor to conduct post-market studies as a “condition of approval” under authority of 21CFR814.82(a). Requirements can include “continuing evaluation and periodic reporting on the safety, effectiveness, and reliability of the device for its intended use.” Approximately one-half of original PMAs that are approved include conditions of approval study requirements.

CDRH staff develop requirements for conditions of approval studies by working with other Center experts to identify issues of safety and/or effectiveness that should be examined in postmarket reports. The studies are designed in collaboration with Center staff and industry. Once the Postmarket Plan is developed, it may be presented during an Advisory Panel Meeting. Interim and final post-approval study reports are reviewed when submitted by industry. Post-approval studies attempt to balance least burdensome provisions with scientifically effective approaches, and focus on public health objectives. Other elements of study design (e.g., outcomes of interest, sample size, etc.) are based on the specified objective of the study.

A recent evaluation of Conditions of Approval Postmarket Studies revealed deficiencies regarding the quality of such studies that address specific premarket questions in the postmarket arena.²⁸ A new pilot approach is successfully tracking postmarket commitments, facilitating collaborative development of higher quality studies, and building accountability for postmarket deliverables.

It is important for the premarket review staff to highlight information about potential issues with new devices for the postmarket assessment staff. Concern about potential device hazards are discussed with the post-market staff so that the device can be properly monitored for these specific concerns as the device moves into community practice.

- 522 Study

Section 522, mandated in 1990 under the Safe Medical Device Act and amended under FDAMA in 2000, gives CDRH the authority to require postmarket study requirements. CDRH may order a device manufacturer to conduct a postmarket study for a Class II or Class III device if the device:

²⁸ Brown SL, Bezabeh S, Duggirala HJ. Center for Devices and Radiological Health Condition of Approval Studies as a Postmarket tool for PMA approved cohort 1998-2000. www.fda.gov/oc/whitepapers/epi_rep.pdf. 2005. Accessed November 2005.

- 1) is intended to be implanted in the human body for more than one year,
- 2) is life-sustaining or life-supporting (and used outside a device user facility), or
- 3) failure would reasonably be likely to have serious adverse health consequences.

Prior to issuing an order for a postmarket study, CDRH will discuss the potential public health concern with the firm. Upon receiving an order to conduct a study, the manufacturer has 30 days in which to submit its study plan. By statute, studies are limited to 3 years, however, longer studies may be carried out as agreed upon by the affected firm. Possible study approaches vary, which allows for the most practical, least burdensome approach to address the potential public health question. Approaches may include a detailed review of the device's complaint history and a review of scientific literature, non-clinical testing of the device, telephone or mail follow-up of a patient sample, development of device registries, observational studies, and rarely, randomized controlled trials.

Problem Assessment Groups

Postmarket Issue (PMI) Action Teams

PMI Action Teams develop a Center analysis of a safety issue with a marketed medical device or radiation-emitting product. The team determines the most effective approach to mitigating risk associated with the use of the device. PMI Action Teams may be product-specific or may pertain to a general category of devices.

PMI Action Teams are convened to:

- confirm that the issue has potential public health impact, requiring Center-wide participation to manage it;
- delineate the nature and extent of the issue, if possible;
- develop recommendations for solution strategies for Center management decision-making.

Once recommendations for solution strategies are developed and ranked, concurrence is sought from CDRH Senior Staff. The process is dependent on the criticality, visibility, and complexity of the issue. It can range from informal briefings of Office Directors to a formal presentation to Senior Staff. The PMI Team determines the most appropriate process to inform senior management and to gain concurrence for recommended solution strategies. Once the Team has concurrence from CDRH Senior Staff, the appropriate Office(s) or Program(s) take(s) the lead in implementing the recommendations and the Team is disbanded.

- External Working Groups

Occasionally, the Center will work with external groups to examine problems, determine appropriate solutions to problems and even assist with implementation of solution strategies. These meetings bring national expertise together to address difficult and often, complex issues. The goal is to develop and implement various tools, procedures, and educational documents for health care providers and users to address adverse outcomes associated with the use of medical devices.

- Health Hazard Evaluations (HHE)

Health Hazard Evaluations are internal procedures used to assess the risk of medical device incidents and adverse outcomes, and to guide recall classifications. The information is used to mitigate health hazards and provide the basis for preventive action. When CDRH receives notification of a potential public health hazard, the Center conducts an HHE to assess the risk of a postmarket safety problem and determine if a recall is warranted. When there is no precedent to use as a reference, an HHE Committee is convened.²⁹ The HHE Summary states the likelihood of the occurrence of the health hazard following use of the device that is being recalled, or considered for recall, and the likelihood of exposure to a defective device. A Class I recall signifies a higher risk usually associated with death and a high likelihood of recurrence.

Discussion - Postmarket Problem Assessment

The ability of CDRH analysts to assess medical device issues is limited for both practical and regulatory reasons. Access to accurate and timely information is critical to the Center's postmarket problem assessment functions. Currently, data and device experience information are collected through a variety of mechanisms for specific purposes. The information is received by the individual offices within the Center, and each has a specific scientific and regulatory role for utilizing the information. Sharing this information across the Center, comparing the information, and reviewing it in the aggregate for problem assessment, although desirable, continue to be significant challenges. The broad use of scientific, human factors, clinical specialty, and laboratory expertise in collaborative review has also not been fully realized.

Another major constraint is the lack of objective data about device use and device-related problems. As noted in the Appendices attached to this document, documentation of either device use, or device related problems, in health care settings is sporadic. CDRH's problem assessment program could be improved by expanding access to additional data

²⁹ The HHE Committee has a 2 day (work day) time frame to complete, endorse, and forward the HHE form to the Center recall unit.

sources, such as health care networks' and practitioners' experiences with the use of medical devices. Human Factors reviews of 1) user's experiences with medical devices, 2) usability test data, and 3) device use information contained in adverse event reports are important components of assessing use error problems. Improving the quality of information about the use of medical devices will enhance the Center's ability to more efficiently incorporate human factors and usability reviews, and further define and minimize user error problems. As mentioned earlier, standardization of device nomenclature used in routine documentation of devices in the health care industry would also improve our ability to compare such information between databases.

One result of this lack of detail about device use and device related problems is that any new questions, or issues that are identified, require the initiation of a new review of the data, or a new data collection effort, which is not an efficient or timely exercise. The development of "real-time" systems could decrease the impact of time constraints imposed by regulatory actions. As a result, three areas remain as key areas for improvement in postmarket problem assessment for the Center. They include enhancements to the data and information to be collected, development of data systems that allow comparative reviews of data, and improved Center-wide access to informative databases.

Limits imposed by the regulatory environment are most apparent when postmarket studies are mandated. The Agency levies these studies on identified manufacturers of specific products. In doing so, there is no intent for comparative analyses, or pooled analyses of data submitted by manufacturers of similar products. Another problem is that each required study requires new data collection. In the aggregate, however, these postmarket studies could be a valuable tool to obtain and compare device use information in marketed medical devices. The Center could benefit from cross-office collaborative reviews of information from postmarket studies and increased consideration of such information when new device applications are reviewed.

Access to accurate and timely information is important for problem assessment. The Center is developing an Information Technology Strategic Plan. As part of this plan, the Center is assessing the postmarket business processes, what information is needed, and available for postmarket assessments.

CDRH's ability to continue independent data development in our laboratory facilities is beneficial. The nature of laboratory research and analysis requires a longer time line than some of the other assessment tools. It is important that CDRH continue to involve the laboratory in long term planning and provide the resources necessary to keep pace with evolving technology. We could improve our postmarket assessments by increasing the utilization of laboratory capabilities to include rapid testing/characterization of materials and validation of device usability interfaces.

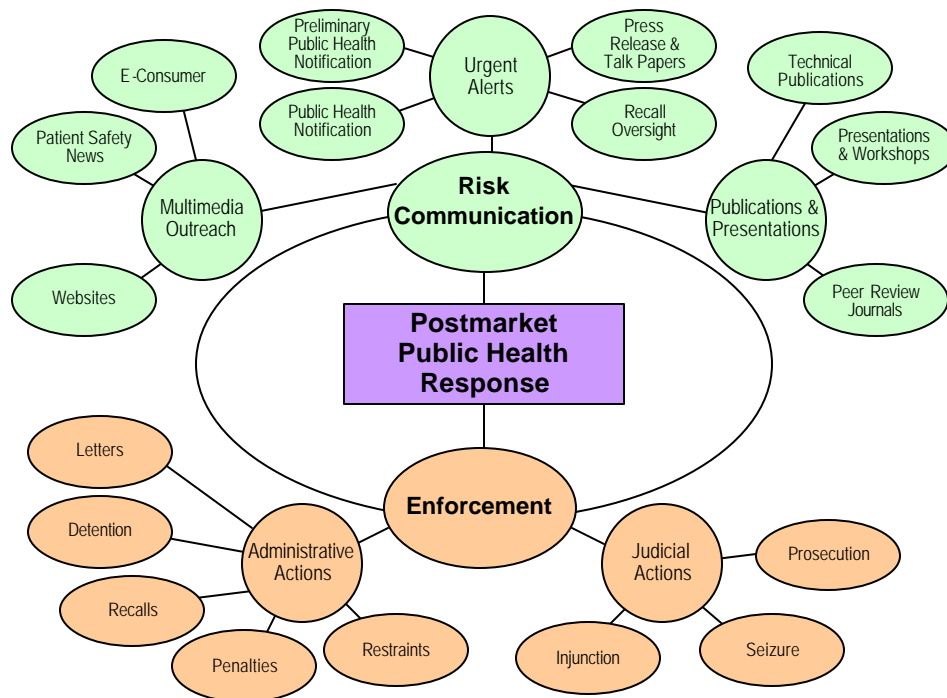
Several postmarket tools that are currently available may have additional postmarket assessment potential that is not yet realized. These include review and analysis of information contained in manufacturers' annual reports, postmarket studies, and Section

522 studies. CDRH continues to use Post-market Issue Action Teams and epidemiological expertise to monitor and assess Condition of Approval and Section 522 Studies; however, utilization of additional Center expertise in both the planning of the studies and the review of the reports may enhance the utility of the information garnered from these reports. Other potentially underutilized sources of expertise and information are external working groups that can provide solutions that may not be generated by intra-agency groups. External working groups offer an opportunity to build trust with our public health partners and increase the likelihood that our solutions are implemented effectively. Public advocacy organizations can be included in working groups and may provide valuable insight into the needs of device users.

Postmarket Public Health Response

The following model depicts the major tools used in the CDRH postmarket public health response process. Postmarket public health response tools are used to carry out the Center’s postmarket regulatory authority, to ensure that postmarket medical devices remain safe and effective in the clinical and home settings, and to inform the public, industry, and health care professionals about risks associated with the use of medical devices as they are utilized in health care delivery.

These tools are directly linked to the CDRH Pre-market process by providing information to be considered in the review of the next generation of medical devices. Additional links are maintained with CDRH’s external partners to assist in developing and disseminating information.



The CDRH postmarket public health response model is divided into two key approaches that provide CDRH with postmarket risk management and risk communication tools. The key areas are Risk Communication and Enforcement. Risk communication strategies are designed to resolve problems through interactive communication with our public health partners and device users. Strategic risk communication involves dialogue with device users to frame and provide context to information that is disseminated. The goal is to inform the public about imminent health hazards, safety concerns and recommendations and to provide device specific education and advice. The audience, determined by the nature of the problem, includes health care practitioners, caregivers, patients, and medical device manufacturers.

Enforcement strategies are also used to ensure industry compliance with CDRH laws and regulations, or to make them aware of specific risks that may not have been previously identified. The enforcement actions include both Administrative Actions and Judicial Actions and they are based upon information obtained through the postmarket problem identification and assessment processes, including information collected from inspections.

Risk Communication

CDRH risk communication programs and projects are generally directed to a specific audience. Outreach efforts usually target health care professionals and allied professions supporting medical components or delivery of care, medical device industry regulatory affairs personnel, technical staff, and consultants, and the broader public audience characterized as patients, caregivers, and consumers. Risk communication strategies for each group are summarized below.

Health Care Personnel

Health care personnel need to be informed about issues so that they may minimize adverse events associated with the use of medical devices. Thus, they will need current information on new products, as well as safety notifications and information on recalls. They may also need training in order to recognize factors that contribute to errors and problems when using medical devices.

Outreach to health care professionals must also focus on improving the ways in which they interact with the FDA, particularly as they interact in reporting adverse events. This would include both mandatory (MDR) and voluntary (MedWatch and MedSun) reporting systems. In each of these areas, health care professionals need to be informed about the types of information the FDA needs in order to generate accurate data about problems and issues with medical devices. If CDRH can provide better guidance on what types of information need to be reported, both pre- and post-market activities will benefit from these improved reports.

Medical Device Industry

Communication between the CDRH and the medical device industry encompasses both the dissemination of guidance and standards information, as well as information about compliance with CDRH regulations and enforcement actions.

Currently, written guidance documents are maintained on the CDRH internet facility under the “Device Advice” website. Additional materials are available from the human factors portion of the CDRH website. This website provides direct guidance materials as well as links to resources provided by other agencies (both government and non-government sources). Oral presentations are given at numerous conferences (such as AAMI) as well as at individual industrial sites. Guidance material is critically important to outreach as better-informed designers will develop improved devices for review; better-informed studies will lead to reduced problems in certification. Information about compliance and enforcement is generally disseminated directly to affected firms, however, major changes to compliance and enforcement activities that affect a substantial portion of the industry are disseminated through other communication mechanisms.

Public Communication

CDRH shares risk communication information with the public primarily through leaflets and internet sites. Leaflets can be mailed out to individuals or made available on location at conferences. The website offers materials on a wide variety of topics of interest to consumers. Information relevant to particular age groups (e.g., children or the elderly) has been developed with those consumers’ limitations in mind (e.g., reading level or accessibility needs). These communication efforts can be used to inform the public about what to look for in selecting medical devices and products, the availability of new medical devices, recalls, safety information, and how to report adverse events associated with the use of medical devices.

CDRH uses a variety of outreach tools to alert device users to potential risks. The tools include Urgent Alerts, Multimedia Outreach, Technical Publications, Presentations, and Workshops. These tools utilize a variety of mechanisms to convey risk messages including broadcast media (press releases, talk papers, web-based news programs, websites, and television interviews), public health notifications, patient notifications, and public meetings. In addition, staff presentations, CDRH workshops, and technical publications, such as standards and guidance documents convey important safety information to significant stakeholders. The goal is to ensure that the health care practitioners, industry, and the public understand the risks and act appropriately to minimize such risks.

CDRH staff utilize targeted risk communication tools depending on the urgency of the message, the intended target audience, and the outreach goals. An urgent alert

mechanism is used when the risk associated with a device problem is greatest. Multimedia outreach tools such as website linkages are readily available to keep the health care community informed about public health problems. CDRH periodically evaluates the effectiveness of its risk communication efforts through surveys, usability testing of electronic communication, and qualitative research such as focus groups.

Urgent Alerts

When a post-market assessment determines that a public health problem is an imminent health hazard, it is important that CDRH alert health professionals and the affected population. CDRH utilizes experts from all parts of the Center to develop urgent alerts.

Preliminary Public Health Notification

The Preliminary Public Health Notification is an early alert issued to health care practitioners about a device risk. A key determination triggering the issuing of a Preliminary Public Health Notification is the urgency of the need for the health care community to have the existing information in order to make informed clinical decisions about the use of a device or device type, even though the information is often incomplete. Factors used to determine the urgency include the severity of the potential risk, the population likely to be at risk, the likelihood that adverse events may occur and the need for information and feedback from the health care community. The judgment of Center experts is relied upon to determine the impact of these factors. Often, the problem is being actively investigated by the Center, the industry, another agency, or some other reliable entity, so we expect to update the Preliminary Public Health Notification when definitive new information becomes available.

The Preliminary Public Health Notification contains

- our current information on the problem,
- our analysis of the existing data with a preliminary finding, and
- preliminary or interim recommendations, usually general reminders (e.g., increase observation of the patient, read the device labeling, and/or report adverse events).

The decision to issue a Preliminary Public Health Notification often comes from a Postmarket Issue Action Team or as the result of review of a recall by the Center. CDRH publishes the Preliminary Public Health Notification on the CDRH/FDA Web Page and advertises the publication on an office listserv, the MedWatch listserv, and any mechanism thought to be necessary to assure that the target audience is made aware of its publication.

Preliminary Public Health Notifications are updated as frequently as necessary to keep the health care community aware of the problem. When the Agency understands the problem and is able to provide recommendations to mitigate the risk,

a Preliminary Public Health Notification will be replaced with a Public Health Notification.

Public Health Notification

Public Health Notifications are important messages about risks associated with the use of medical devices. They are placed on the CDRH/FDA Web Page and may be disseminated in additional ways to assure that the message reaches the target audience. Public Health Notification recommendations usually come from a Postmarket Issue Action Team (PMI team), but in unusual circumstances the decision to issue a Notification may be made without convening a PMI team.

Public Health Notifications are issued when:

- the information is important in order to make informed clinical decisions about the use of a device or device type,
- the information is not readily available to the affected target, and
- CDRH recommendations will help the health care practitioner mitigate or avoid the risk

The decision to issue a Public Health Notification is dependent upon the quality of the information, the significance of the risk, the population at risk, the nature and frequency of adverse events, the urgency of the situation, and the expectations of the public.

Recall Oversight and Device Tracking

By law, the Center may require manufacturers to track Class II and Class III devices. In some instances, manufacturers have used these same tracking systems to conduct voluntary recalls. CDRH participates by providing oversight for the process.³⁰ Companies prepare and send letters to physicians or patients notifying them of potential safety issues. To minimize risk, press releases are also required for Class I recalls. As part of the oversight function, CDRH and the FDA field staff guide the development of these communications and include questions anticipated from doctors and patients.

³⁰ Manufacturers of medical devices implement tracking procedures and collect information required by CDRH's regulation (21 CFR 821, as amended). Permanently implanted devices and life-sustaining or life-supporting devices that are intended for use by a single patient over the life of the device must be tracked to the patient using the device. Manufacturers are required to audit their tracking system, which requires effective communication through the chain of distribution. Manufacturers are obligated to ensure that distributors and hospitals comply with their information reporting obligations. Final distributors of a tracked device, which includes doctors and hospitals, must report to the manufacturer, among other items, the name, address, and telephone number of the patient to whom it distributed the device, as well as the prescribing physician and physician who regularly follows the patient [21 CFR 821.30(b)].

Press Releases and Talk Papers

Press releases and talk papers approved by the Center are issued to the media by FDA's Office of Media Relations whenever there is a need to alert the broader public to a potential health risk associated with an FDA-regulated product. In addition to Class I recalls, press releases are usually issued for seizures. Press releases and talk papers are essentially the same type of document, except that press releases contain a quote from an agency official. The quote is used to emphasize the importance of the message. Press releases and talk papers are distributed to a list of critical media nationwide via a listserv. They are also posted on FDA's and CDRH's web sites.

Multimedia Outreach

CDRH has established a number of tools for providing consistently available information about public health concerns to the health care community and the general public. Several innovative efforts in improved risk communication have their origins in CDRH, such as the Patient Safety News network which disseminates information via a video format accessible through one of the Center's website links. CDRH also has developed a number of relevant and consumer-friendly web pages addressing issues with commonly used medical devices.

Patient Safety News

CDRH leads the Agency's production of FDA Patient Safety News (PSN), a monthly television news show distributed by CDRH to health care practitioners. FDA PSN is a major agency vehicle for communicating FDA safety messages about medical products to physicians, nurses, pharmacists, risk managers and educators across the nation. Now in four years of production, FDA PSN incorporates stories from FDA's three medical product Centers (CDER, CDRH and CBER) on medical errors, patient safety, recalls and alerts, and newly approved drugs, devices and biological products. Since its inception in 2002, FDA PSN has covered over 250 separate stories designed to reduce medical errors and improve the safety of FDA-regulated medical products. This year, FDA PSN received an Award of Excellence from the National Association of Government Communicators.

The show is broadcast each month on several medical satellite TV networks that bring continuing education for health professionals to over 4,500 U.S. hospitals and long-term care facilities. The show also has its own website (www.fda.gov/psn), which receives about 6,000 "hits" per month, an increase of about 50% over the number of FY-03 viewers. On the site, users can view current or past editions of the show, search for individual stories, get more information on any story, e-mail stories to other people, and report problems through MedWatch. This year, users were also able to download a video story to their own computer,

network or even a DVD for viewing then or at a later time. Over 2500 web site users have joined a listserv so they can be automatically notified about the release of each month's show. An FY-04 survey of these listserv subscribers indicated that 94 percent of respondents used the FDA PSN safety recommendations [documented as "used frequently" (41 percent) or "used occasionally" (53 percent)].

E-Consumer Initiative

This CDRH initiative is designed to facilitate the Center's ability to reach the public with information about medical devices using electronic media. It incorporates communication technologies that will provide timely, targeted information in user-friendly formats depending on the needs of the target audience. Tasks under this initiative include developing an easy-to-use database of CDRH regulated products (Devices@FDA), providing a list of routinely-asked questions and answers, establishing a method of collecting and disseminating CDRH news (GovDocs GovDelivery ® email subscription management system), and improving CDRH web pages through needs assessments, user satisfaction surveys and analysis studies, and implementation of internal web maintenance policies and content improvement. See Appendix F (CDRH E-Consumer Initiative) for additional information.

Websites

CDRH communicates postmarket safety information through a variety of public websites.

- *Medical Device Safety* – This website presents a collection of medical device safety information (e.g. recalls, public health notifications, safety tips, “Dear Doctor” letters, etc.) for health care professionals. The site is updated regularly to feature high-priority risk messages. During the past year, CDRH conducted audience analysis and usability studies on this site in order to make it more accessible and understandable to practitioners.
- *CDRH Consumer Website* – The CDRH consumer website provides a collection of information about specific devices and device issues for a patient/consumer audience. It includes links to postmarket safety information (including Class I recalls and Public Health Notifications) as well as information geared toward individuals who use devices in their homes.
- *Disease-Specific Web Pages (FDA Diabetes Information, Heart Health Online)* – CDRH coordinates FDA's disease-specific websites on diabetes and heart disease. These websites are designed to educate patients and caregivers about the types of interventions involving medical devices that prevent and treat disease. Each includes links to appropriate medical device patient labeling and postmarket safety information.

- *Device-Specific and Topic-Specific Web Pages (i.e. LASIK, Phakic Lenses, Whole Body CT Scanning, Cochlear Implants, etc.)* – CDRH’s device-specific Web pages provide coordinated postmarket information about specific types of devices. These web pages give patients and health care professionals easy access to descriptive information, indications for use, risks and precautions, and specific safety information. Additionally, CDRH’s in-vitro diagnostic products’ and devices’ website (www.fda.gov/cdrh/oivd) is provides comprehensive, total life cycle information for in-vitro diagnostic products.

Traditional Publications and Presentations

Peer Review Journals

Peer-reviewed scientific and clinical articles are effective mechanisms for alerting practitioners to public health problems related to devices. Articles discuss both new and well-characterized device risks (for on- and off-label use), benefits, and the potential public health impact associated with the use of devices. All of CDRH’s analytic groups publish their findings in peer-reviewed journals. Publications include laboratory based science from CDRH laboratory experts, issues concerning statistical science, epidemiologic studies of postmarket issues, analyses of MAUDE data and studies regarding methodology for epidemiologic and surveillance studies of devices. Staff also contribute to journals such as *Nursing 2005* to highlight case reports of preventable device injury and recommend means to mitigate such occurrences. Other publications target human factors issues and articles related to the considerable expertise of various clinical disciplines in the Center.

Technical Publications

CDRH has printed numerous technical publications, such as guidance documents, and “recognized” a variety of medical device standards developed through joint participation with industry and outside organizations. These documents are either available through CDRH’s websites or through links to standards organizations. They are often the subject of CDRH’s presentations and workshops and often requested through the CDRH Device Advice webpage.

Presentations and Workshops

CDRH staff develop and present educational material at scientific meetings, industry workshops, and public hearings. Abstracts for scientific and clinical meetings span topics similar to the information presented in journal publications. Information developed for presentations to the industry focuses on solutions for identified systemic problems and industry trends. Human factors information and workshops on usability of medical devices are topics of interest to industry that help to minimize use error problems.

Enforcement

Enforcement actions, both administrative and judicial, are a critical component of the CDRH postmarket program. Administrative actions include Letters, Detentions, Recalls, Penalties and Restraints. Judicial actions include Seizures, Injunctions, and Prosecutions.

Administrative Actions

CDRH is authorized to use a variety of administrative actions to resolve public health issues that are related to non-compliance with FDA laws and regulations. The categories include information dissemination through letters, authorization to detain devices which present a health hazard, and a variety of mechanisms to restrain and control companies when there are problems with data integrity. A public health problem can be resolved by a device recall, or CDRH can initiate an administrative penalty.

Letters

Warning Letters

A Warning Letter is a correspondence that notifies regulated industry about CDRH documented violations. Typically, a Warning Letter informs a firm that the Center considers one or more of its products, practices, processes, or other activities to be in violation of the FFD&C Act, its implementing regulations and/or other federal statutes. Warning Letters are used for violations of regulatory significance, i.e., those that may actually lead to an enforcement action if the documented violations are not promptly and adequately corrected. A Warning Letter is the Center's principal means of achieving prompt voluntary compliance with the Act.

Untitled Letters

An untitled letter is a correspondence that cites violations that do not meet the threshold of regulatory significance that is used to trigger the issuance of a Warning Letter. Therefore, when circumstances warrant the issuance of an untitled letter to regulated industry, it is formatted in a manner that clearly distinguishes it from a Warning Letter. Industry is expected to respond in writing to Untitled Letters.

Detentions

Administrative Detention

Section 304(g) of the FFD&C Act authorizes FDA to detain devices intended for human use for a period of up to 30 calendar days. The intent is to protect the

public by preventing distribution or use of violative devices until CDRH has had time to consider a regulatory action such as a seizure.

Import Detention

An import detention is similar to an administrative detention. It is an enforcement procedure designed to protect the consumer from imported adulterated or misbranded product by placing the product in secured storage.

Recalls

When a device related public health problem is identified, the recall process is an important problem resolution tool. If there is a serious health hazard and a firm does not initiate a voluntary recall, CDRH is authorized to mandate a recall action.

Market Withdraw

A Market Withdraw is a voluntary action by a company to remove a product from commerce. The withdrawn product is not considered to be in violation of the law.

Voluntary Compliance: Recalls

Recalls usually are conducted on a voluntary basis. In 1990, Section 519(f) of the Act was amended by the SMDA, which authorized CDRH to issue reporting and record keeping requirements concerning the recall activities. Congress established this statutory requirement because it wanted to ensure that device manufacturers and importers would conduct recalls and notify CDRH in a timely fashion.

Firms are required to conduct effectiveness checks to make sure the users or consignees have received notice of the correction or removal, and that they have taken the appropriate action. FDA Field staff will audit the firm's effectiveness checks. When a correction or removal involves a device that poses substantial risk of serious injury or death, the Agency may contact each user or consignee to ensure the appropriate action has been taken.

Mandatory Recalls

When a firm fails to correct or remove dangerous devices from the market promptly, and CDRH finds that there is a reasonable probability that a device would cause serious adverse health consequences or death, the Center will issue a cease distribution and notification order. The order requires the firm/responsible person to immediately 1) cease distribution of the device; 2) notify health professionals and device user facilities of the order; and 3) instruct the health professionals and device user facilities to cease use of the device (21 CFR 810).

Even though this action is rarely used, the Center is required to make a weekly Enforcement Report to the public that describes each new mandatory recall issued under 21 CFR 810.13. Recall actions are also published on various Agency and Center Websites.

Penalties

CDRH has the authority to impose fines on companies for non-compliance with regulations and to ban products which present a public health hazard.

Civil Money Penalties (CMP)

Civil money penalty actions authorized by the Safe Medical Devices Act of 1990 (SMDA) are utilized in situations in which a firm continues to violate the GMP, MDR, and/or BIMO regulations, there is a reasonable probability that the firm will likely produce nonconforming and/or defective finished devices, and seizure or injunction is not appropriate or necessary to bring about corrective action.

CMP is a remedial non-punitive action designed to influence future conduct of a firm either directly, by affecting current violative conduct, or indirectly, by serving to deter future violative conduct.

Banning of Products

When a device presents a substantial deception or an unreasonable and substantial risk of illness or injury that cannot or has not been corrected, CDRH has the authority under CFR 895 to ban the device. Because of the extensive review and approval process, and the general oversight of medical devices, the Center rarely uses this authority.

Restraints

Data integrity is an essential element in both pre-approval and post-approval studies. Devices may be restrained from the market based upon a question regarding the integrity of data submitted for the device approval.

An Integrity Hold is an action that places a device application “on hold” due to questions regarding the integrity of the data supporting the application and system-wide failures at the sponsor level to assure CDRH confidence in the quality of the research. An Integrity Hold not only prevents approval of a pending device until there is a determination that the data is valid and in compliance with device regulations, it can also impact approved devices. CDRH has terminated the

marketing of approved devices when the data that justified the approval was determined to be of questionable integrity.

Judicial Actions

Injunction

An injunction is a civil action taken against an individual or firm seeking to stop continued production or distribution of a violative product. A civil restraint order is issued by a federal court to prohibit violations of the Act.

Seizure

A seizure is a judicial civil action in which goods are “arrested”. It is an action taken to remove a product from commerce because it is in violation of the law. CDRH initiates a seizure by filing a complaint with the U.S. District Court where the product is located. A U.S. marshal is then directed by the court to take possession of the goods until the matter is resolved. FDA’s authority for processing a seizure is found in 21 U.S.C. 334.

Prosecution

A prosecution is a criminal action taken against a company or individual, with a charge of violation of the law. A criminal or civil sanction is directed against a firm and/or responsible individuals.

Discussion-Postmarket Public Health Response

Solutions to safety issues identified with medical devices can be divided into two distinct categories: risk communication and enforcement activities. However, to have an effective postmarket program, these two program areas should be closely linked and coordinated. For example, timely and understandable recall information should be disseminated to the health care providers, appropriate industry, and the public. Information from recalls that is available to specific offices within the Center could also provide valuable insight to CDRH premarket reviewers and also, generically, to other medical device firms considering safety modifications.

The process used to develop messages to users about risk and risk prevention ideally should begin very early in the problem assessment process and includes developing teams

with both subject matter experts and risk communicators when problems are first identified. CDRH risk communicators monitor the scientific literature regarding effective development of risk communication messages and have begun using a technique called message mapping that uses risk communication templates to frame risk messages early in the process. Without a coordinated approach to developing risk messages, enforcement activities may move so rapidly that they lose the opportunity to ask for answers to questions users may consider very important. CDRH staff have also begun work on improving risk messaging about recalls by developing a plain language definition of recalls and improving public access to recall information on its website. Increasing the use of risk communication expertise and techniques early will improve both the timeliness and content of the Center's risk communication or prevention messages to users.

Dissemination of information via a multimedia approach is important in the current environment. Although Preliminary Health Notifications may save lives, the preliminary information is incomplete and final recommendations are not possible. Press releases are not a comprehensive mechanism for dissemination of potential health issues. They are used to disseminate "significant news". CDRH could improve our ability to rapidly provide health hazard information by increasing our access to external databases and promoting collaborative relationships throughout the health care community. Improvements to our web site could increase the availability of information about device adverse reactions, home health considerations, and patient safety to interested groups.

CDRH has a variety of excellent communication tools in place but there is an urgent need to market the vast amount of information available. The FDA/CDRH Web sites should be a primary search site for consumers and health care professionals. CDRH has also done a significant amount of focus group testing and evaluation of the risk communication materials that have been used, and it is important that more of this work be done so that we know we are meeting the needs of our customers.

Effective risk communication depends upon an interactive process that allows CDRH to:

- identify and understand who the audience(s) is
- identify the questions different audience(s) will ask on behalf of patients,
- translate technical risk information into culturally and socially appropriate communication, and
- correctly identify the most effective way to distribute messages.

A holistic approach to our external communication includes coordinating complementary messages across broadcast, print, and electronic media with thought given to which tools are most appropriate for our target audience and our communication goals.

CDRH staff from specific offices review letters to patients and physicians. This review process represents an opportunity to provide messages consistent with other risk communication messages that CDRH develops and distributes. This process would benefit from a broader review process involving a variety of CDRH offices and expertise.

Our ability to resolve public health problems based on enforcement is limited by the scope of FDA regulations and laws. Regulation of foreign and domestic firms differs. The review and revision of device regulations should help “level the playing field” between the foreign and domestic based firms and prevent future cases of unapproved devices entering the U.S.

Administrative actions are designed to rapidly resolve issues of non-compliance which can result in health hazards. Judicial actions are more resource intensive than administrative actions. The development of accessible corporate data systems, including tracking systems and electronic document repositories, will enhance our administrative and judicial action processes. Additional issues resulting in delays in the prosecution process are lack of Field staff and administrative delays in processing paperwork.

CDRH Continuous Improvement

After-Action Reviews

Several years ago, under a Continuous Improvement Process (CPI) initiative, a CDRH team developed a process and accompanying materials to institute After Action Reviews (AARs). Procedures and other related documents are stored in the After Action Review eRoom.

AARs may be requested by anyone at any time, although they are usually requested at the end of an event, such as a recall or the publication of a Public Health Notification. AARs can be requested to review an action or event that was problematic but also to review an event that was successful. Several staff in the Center are trained in facilitating these meetings and acting as “scribes” to document the lessons learned.

To date, AARs have been held for a number of high profile actions, and a few lower level operational issues. Although this process is still in the development stage, feedback from the participants in the AARs that have been done have felt that their participation was beneficial. This process needs additional support to have AARs more routinely used throughout the Center and the better understand how the lessons learned can be captured and distributed to the rest of staff.

Education and Training

CDRH postmarket safety processes, linked to CDRH premarket programs, are supported by CDRH’s internal training initiatives. CDRH remains committed to improving government human resources with skill and knowledge to deal with future medical device issues and priorities, including those related to postmarket activities.

Competencies

CDRH Staff College's new voluntary Competency Development Program will enhance CDRH's approach to staff development. Based on results of recent research and experience from the public and private sectors, CDRH Staff College has developed a "competency model" that will serve as the foundation for all future CDRH professional development activities. The competencies enable employees to pinpoint the training and development opportunities needed to succeed. As a result, CDRH will be in a position to fulfill its mission and achieve its long-term goals. Initially, Staff College is introducing the Core Business and Science Competencies as they consist of the skills, knowledge and abilities needed by all CDRH employees. In the future, Staff College intends to move toward development of core competencies for broad job categories, such as scientific reviewer or manager. Ultimately, job-specific competencies will be developed to identify those specialized or technical skills and knowledge that apply directly to individual job positions, including competencies in the postmarket area.

New Employee Orientation

CDRH's new employee training will be implemented in FY2006. It will provide an initial competency based knowledge in support of overall education for CDRH employees, to include pre and postmarket activities.

Science and Regulatory Education Programs

Staff College plays an integral part in CDRH's staff growth by developing and delivering a network of educational programs to meet the regulatory and scientific needs of CDRH. Opportunities for learning include live satellite teleconferences, distance learning telecasts, and online training courses. Sponsorship of the following seminars, courses and lectures enhance the postmarket expertise of staff and contribute to achieving CDRH's mission to ensure safety and effectiveness associated with the use of marketed medical devices.

- Bench to Bedside

- Categorical Data Analysis

- Biostatistics

- Clinical Trials

- Human Factors

- Total Product Life Cycle (TPLC) – A case study of a specific device problem following a device as it is used, and tracking of adverse events while understanding the roles of each office within CDRH in advancing a medical device to market.

- Medical Device Risk Management for Reviewers

- Risk Communication

- Quality Systems

- Adverse Events

- Product Recalls

Basic Epidemiology
Epidemiology Grand Rounds
Post Market Issues Action Teams

Appendices

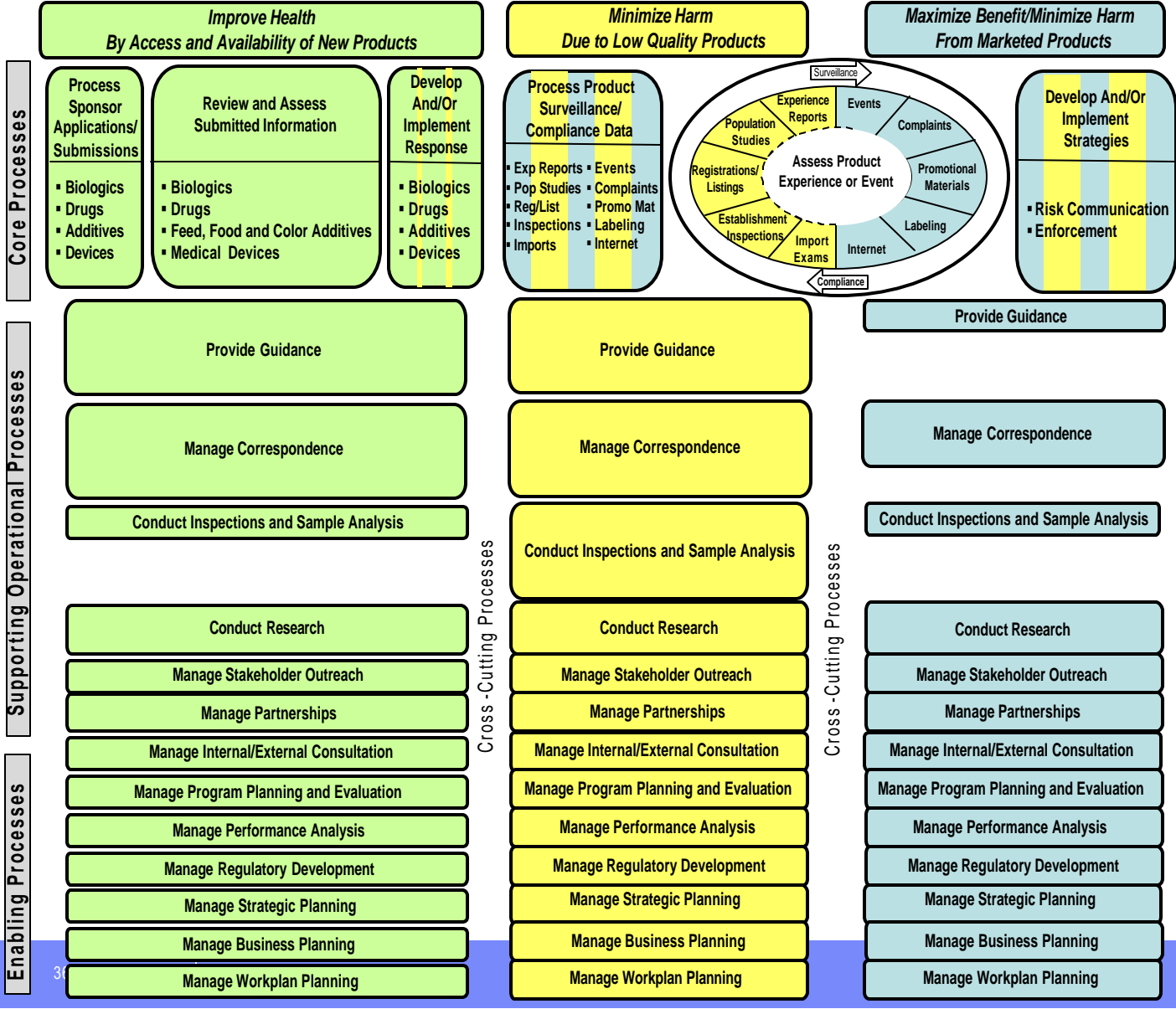
Appendix A - Agency Perspective of the FDA Core Work Processes

This model demonstrates the core work processes of the FDA. The scope of the post-market safety framework is defined by the sections entitled “Minimize Harm Due to Low Quality Products” and “Maximize Benefits/Minimize Harm from Marketed Products”. This includes all post-market input signals, the mechanisms by which we study/examine these signals, and outputs including compliance actions, outreach or perhaps changes in premarket evaluations. Guidance is cited here as part of the supporting operational processes as it directly pertains to the post-market evaluation of device safety.

Figure A. Core Work Processes of the Agency with the Postmarket Safety Network defined in blue and yellow



The Full FDA Model, which includes strategic, supporting, and enabling processes



Appendix B – Epidemiologic Aspects of Postmarket Medical Device Safety

Estimates of the Frequency of Adverse Medical Device Events (AMDE)

Understanding the scope and nature of AMDE for all devices is important for measuring their impact on public health and designing the most effective postmarket strategies.

Although literature on AMDE related to specific devices exists in the cardiology,^{31, 32, 33, 34, 35} orthopedics,^{36, 37, 38} and anesthesia^{39, 40} specialties. CDRH has been responsible for the conduct of a high proportion of studies of the overall frequency of AMDE.

To measure the frequency of serious adverse medical device events that occur outside hospitals, CDRH funded a one year study of visits to emergency departments.⁴¹ The results showed that in a one year period, 452,000 visits to emergency departments were for injuries associated with medical devices. Of these, 58,000 patients died there or were hospitalized.

All other studies we know of focused on hospital-based measures of adverse event rates. An FDA-funded study evaluated different types of surveillance systems in a tertiary care

³¹ Chittock DR, Dhingra VK, Ronco JJ, Russell JA, Forrest DM, Tweeddale M, Fenwick JC. Severity of illness and risk of death associated with pulmonary artery catheter use. *Crit Care Med* 2004; 32:911-915.

³² Chugh A, Scharf C, Hall B, Cheung P, Good E, Horwood L, Oral H, Pelosi F Jr, Morady F. Prevalence and management of inappropriate detection and therapies in patients with first-generation biventricular pacemaker-defibrillators. *Pacing Clin Electrophysiol.* 2005;28(1):44-50.

³³ Pratt TR, Pulling CC, Stanton MS. Prospective postmarket device studies versus returned product analysis as a predictor of system survival. *Pacing Clin Electrophysiol.* 2000;23(7):1150-5.

³⁴ Rosenqvist M, Beyer T, Block M, den Dulk K, Minten J, Lindemans F. Adverse events with transvenous implantable cardioverter-defibrillators: a prospective multicenter study. European 7219 Jewel ICD investigators. *Circulation.* 1998;98(7):663-70.

³⁵ O'Shea JC, Kramer JM, Califf RM, Peterson ED. Part I: Identifying holes in the safety net. *Am Heart J.* 2004;147(6):977-84.

³⁶ Taylor HD, Dennis DA, Crane HS: Relationship between mortality rates and hospital patient volume for Medicare patients undergoing major orthopedic surgery of the hip, knee, spine, and femur. *J Arthroplasty* 1997; 12: 235-242.

³⁷ Parvizi J, Sullivan TA, Trousdale RT, Lewallen DG. Thirty-day mortality after total knee arthroplasty. *J Bone Joint Surg Am.* 2001; 1157-1161.

³⁸ Gill GS, Mills D, Joshi AB: Mortality following primary total knee arthroplasty. *J Bone Joint Surg Am.* 2003; 85:432-435.

³⁹ Beydon L, Conreux F, Le Gall R, Safran D, Cazalaa JB, and the members of the 'Sous-commission de Materiovigilance' for Anaesthesia and Intensive Care. Analysis of the French health ministry's national register of incidents involving medical devices in anaesthesia and intensive care. *Br J Anaesth* 2001; 86:382-387.

⁴⁰ Lin L, Vicente KJ, Doyle DJ. Patient safety, potential adverse drug events, and medical device design: a human factors engineering approach. *J Biomed Inform.* 2001;34(4):274-84.

⁴¹ Hefflin BJ, Gross TP, Schroeder TJ. Estimates of medical device-associated adverse events from emergency departments. *Am J Prev Med* 2004; 27(3):246-253.

hospital that included an online incident reporting system, computer flags, and a retrospective method using discharge claim ICD-9 CM codes.⁴² The detection rates for each system were significantly different: 1.6/1000 discharges for online reports, 27.7/1000 discharges for computer flags, and 64.6/1000 discharges for ICD-9 codes in the discharge claims. More AMDEs were recorded in computerized patient records reflecting real-time in-hospital AMDE (17 fold) and discharge codes (40 fold) reflecting either reason for admission (approximately 55%) or in-hospital AMDE (approximately 45%) than were in the hospital's AMDE database. This showed that more intense systems tend to capture more AMDEs than the traditional passive systems.

Published studies have shown consistent estimates of AMDE (see Table B-1 in this appendix). Expressed per 1000 patient days, the hospital-wide rates were 15 in the Samore et al records-based study⁴² and 6.3 in the more recent estimate from hospital discharge claim diagnosis codes.⁴³ Other estimates were for a neonatal ICU (>16)⁴⁴ and a pediatric ICU (>19).⁴⁵ The definition of AMDEs in the studies represented in Table B-1 met at least one of the following criteria: prolonged hospitalization, resulted in permanent severe harm, or required medical or surgical intervention.

Given the emphasis placed by the Institute of Medicine report, *To Err is Human*,⁴⁶ on the importance of adverse drug events, it is interesting to note (see Table B-1) that the rates reported for medical devices have been comparable to those for drugs (expressed per 1000 admissions): for adverse drug events in hospitals (10,⁴⁷ 2.3,⁴⁸ 12⁴⁹), hospital general medical service (3),⁵⁰ geriatric and internal medicine clinical centers (4.8),⁵¹ a medical ICU (19),⁴⁹ and a surgical ICU (11).⁴⁹ In published studies where we were able to directly compare the rates of device versus drug adverse events (again, per 1000 patient days), the rates for devices were in similar range (>16 related to devices and 20

⁴² Samore MH, Evans RS, Lassen A, Gould P, Lloyd J, Gardner RM, Abouzelof R, Taylor C, Woodbury DA, Willy M, Bright RA. Surveillance of medical device-related hazards and adverse events in hospitalized patients. *JAMA* 2004; 291:325-334.

⁴³ Bright RA, Shen J. Use of a free, publicly-accessible data source to estimate hospitalizations related to adverse medical device events. Draft manuscript, 2005.

⁴⁴ Frey B, Kehrer B, Losa M, Braun H, Berwenger L, Micallef J, Ebenberger M. Comprehensive critical incident monitoring in a neonatal-pediatric intensive care unit: experience with the system approach. *Intensive Care Med* 2000; 26:69-74.

⁴⁵ Stambouly JJ, McLaughlin LL, Mandel FS, Boxer RA. Complications of care in a pediatric intensive care unit : a prospective study. *Intensive Care Med* 1996; 22:1098-1104.

⁴⁶ Kohn L, Corrigan J, Donaldson M. *To Err is Human: Building a Safer Health System*. 1st ed. Washington, DC: National Academy Press; 2000.

⁴⁷ Bates DW, Leape LL, Petrycki S. Incidence and preventability of adverse drug events in hospitalized adults. *J Gen Intern Med* 1993; 8:289-294.

⁴⁸ Hanesse B, Legras B, Royer RJ, Guillemin F, Briancon S. Adverse drug reactions: comparison of two report methods. *Pharmacoepidemiol Drug Safety* 1994; 3:223-229.

⁴⁹ Bates DW, Cullen DJ, Laird N, Petersen LA, Small SD, Servi D, Laffel G, Sweitzer BJ, Shea BF, Hallisey R, Vander Vliet M, Nemeskal R, Leape LL. Incidence of adverse drug events and potential adverse drug events: implications for prevention. *JAMA* 1995; 274:29-34.

⁵⁰ Chaudhry SI, Olofinboba KA, Krumholz HM. Detection of errors by attending physicians on a general medicine service. *J Gen Intern Med* 2003; 18(8):595-600.

⁵¹ Carbonin P, Pahor M, Bernabei R, Sgadari A. Is age an independent risk factor of adverse drug reactions in hospitalized medical patients? *J Am Geriatr Soc*. 1991 Nov;39(11):1093-9.

Table B-1. Literature that has estimated the rates of hospital adverse events.

Paper	Population	Adverse event rate (# /1000 patient days)		
		All	Drug related	Device related
Samore et al 2004 ⁴²	Adult tertiary hospital			15
Bright and Shen manuscript ⁴³	All US hospitals			6.3
Bates et al 1993 ⁴⁷	Urban tertiary hospital		10	
Hanesse et al 1994 ⁴⁸	French hospitals		2.3	
Bates et al 1995 ⁴⁹	Hospital		12	
Chaudry et al 2003 ⁵⁰	Hospital general medicine service	9.3	3	
Carbonin et al 1991 ⁵¹	41 Italian geriatrics and internal medicine clinical centers		4.8	
Frey et al 2000 ⁴⁴	Neonatal ICU	67	20	>16
Stambouly et al 1996 ⁴⁵	Pediatric ICU	27	3	>19
Bates et al 1995 ⁴⁹	Medical ICU		19	
Bates et al 1995 ⁴⁹	Surgical ICU		11	

Note: ICU= Intensive Care Unit.

related to drugs in the Frey et al study) or greater (>19 device-related and 3 drug-related in the Stambouly et al study).

On a national basis, Bright and Shen⁴³ estimated that 1.1 million AMDE were documented in hospital medical discharge records in 2003; about 486,000 were the principal diagnosis and probably were the reason for admission and the remaining 647,000 secondary diagnoses probably occurred during the hospitalization. Since the Samore et al study⁴² showed that not all AMDE found by other means were in the discharge record, the Bright and Shen estimates are probably undercounts. Nevertheless, compared to the total number of reports received by CDRH that year (160,000), it is clear that underreporting by device users continues to be a problem.

Underreporting of Adverse Medical Device Events

The only tool established by law for surveillance of unknown or unanticipated problems is the collection of adverse event (AMDE) reports.⁵² Given its importance, understanding why AMDE are underreported by medical device users is critical.

⁵² Even though Section 522 is labeled “surveillance”, under the definitions adopted for this paper, it is an authority to require specific studies, generally hypothesis-driven, rather than an authority to require surveillance.

Barriers to recognizing and reporting AMDE

There are many barriers to reporting AMDEs to CDRH. These barriers include recognition of a device event, reporting within the institution, and reporting to FDA. First, there are barriers to recognizing a potential relationship between a medical device and adverse medical device event (AMDE). A few reasons for this lack of recognition include that the AMDE can be reasonably explained by other causes, the AMDE is a common condition, there was a time delay from device use to the AMDE, or the AMDE occurred in an organ system different from the one being treated with the device.

Second, there are many barriers to reporting AMDE once the potential relationship between the medical device and adverse event is recognized. Some reasons are related to the seeming triviality of the AMDE, such as the AMDE having resolved or already “known” (already listed in the label or otherwise publicized). Furthermore, the health care provider could be very busy, assume that others have already reported this event, may not see that reporting would be useful, could be concerned about being blamed for the AMDE, or may be unaware of the FDA medical device reporting program. In addition, an individual provider may be collecting a series of cases for publication, and therefore decide not to report.

One of the most significant barriers specific to reporting events with medical devices is the general lack of recognition of medical devices as products related to adverse events (AE). In studies of AE, AMDE were often not explicitly reported in a medical device category.^{53, 54, 55} In a study by Frey et al,⁴⁴ only 1 category of medical care problems was specified as being device related (“equipment dysfunction”, 15 problems), yet many (36 of 134) of the problems described in the other non-drug categories (“management/environment”, “procedures”, “respiration”, and “nosocomial infections”) that were described in the text related to devices. Another significant barrier to reporting is that documentation of device use is often missing from patient records.^{42, 56, 57} When documentation is present, the lack of a standard identification system for devices (addressed later in this appendix) hampers understanding of the AMDE.

⁵³ Brennan TA, Leape LL, Laird NM, et al. Incidence of adverse events and negligence in hospitalized patients. Results of the Harvard Medical Practice Study I. *N Engl J Med*. Feb 7 1991;324(6):370-376.

⁵⁴ Wilson RM, Harrison BT, Gibberd RW, Hamilton JD. An analysis of the causes of adverse events from the Quality in Australian Health Care Study. *Med J Aust* 1999 May 3;170(9):411-5.

⁵⁵ Thomas EJ, Studdert DM, Burstin HR, Orav EJ, Zeena T, Williams EJ, Howard KM, Weiler PC, Brennan TA. Incidence and types of adverse events and negligent care in Utah and Colorado. *Med Care*. 2000 Mar;38(3):261-71.

⁵⁶ Bright RA, Mermel L, Richards C, Eakle MR, Yoder D. Mechanical and allergic adverse events related to central vascular catheters: epidemiology in the Medicare in-hospital population, 2002. Poster presented at the International Conference on Pharmacoepidemiology, Bordeaux, France, August 2004.

⁵⁷ Brennan TA, Localio AR, Leape LL, et al. Identification of adverse events occurring during hospitalization: a cross-sectional study of litigation, quality assurance, and medical records at two teaching hospitals. *Annals Intern Med*. 1990;112:221-226.

There are many other barriers to recognizing and reporting AMDE that are specifically related to the involvement of medical devices. Instructions for device use are generally written in medical jargon for health care providers and difficult for lay users or patients to understand and follow. Other contributors to AMDE that complicate reporting include adverse interactions between the device and other therapies and complex multi-device situations. For diagnostic devices, it can be difficult to recognize false positive and false negative results. Re-used devices can present their own problems: devices manufactured for single use may be reprocessed for further use while devices meant for multiple uses are refurbished and may get replacement parts made by other manufacturers; it can be difficult to understand what went wrong.

A major barrier to reporting is that devices are most often thought to injure as a result of device failure or “user” error. However, human factors analysis and patient safety research has revealed difficulties with trying to assign one or the other of these causes; for example, design flaws make error-free use difficult^{1, 2, 3, 4, 5, 6, 7, 9, 33, 58, 59} and poor maintenance can lead to device failure.^{8, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70} Infusion pumps and defibrillators have drawn particular attention by researchers in the human factors field for

⁵⁸ Maisel WH, Sweeney MO, Stevenson WG, Ellison KE, Epstein LM. Recalls and safety alerts involving pacemakers and implantable cardioverter-defibrillator generators. *JAMA*. Aug 15 2001;286(7):793-799.

⁵⁹ Ward JR, Clarkson PJ. An analysis of medical device-related errors: prevalence and possible solutions. *J Med Eng Technol*. Jan-Feb 2004;28(1):2-21.

⁶⁰ Ramsey AH, Oemig TV, Davis JP, Massey JP, Torok TJ. An outbreak of bronchoscopy-related Mycobacterium tuberculosis infections due to lack of bronchoscope leak testing. *Chest* 2002; **121**:976-981.

⁶¹ Agerton T, Valway S, Gore B, Pozsik C, Plikaytis B, Woodley C, Onorato I. Transmission of a highly drug-resistant strain (Strain W1) of Mycobacterium tuberculosis. Community outbreak and nosocomial transmission via a contaminated bronchoscope. *JAMA* 1997; **278**:1073-1077.

⁶² Kressel AB, Kidd F. Pseudo-outbreak of *Mycobacterium chelonae* and *Methylobacterium mesophilicum* caused by contamination of an automated endoscopy washer. *Infect Control Hosp Epidemiol* 2001; **22**: 414-418.

⁶³ Kolmos HJ, Lerche A, Kristoffersen K, Rosdahl VT. Pseudo-outbreak of pseudomonas aeruginosa in HIV –infected patients undergoing fiberoptic bronchoscopy. *Scand J Infect Dis* 1994; **26**: 653.

⁶⁴ Bryce EA, Walker M, Bevan C, Smith JA. Contamination of bronchoscopes with Mycobacterium tuberculosis. *Can J Infect Control* 1993; **8**: 35-36.

⁶⁵ Fraser VJ, Jones M, Murray PR, Medoff G, Zhang Y, Wallace RJ Jr. Contamination of flexible fiberoptic bronchoscopes with Mycobacterium chelonae linked to an automated bronchoscope disinfection machine. *Am Rev Respir Dis* 1992; **145**: 853-855.

⁶⁶ Gubler, JG, Salfinger M, von Graevenitz A. Pseudoepidemic of nontuberculous mycobacteria due to a contaminated broncoscope cleaning machine. Report of an outbreak and review of the literature. *Chest* 1992; **101**:1245-1249.

⁶⁷ Bronchoscopy –related infections and pseudoinfections – New York, 1996 and 1998. *MMWR* 1999; **48**: 557-560.

⁶⁸ FDA and CDC Public Health Advisory: Infections from Endoscopes Inadequately Reprocessed by an Automated Endoscope Reprocessing System. <http://www.fda.gov/cdrh/safety/endoreprocess.html> . (Accessed 6/3/05).

⁶⁹ Kirschke DL, Jones TF, Craig AS, Chu PS, Mayernick GG, Patel JA, Schaffner W. Pseudomonas aeruginosa and Serratia marcescens contamination associated with a manufacturing defect in bronchoscopes. *N Engl J Med* 2003; **348**: 214-20.

⁷⁰ Srinivasan A, Wolfenden LL, Song X, Mackie K, Hartsell TL, Jones HD, Diette GB, Orens JB, Yung RC, Ross TL, Merz W, Scheel PJ, Haponik EF, Perl TM. An outbreak of Pseudomonas aeruginosa infections associated with flexible bronchoscopes. *N Engl J Med* 2003; **348**: 221-227.

being difficult to use successfully.^{9, 33, 71, 72} An area where anesthesiologists, epidemiologists, and human factors engineers (including from FDA) have worked together and continuous improvements have occurred in deliberate cycles is anesthesia safety.⁷³ The complexity of determining root cause of AMDE has led the human factors team at CDRH to advocate using “use-related error” as a blame-neutral term.¹⁰ To illustrate the current ease with which users tend to be blamed for AMDE, note the excerpt from the United Kingdom web page in Figure B. All the items in the figure put the onus on the user rather than on the manufacturer to redesign the devices to make them easier to use. The issue of “user error” is important because AMDE are less likely to be reported if the user rather than the device is seen as being “at fault.”^{74, 75}

Incompleteness of Reports

Adverse medical device reports also commonly suffer from the following deficiencies:

Little or no data on the extent of device use. The nature of AMDE reports emphasizes cases of adverse outcome and ignores instances of successful use. There is no inherent mechanism for reporting the total amount of both successful and unsuccessful device use.

Limited coded or free text information.⁷⁶ The report narratives submitted by manufacturers are frequently incomplete and may gloss over underlying problems. Many significant problems are discovered and addressed by the manufacturers well before CDRH recognizes the problem or takes action. Conversely, manufacturers may choose not to inform FDA in a timely fashion.

Inadequate product group categorization (e.g., procodes may contain more than one generic device group, products that should be grouped under one procode are distributed among more than one, and the types of products intended to be included under some procodes are unknown).

For some product classes (e.g., multi-device systems, etc.), difficulty inferring which product seems to be associated with the AMDE.

All these deficiencies contribute to difficulties in analyzing adverse events.

⁷¹ Gosbee J. Who left the defibrillator on? *Jt Comm J Qual Saf.* May 2004;30(5):282-285.

⁷² Rothschild JM, Keohane CA, Cook EF, et al. A controlled trial of smart infusion pumps to improve medication safety in critically ill patients. *Crit Care Med.* 2005;33(3):533-540.

⁷³ Pierce, EJ Jr. The 34th Rovenstine Lecture. 40 years behind the mask: safety revisited. *Anesthesiology.* 1996;84(4):965-75.

⁷⁴ Cook DM. Iatrogenic illness: a primer for nurses. *Dermatol Nurs.* Feb 2002;14(1):15-20, 52.

⁷⁵ Mosenkis R. Human factors in design. In: van Gruting C, ed. *Medical Devices: International Perspectives on Health and Safety.* New York: Elsevier; 1994:41-51.

⁷⁶ Kaye R, North R, Peterson M. UPCARE: an analysis, description, and educational tool for medical device use problems. https://www.medsun.net/participants/Uploads/kaye_2491.pdf. 2003. Accessed November 2005.

Other Problems with the Adverse Event Reports System

Most reports are from manufacturers and are based on reports they received. Relatively few reports come to FDA directly from health care providers or patients. Health care facilities may feel that there is no benefit to reporting to FDA and have concerns about FDA regulatory authority, although FDA's only regulatory functions with respect to providers regard User Facility Reporting and reuse of single-use devices.⁷⁷ Individual health care providers and consumers are often unaware of the reporting system for problems with medical devices.⁷⁷

An example is the model provided by research on methods for surveillance of adverse drug events (ADE). The scientific literature is quite well developed on the topics of adverse drug events descriptions, development of drug surveillance systems, and prevention of adverse drug events; these are a major focus of the US Institute of Medicine report, *To Err is Human*.⁴⁶ A number of other papers have also found that soliciting actual or potential adverse events of all types yields more reports than the routine incident reporting system^{78, 79, 80} or criteria-driven record review.^{81, 82} Some studies found that solicitation did not yield substantially higher numbers than other methods, but did reveal significant numbers that were not otherwise found.⁸¹

Lack of Documentation in Health Care Records of Device Use and Device-Related Problems

There have been some published indications that most problems with devices are not captured, as indicated by studies of all types of patient safety problems^{53, 54, 55} as well as the studies of AMDE underreporting. Reliable information on device exposure would require documentation of device exposure on a routine basis. This has been problematic, as shown by Samore et al,⁴² Hefflin et al,⁴¹ and research in progress on central vascular catheters.⁵⁶

The poor quality of documentation of device use is an important challenge to the design of medical device surveillance programs. Exposure to some devices, generally

⁷⁷ Field M, Tilson H, eds. *Safe Medical Devices for Children*. Washington, DC: The National Academies Press; 2005.

⁷⁸ Classen DC, Pestotnik SL, Evans RS, Burke JP. Computerized surveillance of adverse drug events in hospital patients. *JAMA* 1991; 266:2847-2851.

⁷⁹ Cullen DJ, Bates DW, Small SD, Cooper JB, Nemaskal AR, Leape LL. The incident reporting system does not detect adverse drug events: a problem for quality improvement. *Jt Comm J Qual Improv* 1995; 21:541-548.

⁸⁰ Jha AK, Kuperman GJ, Teich JM, Leape L, Shea B, Rittenberg E, Burdick E, Seger DL, Vliet MV, Bates DW. Identifying adverse drug events: development of a computer-based monitor and comparison with chart review and stimulated voluntary report. *JAMIA* 1998;5:305-314.

⁸¹ O'Neil AC, Petersen LA, Cook EF, Bates DW, Lee TH, Brennan TA. Physician reporting compared with medical-record review to identify adverse medical events. *Ann Intern Med*. Sep 1 1993;119(5):370-376.

⁸² Michel P, Quenon JL, de Sarasqueta AM, Scemama O. Comparison of three methods for estimating rates of adverse events and rates of preventable adverse events in acute care hospitals. *BMJ*. Jan 24 2004;328(7433):199.

disposable single use devices such as gloves, gauze, and syringes, is virtually never recorded. Exposure to equipment is generally presumed, such as infusion pumps for delivery of intravenous drugs, but the type of or specific pump is generally not noted in records. Use of short term implants such as catheters is also usually documented only in a general manner. Permanent implants are generally well noted in the surgical chart, although the recent profusion of barcoded stickers provided with the equipment has resulted in confusion regarding which stickers indicate insertion and sizing tools and which indicate the permanently placed items; barcodes are proprietary and there are no publicly available comprehensive catalogs one can use to look up a code on a sticker to find out the device type and size. Because of the general lack of explicit documentation of device use, implicit data such as procedure codes have been used to indicate device use. For procedures that can be performed on either one or both sides of the body (such as on the eyes, hips, or knees), codes can be difficult to use because they do not indicate which side was involved. Furthermore, almost all procedure codes are not specific to device use; for example, many codes related to cardiovascular prosthesis refer to animal tissue as well as artificial devices.

An associated problem is the general lack of documentation regarding problems related to device use. In every surveillance system or epidemiologic study, it is important to accurately characterize the exposure for each person. When medical device use is the exposure, the data collector must gather the type of device and characteristics of its use. The quality of documentation of device use is important to the design of epidemiologic studies. The poor quality of documentation in existing sources, such as patient records is detrimental.⁵³ Furthermore, the chart review of central venous catheter use and non-infection problems found that use was more extensively documented when there was a problem,⁵⁶ increasing the likelihood of study bias.

Successful development of active surveillance systems and epidemiologic retrospective study designs will require the development of the following:

A rational system of codes for devices, such as the Unique Device Identifiers being developed in conjunction with the Global Medical Device Nomenclature.
 Routine documentation in patient records of device use and device-related problems.

If the device codes are placed on devices and device users recognize that the code describes the device, using the code in documentation and reporting will enhance communication of which device is being described.

Routine documentation of device use and device related problems will allow the possibility of surveillance and conducting epidemiology studies based on records. It has already been well established in other areas of surveillance and epidemiology, such as for drugs and consumer products, that using available records decreases the cost of studies tremendously and also has other methodological advantages.

ONE LINERS

Vapour Trail

MHRA is aware of an incident where an overfilled anaesthetic vaporiser resulted in the administration of an overdose of the anaesthetic agent with resulting patient bradycardia and hypotension. Investigation revealed that the vaporiser was tilted whilst being filled, thus overcoming internal safety features, allowing it to be overfilled.

When filling all types of anaesthetic vaporisers, follow the manufacturer's instructions precisely. Never tilt the vaporiser to increase the flow of anaesthetic agent as this can flood the internal chambers. Always follow the Association of Anaesthetists of Great Britain and Ireland's pre-use checks and other actions outlined in the MHRA Medical Device Alert 2003/039.



Fracture Line

MHRA has received a report of damage to the tip of a multi-parameter neonatal sensor during removal, which may have been caused by cross-clamping the sensor on the removal from the umbilical artery catheter. This resulted in a fragment of the sensor remaining in situ.

During removal of the sensor, follow the manufacturer's instructions and ensure that the sensor has been fully retracted before crimping or clamping the artery catheter. Do not use forceps or surgical clamps. Wherever possible remove the catheter and sensor together.

Footsore?

The MHRA has been made aware that wheelchair users who have diabetes are vulnerable to injuries or pressure ulcers of the feet, in addition to the more obvious load bearing areas such as ischial tuberosities.

Risk to the feet should always be checked, especially if the patient cannot wear normal footwear. The NHS trust supplying the wheelchair should be contacted for appropriate foot support or padding.

Jaws!

MHRA is aware of incidents where there have been slippages of liga clips following abdominal surgery leading to serious outcomes. These were due to the fact that the jaws of the applicator had become over-stressed resulting from the use of larger sized clips than intended.

Always ensure that the applicator is adequately maintained and only use clips specified in the instructions for use.



Pole Dancing

MHRA has received reports of monitor pole stands being used when the pole had become loose on its base. The pole stands became live because the monitor's mains cable became trapped between the pole and the base of the stand.

Users should always check the security of the pole and base of monitor or drip set stands to ensure mains cables (from monitors or pumps) cannot be trapped.

Rate Limiting?

MHRA continues to receive reports of pre-filled glass syringes that cannot be connected to some types of needle-free IV connectors. This has the potential for delay in administering treatment. Although adapters are available, MHRA has also received one report in which the adapter was left connected, resulting in an open-ended line posing a risk of infection.

Ensure that pre-filled syringes are compatible with the needle-free connector in question. Details of the size limits to ensure compatibility are provided in the instructions for use. If using an adapter to connect the syringe, ensure that this is removed from the connector after use.



Spark Gap

A defibrillator failed to charge in use because, although the paddle cable was connected, there had been failure to tighten the connector's locking ring.

Users of defibrillators should ensure the paddles are attached to the defibrillator in accordance with the instructions for use.



Published by the MHRA, an executive agency of the Department of Health. The MHRA was formed from a merger of the Medical Devices Agency (MDA) and the Medicines Control Agency (MCA) on 1 April 2003. If you would like to discuss or report an incident involving a device, contact us on: 020 7972 8123 (medical), 8128 (nursing) or e-mail: devices@mhra.gsi.gov.uk

Issue 25
Jan 2004

www.mhra.gov.uk

Figure B. A "One Liner" from the UK which places all responsibility for problems on the user.

([http://devices.mhra.gov.uk/mda/mdawebsitev2.nsf/e8be0ee313c493aa80256bbb00307b2e/33916896eddb6c3380256e2200535602/\\$FILE/issue%2025.pdf](http://devices.mhra.gov.uk/mda/mdawebsitev2.nsf/e8be0ee313c493aa80256bbb00307b2e/33916896eddb6c3380256e2200535602/$FILE/issue%2025.pdf))

Appendix C –MAUDE Reports

Table C. MAUDE Reports received from users and manufacturers.

A. INDIVIDUAL		<1985	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
MFG /1:	Death	13	585	543	516	565	730	951	1133	1528	1339	1870
	Injury	109	9483	11738	9589	8366	9845	11809	18521	52894	61885	79537
	Malfunction	28	8812	7096	7596	6677	9298	16840	24796	21583	45608	48629
	Other	2	62	10	5	7	7	4	15	13	38	35
	SUBTOTAL	152	18942	19387	17706	15615	19880	29604	44465	76018	108870	130071
UFR /2:	Death								7	287	250	266
	Injury								2	1285	1229	2338
	Malfunction								6	1083	988	989
	Other								0	142	337	554
	SUBTOTAL		0	0	0	0	0	0	15	2797	2804	4147
DIST/IMP /3:	Death									11	18	49
	Injury									251	1103	1803
	Malfunction									33	139	274
	Other									6	13	121
	SUBTOTAL		0	0	0	0	0	0	0	301	1273	2247
VOL 4/:	Death		31	27	21	32	19	319	32	4	5	61
	Injury		345	482	288	194	364	140	54	77	280	1292
	Malfunction		520	472	349	294	255	252	85	95	167	1508
	Other	22602	2097	2170	1827	1716	1664	1894	3610	4439	3013	2015
	SUBTOTAL	22602	2993	3151	2485	2236	2302	2605	3781	4615	3465	4876
	TOTAL	22754	21935	22538	20191	17851	22182	32209	48261	83731	116412	141341
B. SUMMARY 5/:												
	TOTAL											
	GRAND TOTAL	22754	21935	22538	20191	17851	22182	32209	48261	83731	116412	141341

*Individual report counts are based on "date received" for 1985-2002; "date entered" from 2003 to the present.
 **CY2005 represents the most current data retrieval for MDR reports entered into the MAUDE database through 7/31/05; and ASR reports received and entered into the ASR database through 8/10/05. These reports are submitted to FDA on 1/31, 4/30, 7/31 and 10/31 and are related to the preceding reporting quarter. The yearly report counts will be updated periodically to account for delayed data entry issues (e.g. backlog of unentered reports).
 1/: Manufacturer Reports - received since 12/84 (MDR Regulation 12/13/84)
 2/: User Facility Reports- received since 1992 (Safe Medical Devices Act (SMDA) 1990)
 3/: Distributor and Importer Reports - received since 1992 (SMDA 1990). Distributors reported until 2/19/98 as a result of the FDA Modernization Act of 1997 (FDAMDA)
 4/: Voluntary Reports - received 1973 - 1992 (Medical Device Laboratory Product Problem Reporting Program (PRP) and 1992 - Current (MedWatch Program)
 5/: Summary Reports- received from manufacturers who have been granted exemptions (beginning 1995) to reporting individual adverse events

Table C (continued)

A. INDIVIDUAL		1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
MFG /1:	Death	1773	1389	1019	1021	905	1017	1366	1266	1453	1909
	Injury	51752	38236	31122	18554	13073	13646	17354	17955	18775	22894
	Malfunction	50125	37830	32833	31960	29199	27683	29418	36988	35453	20149
	Other	28	631	2299	2485	3140	3132	2960	3544	4063	3732
SUBTOTAL		103678	78086	67273	54020	46317	45478	51098	59753	59744	48684
UFR /2:	Death	211	346	326	273	233	211	240	200	185	229
	Injury	2315	3173	3892	2556	1777	1568	1625	1448	1123	1110
	Malfunction	780	1091	1293	860	738	654	675	729	1001	1531
	Other	657	697	657	446	264	323	274	303	321	504
SUBTOTAL		3963	5307	6168	4135	3012	2756	2814	2680	2630	3374
DIST/IMP /3:	Death	19	27	35	13	11	11	9	7	0	4
	Injury	1661	3606	1364	189	85	55	142	117	186	260
	Malfunction	164	213	169	289	711	536	206	313	665	239
	Other	169	150	70	50	78	619	210	297	92	58
SUBTOTAL		2013	3996	1638	541	885	1221	567	734	943	561
VOL 4/:	Death	73	63	67	75	54	92	102	104	155	110
	Injury	1559	864	835	963	899	1397	1223	1246	1192	1188
	Malfunction	1367	1494	1299	1523	1416	1245	1513	1773	1799	1613
	Other	782	565	405	391	319	373	411	522	590	476
SUBTOTAL		3781	2986	2606	2952	2688	3107	3249	3645	3736	3387
TOTAL		113435	90375	77685	61648	52902	52562	57728	66812	67053	56006
B. SUMMARY 5/:											
TOTAL		2755	6292	21682	36190	36969	46075	65818	79189	91192	104391
GRAND TOTAL		116190	96667	99367	97838	89871	98637	123546	146001	158245	160397

*Individual report counts are based on "date received" for 1985-2002; "date entered" from 2003 to the present.

**CY2005 represents the most current data retrieval for MDR reports entered into the MAUDE database through 7/31/05; and ASR reports received and entered into the ASR database through 8/10/05. These reports are submitted to FDA on 1/31, 4/30, 7/31 and 10/31 and are related to the preceding reporting quarter. The yearly report counts will be updated periodically to account for delayed data entry issues (e.g. backlog of unentered reports).

1/: Manufacturer Reports - received since 12/84 (MDR Regulation 12/13/84)

2/: User Facility Reports- received since 1992 (Safe Medical Devices Act (SMDA) 1990)

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4/: Voluntary Reports - received 1973- 1992 (Medical Device Laboratory Product Problem Reporting Program (PRP) and 1992 - Current (MedWatch Program)

5/: Summary Reports- received from manufacturers who have been granted exemptions (beginning 1995) to reporting individual adverse events

Table C (continued)

A. INDIVIDUAL		2005**	TOTAL
MFG /1:	Death	1492	24,383
	Injury	19077	536,214
	Malfunction	38077	566,678
	Other	4677	30,889
	SUBTOTAL	63323	1,158,164
UFR /2:	Death	119	3,383
	Injury	684	26,125
	Malfunction	1192	13,610
	Other	442	5,921
	SUBTOTAL	2437	49,039
DIST/IMP /3:	Death	4	218
	Injury	156	10,978
	Malfunction	213	4,164
	Other	296	2,229
	SUBTOTAL	669	17,589
VOL 4/:	Death	67	1,513
	Injury	593	15,475
	Malfunction	803	19,842
	Other	315	52,196
	SUBTOTAL	1778	89,026
TOTAL		68207	1,313,818
B. SUMMARY 5/:			
TOTAL		53,993	544,546
GRAND TOTAL		122200	1,858,364

*Individual report counts are based on "date received" for 1985-2002; "date entered" from 2003 to the present.

**CY2005 represents the most current data retrieval for MDR reports entered into the MAUDE database through 7/31/05; and ASR reports received and entered into the ASR database through 8/10/05. These reports are submitted to FDA on 1/31, 4/30, 7/31 and 10/31 and are related to the preceding reporting quarter. The yearly report counts will be updated periodically to account for delayed data entry issues (e.g. backlog of unentered reports).

1/: Manufacturer Reports - received since 12/84 (MDR Regulation 12/13/84)

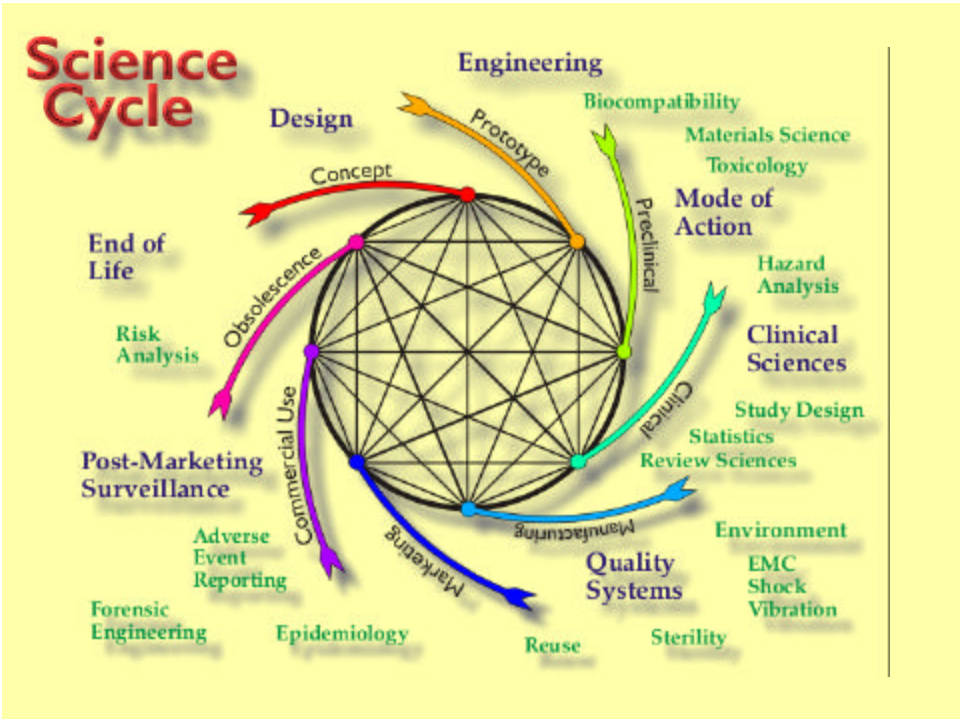
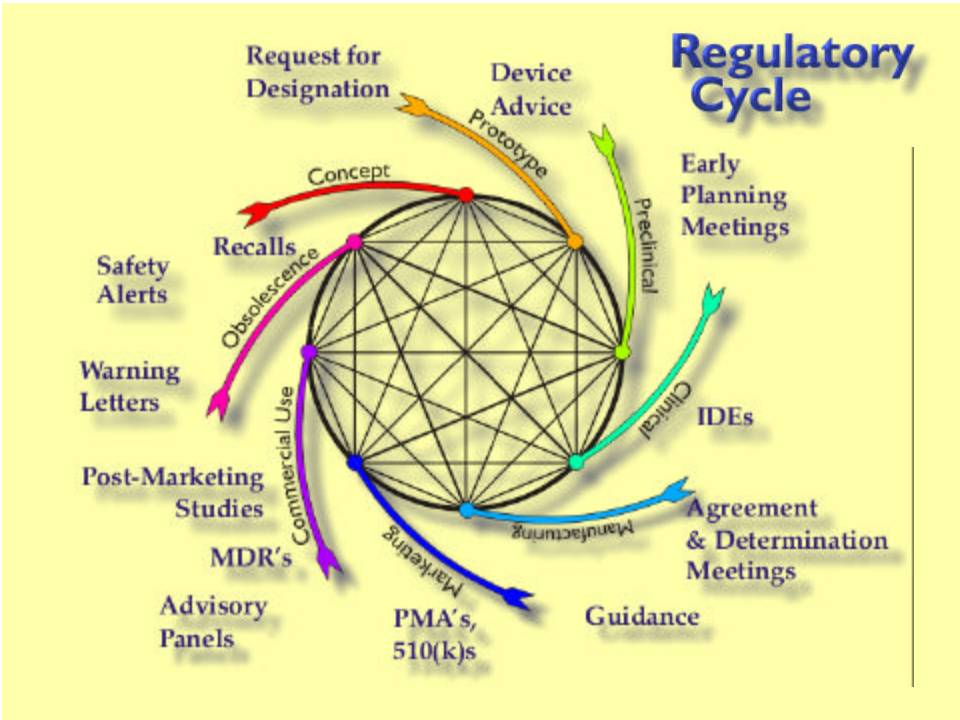
2/: User Facility Reports- received since 1992 (Safe Medical Devices Act (SMDA) 1990)

3/: Distributor and Importer Reports- received since 1992 (SMDA 1990). Distributors reported until 2/19/98 as a result of the FDA Modernization Act of 1997 (FDAMDA)

4/: Voluntary Reports - received 1973 - 1992 (Medical Device Laboratory Product Problem Reporting Program (PRP) and 1992 - Current (MedWatch Program)

5/: Summary Reports- received from manufacturers who have been granted exemptions (beginning 1995) to reporting individual adverse events

Appendix D- CDRH Total Product Life Cycle (TPLC) Model



Appendix E -- Capability Analysis of Surveillance Programs Internal and External to CDRH with Respect to Surveillance Goals

Surveillance Objectives

The main objective of medical device surveillance⁸³ is to detect patterns of actual or potential AMDE. An ideal surveillance program should be based on epidemiologic principles so that inferences can be made about the specific, overall, and relative public health burdens of different types of AMDE. This population-based knowledge would form the basis of more effective efforts to mitigate and prevent device-related AMDE.

A program of surveillance systems should ideally meet all of the following objectives simultaneously:

- Detect rare or unexpected AMDE.
- Find problems in “real” users with multiple co-morbidities (including vulnerable populations) in “real world” settings (including many years after initial device exposure).
- Have complete capture of AMDE and reliable information on device exposure, including the specific nature of the device, brand and model number.
- Allow full appreciation of the public health burden imposed by AMDE of specific natures or related to specific device types.

These objectives combine the purposes of surveillance and the quality of data required to fulfill the purposes.

All individual surveillance systems should be measured against these objectives. Their selection into a program of surveillance systems should be based on their ability to advance the program towards meeting the objectives. In practice, the strategy would be to add systems that have complementary strengths and weaknesses. One should base the surveillance program on a variety of data collection methods that capture information specific to a variety of device types, use settings, and users.

Such a program would effectively and comprehensively support timely and science-based decision-making regarding:

- inspection and other legal decisions
- choice of further laboratory and epidemiologic studies to conduct
- strategies for effective communication to stakeholder communities (sponsors, users, and patients)

⁸³ In this paper, we use “surveillance” to mean “just looking” or “monitoring” for adverse events (AE), as opposed to “epidemiology,” meaning research with a pre-defined objective. (See the two definitions in Rothman KJ, Greenland S, eds. *Modern Epidemiology*, 2nd ed., Lippincott-Raven, Philadelphia, PA, 1998.) There is a multitude of surveillance methods. Data collection methods include anecdotes, surveys, standard data forms, and use of existing data. Data may come from convenience samples, random samples, or all of the population.

measurement of the impact of CDRH on public health
support of the functions of partner agencies, such as CMS, AHRQ, VHA, and DoD.

Surveillance Methods: “Active” vs. “Passive”

The surveillance objectives listed above include:

Complete capture of AEs and reliable information on device exposure.
Calculation of the public health burden imposed by AEs of specific natures or related to specific device types.

Both of these objectives require collecting data that was recorded during routine patient care, or “active surveillance.” In “active” surveillance someone regularly looks for AE to add to the AE database; this may be accomplished by regular solicitation of care providers for reports, regular searching of records for evidence of AE, or regular wholesale downloading of primary patient records.⁸⁴ This active data collection stands in contrast to “passively” waiting for reports of AE, which is defined as “passive” surveillance.⁸⁴ It has already been shown for adverse drug events that active surveillance yields more AE information than passive surveillance.^{78, 79, 80}

The “active” versus “passive” nature of a surveillance system is a relative, rather than absolute concept. For example, MedSun has features of both an active and a passive surveillance system. One active feature of the MedSun program is its intense educational efforts. A passive aspect of the program is the fact that facility representatives wait for reports from within their facilities that are then reported to CDRH. If the facilities actively searched their patient records for evidence of AMDE their program would be more active, and therefore the MedSun system would capture AMDE more completely.

Reliable information on device exposure would require documentation of device exposure on a routine basis. This has been problematic, as shown by Samore et al,⁴² research in progress on central vascular catheters,⁵⁶ and direct observation of device use in hospital intensive care units.

Active surveillance that ensures complete capture of AMDE and reliable information on device exposure for the entire population or a statistical sample of the population also would allow the calculation of the public health burden imposed by AMDE of specific types or related to specific device types. NEISS (discussed later in this appendix) is under development to try to address these objectives.

Capability Analysis

The following tables compare CDRH’s internal and external database capabilities to the surveillance objectives.

⁸⁴ Buehler JW. “Surveillance” In: Rothman KJ, Greenland S, eds. *Modern Epidemiology*, 2nd ed., Lippincott-Raven, Philadelphia, PA, 1998.

Table E-1. Capability Analysis of Surveillance Programs Internal to CDRH. These data systems are explained in the main part of the report, under “Postmarket Problem Identification: Adverse Event Reports.”

System property	System name		
	MDR, ASR, UFR	MedWatch	MedSun
Type of system	Mandatory passive reporting	Voluntary passive reporting	Sentinel passive reporting
Source of AMDE data	Any health care setting	Any health care setting	Volunteer hospitals and nursing homes
Special population(s)	All	All	All
Data available for use within 1 year of AMDE	Y	Y	Y
Device description details	Varies	Varies	Varies
Long term follow-up of individual device user	N	N	N
Detect rare AMDE	Y	Y	N
Detect unexpected AMDE	Y	Y	Y
Find problems in “real” users with multiple co-morbidities in “real world” settings	Y	Y	Y
Complete capture of AMDE	N	N	N
Trends over time can be calculated	N	N	N
Reliable data on device exposure	N	N	N
Allow calculation of the public health burden imposed by AMDE of specific natures	N	N	N
Allow calculation of the public health burden imposed by AMDE related to specific device types	N	N	N

Table E-2-a. Capability Analysis of Programs . These data systems are explained in the main part of the report, under “Postmarket Problem Identification: Public Health Partners.”

System property	System name				
	NEISS	HCUP NIS	JCAHO	CMS data	National registries called for by CMS. 1) Left ventricular assist devices, 2) Carotid stents, 3) maybe ICD for sudden death
Type of system	Active surveillance	Sentinel active surveillance		Administrative files	Registry supplemented by Medicare administrative files
Source of AMDE data	Statistical sample of emergency departments	All discharge claims for a statistical sample of hospitals		CMS administrative files	Registry and administrative files
Special population(s)	All	All		Elderly and disabled	Elderly and disabled
Data available for use within 1 year of AMDE	Y	N		Y?	Probably
Device description details	Type of device	Infer from diagnosis or procedure code		Varies	To be determined
Long term follow-up of individual device user	N	N		Possible if user stays in Medicare	Possible
Detect rare AMDE	N	N		?	Possible
Detect unexpected AMDE	Y	N		?	Possible
Find problems in “real” users with multiple co-morbidities in “real world” settings	Y	Y		Y	Possible
Complete capture of AMDE	Y	N			Possible
Trends over time can be calculated	N	N		Y	Possible
Reliable data on device exposure	N	N		N	Y
Allow calculation of the public health burden imposed by AMDE of specific natures	Y	Y		N	Y for elderly and disabled
Allow calculation of the public health burden imposed by AMDE related to specific device types	N	N		N	Y for elderly and disabled
Mechanisms to convey trends of AMDE event information to interested parties?					

Table E-2-b. Capability Analysis of Programs. These data systems are explained in the main part of the report, under “Postmarket Problem Identification: Public Health Partners.”

System property	System name				
	ACC	NCHS surveys	ECRI	Agreements with states that have reporting	VA nationwide electronic medical record system
Type of system	Registry	Survey	Voluntary passive reporting	?	
Source of AMDE data	Sample of participating cardiac catheterization labs	Statistical sample of providers or patients, depending on the survey	Reports from ECRI clients	?	Medical records
Special population(s)		All		?	Veterans
Data available for use within 1 year of AMDE	Y	N	Y	?	Probably
Device description details	Level of detail determined by study sponsor	Type of device	?	?	Varies
Long term follow-up of individual device user	N	N	N	?	Possible
Detect rare AMDE	N	N	?	?	Possible
Detect unexpected AMDE	N	Y	Y	?	Possible
Find problems in “real” users with multiple co-morbidities in “real world” settings	Y	Y	Y	?	Possible
Complete capture of AMDE	N	N	N	?	Possible
Trends over time can be calculated	Y	N	N	?	Possible
Reliable data on device exposure		N	N	?	Possible for some devices
Allow calculation of the public health burden imposed by AMDE of specific natures	N	Y	N	?	Possible for veterans
Allow calculation of the public health burden imposed by AMDE related to specific device types	N	N	N	?	Possible for veterans
Mechanisms to convey trends of AMDE event information to interested parties?					

Summary of Capability Analysis

To be effective, all of the objectives listed at the beginning of this appendix should be met by a comprehensive surveillance program. It is possible to meet all the objectives in the program as a whole, if it is composed of systems that each contribute to enough of the objectives. An example surveillance system that would meet the objectives and be comprised of two systems would include a passive reporting system to signal rare AMDE and an active surveillance system using a statistical sample of health care settings. This example could meet all the objectives as a whole if practitioners nationwide routinely recorded device use and device-related problems in health care records. This routine documentation would form the requisite infrastructure for any effective AMDE surveillance system. It would support the development of informative codes for electronic records and reporting. It would also be an important resource when CDRH, manufacturers, or other parties want to follow-up on AMDE reports and gather more information about individual events.

Appendix F – CDRH E-Consumer Initiative

CDRH E-Consumer Initiative

Summary of 2004/2005 E-Consumer Initiative and the Future of CDRH Web Communication

Laurie Mendelson
Jay Rachlin

Office of Communication, Education and Radiation Programs
Center for Devices and Radiological Health

E-Consumer Initiative

CDRH 2004/2005 Strategic Initiative:
"Automate a Consumer Information System"

Where do we stand? Under the initiative, we have:

- formed a Center-wide E-Consumer steering committee that develops and vets ideas.
- assigned E-consumer tasks and responsibilities to OCER.
- acquired and developed new technology and software to enhance Web outreach.
- developed new policies and procedures to help CDRH employees improve, develop, and maintain Web pages.

4 Initial E-Consumer Tasks

1. Develop an easy-to-use database of CDRH-regulated products
2. Develop and post a list of routinely-asked questions and answers
3. Develop a method of collecting and disseminating (“pushing out”) CDRH news
4. Improve CDRH Web pages

Task 1: Develop Easy-to-Use Database of CDRH-Regulated Products

Requirements:

- Simple, Google-like search box
- Allows text search without knowing device regulatory classification

Solution:

The screenshot shows the 'Devices@FDA' website interface. At the top, the logo 'Devices@FDA' is displayed in blue and red, with 'release 1.0' written in a small font to the right. Below the logo, the text reads 'A Catalog of Cleared and Approved Medical Devices' and 'A new resource for finding medical device information from FDA. It includes links to the device approval date, user instructions, and other consumer information.' The main search area is titled 'Devices@FDA' and contains a text input field with the placeholder 'Enter a medical device in the space below.' and the text 'pacemaker' entered. Below the input field, there is an 'Optional:' section with 'Approval Date From:' and 'To:' fields. The 'To:' field contains the date '06/07/2005'. At the bottom of the search area, there are 'Search' and 'Clear' buttons, a dropdown menu set to '10', and the text 'Records per Report Page'.

<http://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/>

Task 2: Develop and Post a List of Routinely-Asked Questions and Answers

Requirements:

- Manages and displays questions and answers
- Provides access from every CDRH page
- Allows users to scroll through questions and answers, search by category or keyword, or submit their own question

Solution:

RightNow Technologies® Website Question and Answer System

Task 3: Develop a Method of Collecting and Disseminating CDRH News

Requirements:

- Sends email messages with CDRH news
- Allows users to create individual profiles according to areas of interest
- Allows users to select frequency of messages
- Contains simple and clear subscription points adjacent to specific information

Solution:

GovDocs GovDelivery® Email Subscription Management System

Task 4: Improve CDRH Web Pages

4 Step Process:

Step 1: Understand the CDRH website audience(s) and determine audience needs

Step 2: Improve quality of information (including content, language, and maintenance)

Step 3: Improve design and dissemination

Step 4: Plan for the future

CDRH Website: Where are We Now?



What are We Doing to Improve CDRH Web Pages?

- CDRH Website customer satisfaction survey
- Audience analysis interviews and surveys
- SOP for posting information on the Web (new Websites and questions and answers)
- Focus on plain language and risk communication
- Policies for ensuring websites are maintained
- Usability studies throughout website lifecycles
- Creative dissemination (including RSS)
- New sites or site designs as need arises

A Vision for CDRH Electronic Communication

- A coordinated Web communication program that includes e-consumer initiatives and more
- An easy-to-use, interesting, informative, user-focused CDRH website and CenterNet
- Clear and consistent policies for testing, posting, and reviewing new information
- A CDRH "image" with unique look and feel
- Experienced staff with clear goals, Center-wide support, and outreach plans
- A leadership role within FDA and HHS in developing and applying innovative technology