



Heart Rhythm SocietySM

Draft Recommendations Report
by the Heart Rhythm Society
Task Force on Device Performance
Policies and Guidelines

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SUMMARY OF RECOMMENDATIONS

The Heart Rhythm Society believes that patient and physician knowledge, confidence, and trust can be enhanced and strengthened through:

- Greater transparency in post-market surveillance, analysis, and reporting of information,
- Enhanced systems to increase the return of devices to manufacturers and to improve the analysis and reporting of device performance and malfunction information, and
- Cooperation among industry, the FDA, and physicians to make every effort to prevent injuries and deaths due to device malfunctions.

Specific recommendations for industry, FDA, CMS, Congress, physicians and others, follow.

DEVICE PERFORMANCE

Recommendation

The Heart Rhythm Society recommends that manufacturers establish standards of performance for their devices and the key components including batteries, pulse generators, and leads.

The Heart Rhythm Society recommends that manufacturers publish annually malfunction rates for each device type based on documented device malfunctions reported to the FDA as indexed to the number of devices at risk (implanted) in the US population during the same calendar year.

COMMUNICATION OF DEVICE PERFORMANCE

Recommendations

Industry: At the national Policy Conference on Pacemaker and ICD Performance (17), the Heart Rhythm Society recommended that manufacturers of cardiac rhythm management device provide standardized device performance reports semiannually in hard copy and in a format available to the public on the Internet. The reports should include all device information pertinent to

patient care, and be presented in an unbiased manner and in a consistent and usable format. The Heart Rhythm Society recommends that manufacturers establish expected standards of performance for their particular device models including key components such as batteries, pulse generators, and leads. In addition, the Heart Rhythm Society recommends that manufacturers provide public access to the standards of performance and all information regarding any product performance issues, including sporadic or “component malfunctions” in the semiannual product performance reports. Information should include changes made in response to field observations.

Physicians: The Heart Rhythm Society recommends that physicians (or other medical personnel), in addition to informing patients of procedural benefits and risks, inform patients of expected device performance, including battery life and potential malfunction rate, at the time of initial device implantation and at replacement.

SURVEILLANCE

Recommendations

Industry: The Heart Rhythm Society recommends that cardiac rhythm management device manufacturers develop and utilize wireless and remote monitoring technologies to:

- Identify abnormal device behavior as early as possible.
- Reduce underreporting of device malfunctions by determining the functional status of an implanted device more frequently and more accurately.

FDA: Changes to the current post market surveillance system are required to improve the timely identification of cardiac rhythm management devices that do not perform according to expectations and which may pose a danger to patients.

The Heart Rhythm Society recommends that the FDA enhance the Manufacturer and User Device Experience (MAUDE) database by:

- Utilizing a specialized form for cardiac rhythm management devices to permit better and more precise reporting of adverse events.

- Tracking devices that are returned to manufacturers for analysis and updating publicly available adverse event reports with root cause analyses.

- Facilitating links to data from international sources.

General Recommendation: The Heart Rhythm Society recommends that the NCDR ICD Registry, administered by the Heart Rhythm Society and the American College of Cardiology be modified to:

- Collect detailed device-specific longitudinal performance data including a report of device performance at the time of device replacement or death.
- Collect data regarding adverse device events, date of the event, and the outcome of the event or cause of each patient’s death.

This adjunctive information can assist in tracking device performance and the consequences of malfunctions.

Implementation of this recommendation will require additional funding and resources from the federal government, private payers, device manufacturers, and hospitals.

Congress: The Heart Rhythm Society urges Congress to recognize that post-market surveillance, analysis, and reporting of ICD and pacemaker performance is a high priority for ensuring patient safety. Additionally, Congress is urged to recognize and address the issue that the FDA does not currently have adequate resources to perform this function. The enhancements to the surveillance system that the Heart Rhythm Society recommends, particularly those to the MAUDE database and the NCDR ICD Registry, will require additional resources. The Heart Rhythm Society recommends that Congress ensure that FDA receives the resources and funding necessary to enhance the MAUDE database and provide improved post-market surveillance of pacemakers, ICDs, and leads as described in this section.

Physicians: The Heart Rhythm Society recommends that all devices be returned to the manufacturer for analysis after explantation. This includes returning devices to the manufacturer at the time of device replacement whether the replacement is routine or because of device malfunction.

The Heart Rhythm Society recommends the following actions in order to achieve this goal.

- Post mortem device interrogation, explantation, and return to the manufacturer should be strongly encouraged, particularly in cases of sudden or unexpected death.
- The Heart Rhythm Society should work to educate physicians, nurses, allied health professionals, patients, families, pathologists, and morticians of the importance of notifying the physician following the device immediately after the patient dies and returning the patient’s device to the manufacturer.
- Whenever possible and indicated, patients should be asked to consent for post-mortem ICD evaluation including interrogation and removal. This consent should be legally binding.
- In the absence of prior discussion with the patient, family members should be asked to consent to device interrogation, removal and return to the manufacturer after the patient’s death.

Other Recommendations: The Heart Rhythm Society recommends that physicians be compensated appropriately for post mortem evaluation of cardiac rhythm management devices and reporting of device adverse events. CPT codes should be established for these activities.

ANALYSIS OF DATA – ROLES OF INDUSTRY, FDA, AND PHYSICIANS

Recommendations

The Heart Rhythm Society recommends that experts who are not full-time employees of industry or the FDA should analyze device performance data and provide advice on a regular basis and when life-threatening device malfunctions are identified. The Heart Rhythm Society recommends that these committees advise when and what action is appropriate including physician and patient notification and the necessity of retrieving unmitigated devices from the sales force and from hospital inventories.

Industry: The Heart Rhythm Society recommends that device manufacturers

establish standing independent committees of experts (including physicians and representatives of other disciplines such as engineering, statistics, risk assessment and ethics) to analyze data (including semiannual device performance reports and registry information) regarding cardiac rhythm management device performance. These committees should meet on a regular basis (at least semiannually) as well as on an ad hoc basis and quickly when a life-threatening device defect has been identified. The committees would act much like the data safety and monitoring board for a clinical trial and would advise when and what action (if any) is appropriate, including physician and patient notification and the necessity of retrieving unmitigated devices from the sales force and from hospital inventories. The committees could be organized according to device type (e.g. pacemaker, ICD, leads) and could be either industry-wide or manufacturer specific.

FDA: The Heart Rhythm Society recommends that the FDA establish standing post-market advisory committees that will meet on a regular basis (semiannually) and in a timely fashion on an ad hoc basis to analyze data regarding cardiac rhythm management device performance and to advise when and what action should be taken to address device malfunctions that are identified. The FDA could accomplish this also by extending the scope of the Circulatory System Devices Panel to the post-market period. The Heart Rhythm Society should assist the FDA in identifying individuals who can serve in this capacity.

Congress: The Heart Rhythm Society recommends that Congress ensure that FDA receives the resources and funding necessary to establish and maintain the FDA advisory committee that is described in this section.

TERMINOLOGY AND THRESHOLD FOR ACTIVATION OF DEVICE RECALLS AND ADVISORY NOTICES

Recommendations

Terminology: The Heart Rhythm Society recommends that device manufacturers and the FDA should use identical terminology to classify device malfunctions and communicate them to the public.

Industry: The Heart Rhythm Society recommends that device manufacturers continue to provide the FDA with data regarding device performance at the time that certain problems are identified, as well as in the form of semiannual product performance reports. A malfunction that is associated with a significant risk for death or serious injury, is systematic, and for which there is reason to suspect that it could occur in other patients, merits early review by the advisory committees described in the previous section. Examples of circumstances that, meeting these criteria, that would require early notification of the FDA and its post-market surveillance advisory committee include: 1) Devices that fall outside of FDA approved labeling or the standards of performance, 2) Devices that fail to treat an arrhythmia, pace the heart, or provide inappropriate and potentially life-threatening therapy, and 3) Devices that are unexpectedly inactive (no telemetry and/or unable to be interrogated, or no output for reasons other than normal battery depletion).

FDA: The Heart Rhythm Society recommends that the FDA establish a simple and more intuitive nomenclature to communicate important information about device malfunction or failure of a device to perform according to specifications. Specific recommendations for changes in nomenclature include:

1. Eliminate the term “recall” in public communications regarding implanted devices.
2. Change the term “Class I recall” to “Class I advisory notice or to Class I safety alert.” Class I advisory notices would be those in which device replacement should be considered because of the reasonable probability that the malfunction could result in death or significant harm.
3. Change Class II and III recalls (non life-threatening malfunctions or potential malfunctions) to “advisory notices or safety alerts.”

Threshold for action: The threshold for activation of an advisory notice may vary depending on the frequency of the device performance problem and the clinical implications of the malfunction. A single event, if it is associated with a significant risk for death or serious injury, is systematic, and for which there is reason to suspect

that it could occur in other patients, merits notification of physicians and patients. In such a case, devices that are not implanted and in which the malfunction has not been corrected or addressed adequately should be retrieved from the sales force and hospital inventories. The Heart Rhythm Society considers it to be inadvisable to determine a fixed percentage of device malfunctions or attempt to classify all of the particular types of malfunction that would automatically trigger a notification or advisory. Rather, data should be reviewed on a regular basis by the committees identified in the previous section, in order to determine when a pattern of inadequate device performance exists.

COMMUNICATION AFTER DEVICE MALFUNCTION IS IDENTIFIED

Recommendations

Industry: In addition to physician advisory notification letters, the Heart Rhythm Society supports the use of a standardized Physician Device Advisory Notification format for all manufacturer advisories to physicians regarding potential device malfunction. The Heart Rhythm Society recommends that industry use the Patient Device Advisory Notification letter format to communicate directly with patients.

Manufacturers should make a good faith effort to contact affected patients using the patient's registration information obtained at the implant center at the time of the implant procedure. The definition of such an effort should be determined between the FDA and industry according to guidelines already in place for advisory communications. Whenever possible, physicians should be notified first and patients shortly thereafter. In addition to historical communication methods, physicians and patients could be notified by email to increase the timeliness of communication.

The Heart Rhythm Society also recommends that the standardized physician and patient notifications reside on the manufacturer's website, and that they be linked to the Heart Rhythm Society website and to FDA enforcement reports and other notifications to facilitate easy access to all components of each individual device advisory.

Product advisory notices could also appear in Heart Rhythm, the official journal of the Heart Rhythm Society. Updates to these notifications can be communicated in a similar manner and in the manufacturer's Product Performance Reports.

Advisory notices should include general information regarding the potential clinical implications and appropriate clinical recommendations, and should acknowledge that management decisions are ultimately the decision of the patient in consultation with his or her doctor.

FDA: The Heart Rhythm Society supports a centralized, rather than the current regional system, for communication of device advisory notifications to promote a broader and more inclusive interpretation of the advisory issues. In addition, the unique and specialized nature of cardiac rhythm management device advisories requires a centralized rather than regional intake mechanism to enable accurate interpretation of data on an ongoing basis by key knowledgeable FDA staff and by the other parties such as a post-market physician advisory panel. The Heart Rhythm Society believes that a centralized system will facilitate timely FDA classifications and urges the FDA to classify all advisory notifications and include these data on the Physician Device Advisory Notification form within 30 days.

Congress: The Heart Rhythm Society recommends that Congress ensure that FDA receives the resources and funding necessary to ensure that centralized notification and analysis of pacemaker, ICD, and lead malfunction notifications, as recommended in this section, is accomplished effectively.

Physicians: The Heart Rhythm Society urges physicians to utilize the standardized Physician Device Advisory Notification format to aid in the objective assessment and characterization of all device advisory communications. This format can be used to facilitate quick reference and identify key aspects of the advisory to help guide patient management decisions in an ongoing fashion.

RECOMMENDATIONS FOR CLINICIANS MANAGING DEVICE ADVISORY NOTICES

Recommendations

Physicians:

- The Heart Rhythm Society recommends that physicians and the facilities where ICDs and pacemakers are implanted should monitor local outcomes and adverse events associated with pacemaker and ICD system implantation and removal. Participation in the NCDR ICD Registry will facilitate obtaining this information.
- The Heart Rhythm Society recommends that physicians consider the risk of device removal and reimplantation when making clinical decisions and recommendations to patients who have a device that has or may have a malfunction.
- The Heart Rhythm Society recommends that physicians consider, when appropriate, alternatives to device explantation (reprogramming, enhanced monitoring, etc) that may mitigate the consequences of device malfunction and decrease patient risk.

Guidelines for Decisions on Device Recalls and Notifications

1. Consider device/lead replacement if:
 - the mechanism of malfunction is known and is potentially recurrent,
 - the risk of malfunction is likely to lead to patient death or serious harm, and
 - The risk of replacement is less than or at least not substantially greater than the risk of device malfunction.
2. Consider device/lead replacement in pacemaker-dependent patients for those:
 - patients with an ICD for secondary prevention of sudden death, and
 - Patients with an ICD for primary prevention of sudden death in whom appropriate therapy has been given when the risk of replacement is not substantially greater than the risk of device malfunction.
3. Consider device replacement if the predicted end of life (EOL) is approaching.

4. Consider conservative management with periodic non-invasive device monitoring in patients who are not pacemaker-dependent and those with an ICD for primary prevention of sudden death in whom there is a low probability of future ICD therapy, and the rate of device malfunction is low (<1/1000). Other patients may also be candidates for conservative management.
5. Provide routine follow up for patients with a device malfunction that has been mitigated or corrected by reprogramming the software.
6. Consider conservative management with periodic non-invasive device monitoring in patients where operative intervention risk is high or in patients who have other significant competing morbidities even when the risk of device malfunctions or patient harm is substantial.

INTRODUCTION

The benefits of pacemakers and implantable cardioverter defibrillators (ICDs) have been demonstrated and confirmed by numerous clinical trials (1-14). Use of these devices has expanded dramatically; ICD implants tripled between 2000 and 2005 and over 250,000 are expected to be implanted worldwide in 2006 (15). Thousands of lives have been saved and many more have been improved by these devices. But as is true for all man-made devices, malfunctions in pacemakers and ICDs have and will continue to occur. Timely detection and communication of malfunctions that have the potential to be repetitive, particularly those malfunctions that are life-threatening, is critical to patient safety and to ongoing device improvement.

Recent events have raised important questions about current systems for post-market surveillance and analysis of pacemaker and ICD performance and the communication of that performance to physicians and patients. Recalls or advisories issued by the three largest pacemaker and ICD manufacturers during the last year, and the untimely death of a patient with a device malfunction, have focused attention on the system and the need for reform. On July 18th, 2005, the Institute of Medicine released a study,

“Safe Medical Devices for Children,” that identified shortfalls and recommended changes in the U.S. Food and Drug Administration (FDA) post-market monitoring system for medical devices (16). Whereas that report highlighted many of the shortcomings of current systems for overall device safety, cardiac rhythm management devices present unique issues due to their life-saving nature, their life-long use, and their implantation in the body.

On September 16, 2005 the Heart Rhythm Society, the international leader in science, education and advocacy for cardiac arrhythmia professionals and patients, and the FDA convened a national Policy Conference on Pacemaker and Implantable Cardioverter Defibrillator Performance in Washington D.C. (17). This was not the first time that the society had addressed post-market device surveillance. On March 6, 1995, the North American Society for Pacing an Electrophysiology (subsequently Heart Rhythm Society) convened a Consensus Conference in Toronto, Ontario, to discuss the management of cardiac device recalls after the provincial Ministry of Health issued unique guidelines regarding a lead problem (18). However, the recent Policy Conference in Washington D.C. was more comprehensive in scope and provided an unprecedented opportunity for the major stakeholders — industry, the FDA, cardiac electrophysiologists, nurses, and patients — to discuss challenges, concerns, and opportunities for improving the current system. Participants discussed device performance, post-market surveillance and analysis, communication of device performance to physicians and patients, and clinical decision-making when a malfunction is identified. Underlying many of these issues were three unifying themes; knowledge, confidence, and trust.

Physicians and patients need timely, accurate, and understandable information regarding device performance in order to make appropriate decisions regarding medical care. They want confidence that the implanted device has been manufactured using state-of-the-art materials and techniques and that it will perform reliably. Furthermore, patients need to trust that physicians, industry, and the FDA will act with the best interest of patients in mind.

The policy conference provided the foundation for future discussions and for the creation by the Heart Rhythm Society of a task force that was charged with developing policy recommendations for post-market pacemaker, ICD, and lead surveillance, analysis, and performance reporting and guidelines for clinicians when a device malfunction is identified. This document is the report of the task force's findings, recommendations, and guidelines.

The Heart Rhythm Society believes that patient and physician knowledge, confidence, and trust can be enhanced and strengthened through:

1. Greater transparency in post-market surveillance, analysis, and reporting of information,
2. Enhanced systems to increase the return of devices to manufacturers and to improve the analysis and reporting of device performance and malfunction information, and
3. Cooperation among industry, the FDA, and physicians to make every effort to prevent injuries and deaths due to device malfunctions.

Specific recommendations for industry, FDA, the Center for Medicare & Medicaid Services (CMS), Congress, physicians and others, follow. The recommendations address device performance and communication of device performance, post market surveillance, analysis of data-the roles of industry, FDA, and physicians, terminology and threshold for activation of recalls and advisory notices, communication after device malfunction is identified, and recommendations for clinicians managing device advisory notices.

DEVICE PERFORMANCE AND COMMUNICATION OF DEVICE PERFORMANCE

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Recommendations

Industry:

The Heart Rhythm Society recommends that manufacturers establish standards of performance for their devices and the key components including batteries, pulse generators, and leads.

The Heart Rhythm Society recommends that manufacturers publish annually malfunction rates for each device type based on documented device malfunctions reported to the FDA as indexed to the number of devices at risk (implanted) in the US population during the same calendar year.

DEVICE PERFORMANCE

Despite continual efforts to improve permanent pacemakers, ICDs, and leads, these devices remain subject to malfunction from a variety of mechanisms, some well-defined and understood at the time of device design and manufacture, others recognized only later, and still others which continue to elude complete understanding despite rigorous analysis. Data compiled between 1990 and 2002 from FDA annual reports indicate that the incidence of confirmed device malfunction resulting in device explantation indexed to the number of devices implanted in the same year ranged between about 1.0 and 9.0 per 1000 implanted pacemakers and between about 8 and 40 per 1000 implanted ICDs (19). During this same timeframe, the mean incidence of confirmed device malfunction indexed to the number of devices implanted during the same calendar year resulting in device replacement was about 7 per 1000 for pacemakers and about 20 per 1000 for ICDs. Similar data are not available to assess the malfunction rates for leads.

Device performance can be defined as the percentage of devices that are in service and functioning appropriately in living individuals over time. Overall, device performance depends not only on the characteristics of the device, but on the skill of the implanting physician, the expertise of the physician(s) and other caregivers following the device and managing the patient, and the ability of the patient to comply with recommendations. Devices that are no longer in service may have been removed or deactivated for reasons unrelated to device performance, may have been functioning normally when a patient expired, or may have failed.

A device malfunction occurs when it is implanted and in service and fails to meet the performance specifications (including all claims in labeling) or otherwise perform as intended (Table 1). Whenever possible, device malfunction should be confirmed by laboratory analysis. Devices may malfunction due to relatively infrequent mechanisms that occur as a result of either prospectively understood or subsequently elaborated mechanisms. These malfunctions have become less common as manufacturing techniques have improved; however, the rate is not likely ever to reach zero. The clinical implications of device malfunctions may vary depending on the type of malfunction and the implication of a malfunction for a particular patient's clinical condition. It is important to recognize that devices can malfunction with or without compromising therapy to the patient (Table 1).

Devices may cease to function appropriately due to well-defined mechanisms that are not considered "device malfunction" including "wear and tear" and factors external to the device. Pacemakers and ICDs are expected to "cease to function" over time as a result of normal depletion of the battery energy. Leads are expected to cease to function over time due to wear and tear. There is a range of intervals (measured in years) during which batteries and leads may be expected to cease to function. For batteries, this range depends not only on characteristics of the device but on patient characteristics including the frequency of use (percentage of beats that are paced, pacing and defibrillation thresholds, and the number of arrhythmia episodes that require shock therapy).

Devices can malfunction due to physical and mechanical factors or as a result of software or firmware failures and anomalies. Physical and mechanical malfunction mechanisms of the pulse generator can occur in components, such as the housing (header, can and feed-through), the circuitry (substrate, microprocessor, crystal oscillator), the sensor, antennae and telemetry and the battery. These mechanisms may result in malfunctions that are relatively innocuous or they may cause the device to provide insufficient or inappropriate therapy that could threaten the patient's life. Physical or mechanical malfunction mechanisms of the lead can occur in components, such as the insulation, conductors, terminal pin, or the stimulating electrode. Software or firmware failures and anomalies can occur in either the programmer or the pulse generator. In addition there are clinical complications (such as high pacing capture or defibrillation thresholds) that may be associated with the clinical implementation of the device, but are not clearly directly related to a shortcoming of the device. A list of definitions and examples of malfunction mechanisms appears in Table 1.

In addition to mechanisms that are intrinsic to the device, extrinsic factors (trauma that damages the device, electromagnetic radiation, lead displacement, etc.) may cause ICDs and pacemakers to provide insufficient therapy. Abnormal device function that is the result of such extrinsic factors is considered to be an induced malfunction (Table 1). Furthermore, devices may function normally but provide insufficient therapy, inappropriate therapy, or need to be removed as the result of external factors, including patient factors or actions during or after implant. These circumstances are not considered to be a device malfunction. Examples include a pulse generator that has been removed due to infection or erosion, unless it is shown to be the result of contamination or another defect in manufacturing, connector problems that result from insufficient tightening of set screws, lead perforation, programming arrhythmia detection and therapy parameters, and changes in the patient's response to therapy (increased defibrillation or pacing thresholds). There may be clinical circumstances under which a patient wishes to have the device deactivated, for example, in end-stage heart failure or terminal cancer. A pulse generator that is functioning normally, has been removed or abandoned as the result of a manufacturer's

safety alert or recall, and has been shown to be free of the defect that led to the safety alert or recall, should not be considered to have malfunctioned.

There are multiple obstacles to estimating prospectively the reliability of a pulse generator or lead. This is difficult to do in a time frame that is germane to the patient during the life cycle of a particular device model. However, to interpret the performance of currently implanted systems, it is important to understand the historical performance and malfunction rates of similar devices. There are several data sources from which to make an estimate of reliability for pulse generators and leads. In Denmark, where all pulse generator device implantations are entered into a longitudinal registry, pacemaker generator and pacemaker lead reliability data are available from 1965 to 2004. During that period, the pacemaker generator reliability was 96.7% at 10 years and 95.3% at 15 years (20). Pacemaker lead reliability at 10 years for leads implanted since 1993 was reported as 97% (unipolar) and 97.9% (bipolar) (97%). This changes the reliability of 96.9% (unipolar) and 92.3% (bipolar) for leads at 10 years if all leads implanted after 1965 are included. Although ICDs, cardiac resynchronization devices and ICD lead malfunctions were reported to the registry, an actuarial analysis of the data was not calculated.

There are two other registries that reported device reliability/malfunction rates: the national registry in the United Kingdom reporting pacemaker malfunction rates from 1983 through 2004 and the Bilitch registry reporting pacemaker (1974-1993) and ICD (1988-1993) malfunction rates (21, 22). A meta-analysis of the data from these three registries estimates the pacemaker and ICD malfunction rates indexed to the number of devices at risk for malfunction (19). These data parallel the data analysis from the manufacturer's pacemaker and ICD annual reports submitted to the FDA as reported by Maisel et al (19). From these data, the historical prevalence of devices requiring replacement for malfunction is estimated to have been approximately 1% for pacemakers and 2% for ICDs, but was not calculated for pacemaker and ICD leads or cardiac resynchronization devices.

Based on analysis of returned products, the AdvaMed subcommittee on ICD and

Pacemaker Performance estimated the malfunction rate for ICD generators to be slightly less than 1 in 100 (<1 %) over five years. The subcommittee estimated the malfunction rate for pacemaker generators to be on the order of 0.25% over five years but cautioned that both of these malfunction rates may be understated because not all devices with malfunctions are explanted and returned to the device manufacturer.

The differences in the estimates provide by Maisel et al, and the AdvaMed subcommittee, could be due to differences in the methods used to collect the data. Nevertheless, these two sources provide a range of prevalence of ICD and pacemaker generator malfunction. Furthermore, the disparity amongst the estimates and the absence of data regarding leads and cardiac resynchronization devices points to the need for ongoing and improved data collection and reporting.

COMMUNICATION OF DEVICE PERFORMANCE

Recommendations

Industry: At the national Policy Conference on Pacemaker and ICD Performance (17), the Heart Rhythm Society recommended that manufacturers of cardiac rhythm management device provide standardized device performance reports semiannually in hard copy and in a format available to the public on the Internet. The reports should include all device information pertinent to patient care, and be presented in an unbiased manner and in a consistent and usable format. The Heart Rhythm Society recommends that manufacturers establish expected standards of performance for their particular device models including key components such as batteries, pulse generators, and leads. In addition, the Heart Rhythm Society recommends that manufacturers provide public access to the standards of performance and all information regarding any product performance issues, including sporadic or "component malfunctions" in the semiannual product performance reports. Information should include changes made in response to field observations.

Physicians: The Heart Rhythm Society recommends that physicians (or other medical personnel), in addition to informing patients of

procedural benefits and risks, inform patients of expected device performance, including battery life and potential malfunction rate, at the time of initial device implantation and at replacement.

Manufacturer Product Performance Reports

Product performance reports should focus primarily on providing information that will enable physicians to make clinical decisions and recommendations to patients. The report, or a summary of the report, also should be presented in a form that can generally be understood by the lay public, including patients, their caregivers and families. Graphic representations of performance data over time can be useful and a computer-based report with referential links to useful corroborative information is essential. The report should be indexed and formatted to place the data in the context of other similar devices. Additional referential links should specifically connect to any appropriate field action letters or important communications sent either by the manufacturer or FDA. The product performance reports should be updated at least semiannually. It is understood that the Manufacturer and User Device Experience (MAUDE) database and other sources of device performance information may be updated in the interim and that this interim information will be included in the subsequent semiannual report.

A list of data that the Heart Rhythm Society recommends to be included in the semi-annual product performance reports appears in Table 2. All currently marketed devices, and all discontinued models, must be included until fewer than 500 implanted devices remain. Once a device is dropped from the active report it should be included in an archival report of retired devices. The denominator for the statistical evaluations within a report should be the number of device implantations within the United States; however the number of devices implanted world wide should also be reported. The data should be reported with and without the normal battery depletion events included to clarify the rate of unexpected malfunction mechanisms. In addition, the report should include the number of devices from each family of devices that have been returned to the manufacturer.

The Heart Rhythm Society recommends that the product performance report be publicly available directly on the websites of the manufacturer and that the report, or a link to it, is emailed to physicians who implant or follow pacemakers and ICDs. The websites of the Heart Rhythm Society and other relevant national societies, the FDA and other equivalent governments' agencies should be linked to the product performance report. In addition, the Internet report could be linked to the MAUDE database and other relevant national device databases, to other published communications from the manufacturer or FDA, and to other governments' agency safety alerts and updates. The Heart Rhythm Society recommends that consideration also be given to publishing the information in Heart Rhythm, the official journal of the Heart Rhythm Society.

Physician Communication with Patients

In order to make informed decisions, patients should be informed, not only of the benefits and risks associated with device-related therapy and procedures, but also of the expected performance of the device that they are to receive, including battery life, lead performance and the expected rate of component and device malfunction. Knowledge of these factors will facilitate informed decisions and appropriate expectations for therapy by physicians and patients.

CURRENT PRACTICE

Recommendations

Industry: Until very recently, the manufacturer's product performance reports were provided annually and only in hard copy. The content and appearance of the information in these reports has, to a large extent, been dependent on the manufacturer. Following the Heart Rhythm Society/FDA national Policy Conference on Pacemaker and Implantable Defibrillator Performance (17), the three largest manufacturers of devices agreed to provide semiannual product performance reports in hard copy and on their websites.

Physicians: Physicians typically discuss procedural risks and the expected longevity of the device battery and leads at the time of device implant or replacement. However, it has not been standard practice for physicians

to discuss overall device performance including the rate of unexpected and unpredicted component malfunctions with their patients. It is recommended that such information be included as part of the pre-procedure discussion or decision making process.

TABLE 1. DEFINITIONS OF DEVICE PERFORMANCE

DEFINITIONS

1. **Device Malfunction:** Failure of a device to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling for the device. The intended performance of a device refers to the intended use for which the device is labeled or marketed (FDA Regulations 803.3 (n)). Whenever possible device malfunction should be confirmed by laboratory analysis.

A. Device Malfunction with

Compromised Therapy: A device (pulse generator or lead) that has malfunctioned in a manner that compromises pacing or defibrillation therapy (including complete loss or partial degradation). Some examples include: Sudden loss of battery voltage, accelerated current drain such that low battery voltage is not detected before loss of therapy, sudden malfunction resulting in non-delivery of defibrillation therapy.

B. Malfunction without Compromised

Therapy: A device that has malfunctioned in a manner that does not compromise pacing or defibrillation therapy. Some examples include: error affecting diagnostic functions, telemetry function, data storage; malfunction of a component that causes battery to lose power prematurely but in a time frame that is detectable during normal follow-up before normal function is lost; and mechanical problems with connector header that do not affect therapy.

C. **Induced Malfunction:** A malfunction caused by external factors (e.g., therapeutic radiation, excessive physical damage, etc.) including but not limited to hazards that are listed in product labeling. Damage to a pulse generator caused by a lead malfunction is considered to be a lead rather than a pulse generator malfunction.

D. Normal Battery Depletion occurs when:

1. a device is returned with no associated complaint and the device has reached its elective replacement indicator(s) with implant time that meets or exceeds the nominal (50th percentile) predicted longevity at default (labeled) settings, or
2. A device is returned and the device has reached its elective replacement indicator(s) with implant time exceeding 75% of the expected longevity using the longevity calculation tool available at the time of production introduction, calculated using the device's actual settings.

MECHANISMS OF MALFUNCTION

Device malfunction due to a nonrepetitive mechanism

Often called random component malfunction, statistically independent, usually rare, and non-systematic event. Examples include but are not limited to:

1. Non-battery pulse generator failure may be caused by:
 - a. Electronic component malfunction, including the sensor(s).
 - b. Electrical overstress* in ICDs.
 - c. Housing defects resulting in loss of the hermetic seal, short-circuiting, or connector malfunction.
 - d. Software abnormalities
 - e. Connector malfunction due to inability to position the setscrew.
2. Battery failure may be caused by:
 - a. Premature depletion due to
 - 1) defects in battery manufacture or design, or

- 2) an electromechanical defect not associated with battery depletion.
- 3) Lead failure caused by:
 - a. Disrupted or degraded insulation.
 - b. Conductor fracture or crush.
 - c. Electrode corrosion or metal migration.
 - d. Terminal pin defect or connector mismatch.
- 4) **Electromagnetic interference (EMI).** EMI may cause device malfunction in susceptible models.
 - e. Improperly grounded electric appliances
 - f. Radiation.
 - g. Electrocautery.
 - h. External defibrillation.
 - i. MRI

**Electrical overstress: a term used to describe the damage to electrical components caused by high voltages or currents that develop and arc within the pulse generator.*

Clinical complications affecting device performance

Examples include but are not limited to:

1. Procedure related.
 - a. Lead displacement, including malposition and perforation.
 - b. Phrenic nerve or extracardiac muscle (including diaphragmatic) stimulation.
 - c. Pericardial effusion.
 - d. Pocket complications, including erosion, migration, and infection.
 - e. Tricuspid valve regurgitation.
 - f. Other
2. Physiologic
 - a. Exit block.
 - b. High defibrillation threshold.
 - c. Undersensing.
 - d. Post-procedural atrial fibrillation.
 - e. Oversensing cardiac or extracardiac electrical activity.

TABLE 2 - RECOMMENDED ELEMENTS IN MANUFACTURER PRODUCT PERFORMANCE REPORTS

BY MODEL

- Number of implants
- Estimated number of devices that remain implanted
- Number of devices explanted that have been received by the manufacturer or confirmed to be taken out of service
- Reason for explant (or reason for out of service if device not explanted) if known
 - Normal battery depletion
 - Device upgrade
 - Complication related to another system component or a clinical condition such as infection
 - Other (not a malfunction of the explanted device)
 - Device malfunction
 - Specific confirmed failure mechanism (or clinical observation for leads taken out of service but not returned)
 - Time from implant to malfunction
 - Critical therapy (pacing and shock function) not available or compromised
 - Number of units cumulative observed with this malfunction mechanism (therapy compromised only)
 - Rate of malfunction for observed mechanism and overall for device model and whether restricted to a certain "batch" (therapy compromised only)
- Life Table Survival Curves
- Device Advisories
 - Models affected
 - Root cause of abnormality (if known)

- Number of units with malfunction
- Number of units at risk
- Observed rate of malfunction
- Projected rate of malfunction
- Mitigating factors
- Advisory update since last report
- Number of units explanted due to advisory
 - Analysis of Explanted Returned Product
- Overview of device manufacturing changes made in response to product that did not meet performance expectations

SURVEILLANCE

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Recommendations

Industry: The Heart Rhythm Society recommends that cardiac rhythm management device manufacturers develop and utilize wireless and remote monitoring technologies to:

- Identify abnormal device behavior as early as possible.
- Reduce underreporting of device malfunctions by determining the functional status of an implanted device more frequently and more accurately.

FDA: Changes to the current post market surveillance system are required to improve the timely identification of cardiac rhythm management devices that do not perform according to expectations and which may pose a danger to patients.

The Heart Rhythm Society recommends that the FDA enhance the Manufacturer and User Device Experience (MAUDE) database by:

- Utilizing a specialized form for cardiac rhythm management devices to permit better and more precise reporting of adverse events.
- Tracking devices that are returned to manufacturers for analysis and updating publicly available adverse event reports with root cause analyses.
- Facilitating links to data from international sources.

General Recommendation: The Heart Rhythm Society recommends that the NCDR ICD Registry, administered by the Heart Rhythm Society and the American College of Cardiology be modified to:

- Collect detailed device-specific longitudinal performance data including a report of device performance at the time of device replacement or death.
- Collect data regarding adverse device events, date of the event, and the outcome of the event or cause of each patient's death.

This adjunctive information can assist in tracking device performance and the consequences of malfunctions.

Implementation of this recommendation will require additional funding and resources from the federal government, private payers, device manufacturers, and hospitals.

Congress: The Heart Rhythm Society urges Congress to recognize that post-market surveillance, analysis, and reporting of ICD and pacemaker performance is a high priority for ensuring patient safety. Additionally, Congress is urged to recognize and address the issue that the FDA does not currently have adequate resources to perform this function. The enhancements to the surveillance system that the Heart Rhythm Society recommends, particularly those to the MAUDE database and the NCDR ICD Registry, will require additional resources. The Heart Rhythm Society recommends that Congress ensure that FDA receives the resources and funding necessary to enhance the MAUDE database and provide improved post-market surveillance of pacemakers, ICDs, and leads as described in this section.

Physicians: The Heart Rhythm Society recommends that all devices be returned to the manufacturer for analysis after explantation. This includes returning devices to the manufacturer at the time of device replacement whether the replacement is routine or because of device malfunction. The Heart Rhythm Society recommends the following actions in order to achieve this goal.

- Post mortem device interrogation, explantation, and return to the manufacturer should be strongly encouraged, particularly in cases of sudden or unexpected death.

- The Heart Rhythm Society should work to educate physicians, nurses, allied health professionals, patients, families, pathologists, and morticians of the importance of notifying the physician monitoring the device immediately after the patient dies and returning the patient's device to the manufacturer.
- Whenever possible and indicated, patients should be asked to consent for post-mortem ICD evaluation including interrogation and removal. This consent should be legally binding.
- In the absence of prior discussion with the patient, family members should be asked to consent to device interrogation, removal and return to the manufacturer after the patient's death.

Other Recommendations: The Heart Rhythm Society recommends that physicians be compensated appropriately for the significant time and effort associated with post mortem evaluation of cardiac rhythm management devices and reporting of device adverse events. CPT codes should be established for these activities.

Increased Utilization of Wireless and Remote Monitoring Technologies

The development of remote, automated, wireless or internet based, cardiac rhythm device monitoring systems offers the opportunity to enhance post market surveillance by: 1) identifying abnormal device behavior earlier and 2) automatically and accurately determining the status of certain implanted device functions, thereby decreasing the reliance on reporting by patients and physicians. The outcomes of this increased monitoring that are related to device performance should be incorporated into manufacturers' Product Performance Reports.

MAUDE DATABASE ENHANCEMENT

The current MAUDE system utilizes one form for all medical devices. The Heart Rhythm Society recommends that a specialized form be developed for cardiac rhythm management devices to permit better, more complete, and more detailed reporting of adverse events. Efforts to design and implement a

more robust system for reporting observed device malfunctions could overcome many of the MAUDE database shortcomings and strengthen the current voluntary reporting system by:

- Facilitating the reporting of all unexpected device malfunctions (pacemaker and ICD pulse generator and leads) by healthcare professionals caring for device patients. Normal battery depletions and non-device related malfunctions would not be included.
- Tracking devices returned to manufacturers for analysis. The system could allow individuals (and the public) to track device analysis through the process online, analogous to tracking an overnight package.
- Including in the data base the adjudication of root cause analysis once that has been determined.
- Including data from international sources, which may permit earlier detection of device malfunction for the many devices marketed first in countries other than the United States.
- Employing an Internet-based reporting system with user-friendly format to encourage submission of reports by health care providers.
- Including data elements standardized and modeled after data bases currently in use (UK, Danish, and Hauser) (20, 21, 23) and those recommended by the Global Harmonization Task Force (24) for each device malfunction such as manufacturer, model and serial numbers, dates of implant and failure, signs of failure, clinical consequence, and presumed/actual cause of failure (24).
- Including the number of implants by device model and timely results of engineering analyses to allow determination of malfunction rates.
- Sharing the data publicly on the Internet.
- Including a search engine available for public use.
- Providing an annual report and semi-annual updates.

NCDR ICD REGISTRY

In October 2005, the Center for Medicare and Medicaid Services (CMS) announced that the ICD Registry developed by the American College of Cardiology (ACC) and the Heart Rhythm Society, based on the ACC's National Cardiovascular Data Registry (NCDR), would become the repository of ICD information for all hospitals in the United States where these devices are implanted in Medicare beneficiaries for primary prevention of sudden cardiac arrest. In order to provide information that can be used to assess overall quality, hospitals and physicians will be encouraged strongly to enter all patients receiving ICDs and not just Medicare patients receiving ICDs for primary prevention indications. It is expected that data from over 100,000 patient implants will be entered yearly. The registry will include the clinical characteristics, indication for ICD implantation, and in-hospital, procedure-related outcomes of patients receiving ICDs in order to determine if these are similar to those of patients involved in the randomized trials. Data from the NCDR ICD Registry may ultimately be merged with data from several other national sources including the CMS Death Indices and Medicare Claims Data.

As it is currently configured, several important limitations preclude the use of the NCDR ICD Registry as an effective PM and ICD post market surveillance tool:

- The registry is mandated only for Medicare patients receiving ICDs for primary prevention indications. Whereas hospitals are encouraged strongly to enter all ICD implants (not just those mandated by CMS), this is not required.
- The NCDR ICD Registry is designed to include only those patients receiving ICDs. It does not specifically include pacemakers or leads.
- A goal of the NCDR ICD Registry is to determine whether primary prevention ICD implants are appropriate for Medicare beneficiaries covered by the agency's national coverage determination. As such, the registry will focus on indications for device implantation and short-term outcomes. Detailed device malfunction data will not be collected. CMS has established a goal to develop longitudinal follow-up and merging databases. It

is unclear if or when in the process of developing longitudinal follow-up CMS would prioritize additional device performance data. A registry that monitors PM and ICD performance needs to identify and track device malfunctions and thus requires more comprehensive longitudinal device performance and patient follow-up. To satisfy the need for a longitudinal PM and ICD surveillance registry, data collected should include information on subsequent hospitalizations related to adverse device events, date and cause of a patient's death, and a review of device performance at the time of device replacement or patient death.

- CMS has indicated that it will require registry information only until its questions are addressed which may require two to three years. In addition, whereas the current CMS leadership actively supports the ICD Registry, this level of support may not continue.

The NCDR ICD Registry will provide important information on ICD implant populations, complications, and therapy. NCDR ICD registry data can complement those that are available in the MAUDE database. Whereas, the MAUDE database has the advantage of including pacemakers and ICDs and may include detailed information regarding adverse events, the NCDR ICD registry will have the advantage of including all ICDs implanted for primary prevention of sudden cardiac arrest in the Medicare population. However, because of the limitations outlined above, the NCDR ICD database is not useful as a device "surveillance" tool as currently configured. Significant changes would be required for the NCDR ICD registry to perform the function of an effective surveillance instrument.

CURRENT PRACTICE AND LIMITATIONS

The goal of post-market surveillance is to "enhance the public health by reducing the incidence of medical device adverse experiences" (25). The current surveillance system relies on the FDA, medical device manufacturers, healthcare providers, hospitals and other medical care facilities, and patients to report device malfunctions. Post-market

surveillance, as currently configured, is designed primarily to identify uncommon, but potentially serious, device-related adverse events. The FDA uses several different methods to conduct post-market surveillance including spontaneous reporting systems, analysis of large healthcare databases, scientific studies, registries, and field inspection of facilities.

The FDA depends primarily on a passive adverse event reporting system, relying on patients and the health care industry to identify and report adverse events including rare, serious occurrences. Manufacturers are required to report to the FDA any medical device-related event or malfunction that may have caused or could cause a serious injury or death. Hospitals, nursing homes, and other medical facilities are required to report device-related serious injuries to the manufacturer and device related deaths to both the manufacturer and the FDA.

The FDA annually receives more than 160,000 adverse event reports regarding medical devices of all types, including some that involve pacemakers, ICDs or leads. The vast majority of reports are provided by manufacturers; fewer than 10,000 come directly from medical facilities (26). Healthcare professionals and patients are encouraged, but not required, to report suspected device related adverse events via the FDA program, MedWatch. Suspected events may be reported by telephone, fax, mail, or over the internet (www.fda.gov/medwatch). The FDA receives only several thousand reports via MedWatch each year, and physicians in particular rarely report events (8% of reports) (27).

The MAUDE database was established to assist with adverse event reporting and information dissemination for medical devices of all types (28). It contains hundreds of thousands of adverse event reports, including voluntary reports since June 1993 and manufacturer reports since August 1996. Selected information from this database is publicly searchable via the internet. However, because submitted adverse event reports are often cryptic or incomplete, it is often difficult to determine if a true device malfunction or patient injury has occurred. Furthermore, updated information following manufacturer device analysis is often not included in the publicly available reports. In addition,

multiple reporting (for example by physician, manufacturer, and patient) could result in three reports documented for a single event. FDA analysts use the MAUDE database to detect patterns or events that may warrant further investigation. This surveillance method was never intended nor configured to be utilized for tracking device malfunction rates.

Medical Products Surveillance Network (MedSun)

Spontaneous reporting systems have several additional important limitations. Manufacturers must report those events of which they become aware but they are not required to actively seek out device malfunctions. Importantly, as noted in the recent Institute of Medicine Report, “Safe Medical Devices for Children,” there is significant underreporting of device-related adverse events (16). Studies comparing passive versus active surveillance suggest that less than half of malfunctions may be reported (29). Recognizing this shortcoming, the FDA has established the Medical Products Surveillance Network (MedSun). This active surveillance system utilizes individuals specially trained in device adverse event reporting at a number of medical facilities (primarily hospitals and nursing homes) to identify problems in both device function and user error in the clinical setting. Because MedSun includes only selected facilities and does not include data submitted by manufacturers, detection of relatively rare device performance issues via this surveillance method is difficult. In addition to the MedSun, Pacemaker and ICD manufacturers are required to submit “annual reports”, detailing the number of device implants and the number and type of reported device malfunctions. The malfunctions contained in these reports, however, remain subject to the shortcomings of spontaneous reporting systems.

Other Systems

The FDA may utilize also other methods of post-market surveillance. For example, it may conduct or commission a study to further investigate any issue in more detail. This additional surveillance may take the form of an analysis of complaint information, a field inspection of a manufacturing facility, the initiation of a device registry, or some other investigation. In general, the FDA has the authority to require that manufacturers conduct additional post-market surveillance on any device, when it is deemed appropriate to do so.

ALTERNATIVES

Denmark and England have established comprehensive registries that track the vast majority of, if not all, cardiac rhythm management devices implanted in those countries. In the United States, such a system would:

- Include all patients who receive cardiac rhythm management devices.
- Mandate that all implanted devices be returned to the manufacturer after explant or death of the patient.
- Collect information from all implanted pacemaker and ICD pulse generators and leads and not solely on device failure related events.
- Include data elements used by registries of proven success such as the Danish Registry (20) and the Hauser Registry (23).

Although a single comprehensive cardiac rhythm management device registry has several advantages, the Heart Rhythm Society recognizes that the establishment of such a system is unrealistic at this time due to the significant resources it would require. The recommendations put forward here provide a mechanism for optimizing available registries and databases so as to achieve many of the benefits of a comprehensive registry without investing significantly in additional infrastructure.

ANALYSIS OF DATA – ROLES OF INDUSTRY, FDA, AND PHYSICIANS

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Recommendations

The Heart Rhythm Society recommends that experts who are not full-time employees of industry or the FDA should analyze device performance data and provide advice on a regular basis and when life-threatening device malfunctions are identified.

The Heart Rhythm Society recommends that these committees advise when and what action is appropriate including physician and patient notification and the necessity of retrieving unmitigated devices from the sales force and from hospital inventories.

Industry: The Heart Rhythm Society recommends that device manufacturers establish standing independent committees of experts (including physicians and representatives of other disciplines such as engineering, statistics, risk assessment and ethics) to analyze data (including semiannual device performance reports and registry information) regarding cardiac rhythm management device performance. These committees should meet on a regular basis (at least semiannually) as well as on an ad hoc basis and quickly when a life-threatening device defect has been identified. The committees would act much like the data safety and monitoring board for a clinical trial and would advise when and what action (if any) is appropriate including physician and patient notification and the necessity of retrieving unmitigated devices from the sales force and from hospital inventories. The committees could be organized according to device type (e.g. pacemaker, ICD, leads) and could be either industry-wide or manufacturer specific.

FDA: The Heart Rhythm Society recommends that FDA establish standing post-market advisory committees that will meet on a regular basis (semiannually) and in a timely fashion on an ad hoc basis to analyze data regarding cardiac rhythm management

device performance and to advise when and what action should be taken to address device malfunctions that are identified. The FDA could accomplish this also by extending the scope of the Circulatory System Devices Panel to the post-market period. The Heart Rhythm Society should assist the FDA in identifying individuals who can serve in this capacity.

Congress: The Heart Rhythm Society recommends that Congress ensure that FDA receives the resources and funding necessary to establish and maintain the FDA advisory committee that is described in this section.

CURRENT PRACTICE

The current system is too heavily dependent on industry to detect and report device performance problems. Industry analyzes device performance data and determines initially when a malfunction is likely to be recurrent, the potential frequency of the recurrent malfunction, and the likelihood that the malfunction could do harm to a patient. Physicians are not involved systematically in determining if and when a device safety concern exists or the response to a safety concern. Device manufacturers sometimes convene ad hoc expert advisory committees to analyze data and to provide advice regarding action, but this is neither required nor has it been considered to be standard practice. Furthermore, these committees are convened only when industry has determined that a significant safety concern exists.

The FDA Center for Devices and Radiological Health convenes advisory committees to analyze device information and data from clinical trials prior to approval of those devices for use in patients. These committees are composed of physicians and others with expertise regarding the device that is undergoing evaluation or its use. Candidates are required to disclose relationships and efforts are made to minimize potential conflicts of interest among committee members. However, the FDA does not convene standing committees to analyze post-market surveillance data nor to recommend action when a malfunction is identified.

TERMINOLOGY AND THRESHOLD FOR ACTIVATION OF DEVICE RECALLS AND ADVISORY NOTICES

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Recommendations

Terminology: The Heart Rhythm Society recommends that device manufacturers and the FDA should use identical terminology to classify device malfunctions and communicate them to the public.

Industry: The Heart Rhythm Society recommends that device manufacturers continue to provide the FDA with data regarding device performance at the time that certain problems are identified, as well as in the form of semiannual product performance reports. A malfunction that is associated with a significant risk for death or serious injury is systematic, and for which there is reason to suspect that it could occur in other patients, merits early review by the advisory committees described in the previous section. Examples of circumstances that, meeting these criteria, would require early notification of the FDA and its post-market surveillance advisory committee include:

1. Devices that fall outside of FDA approved labeling or the standards of performance;
2. Devices that fail to treat an arrhythmia, pace the heart, or provide inappropriate and potentially life-threatening therapy;
3. Devices that are unexpectedly inactive (no telemetry and/or unable to be interrogated, or no output for reasons other than normal battery depletion).

FDA: The Heart Rhythm Society recommends that the FDA establish a simple and more intuitive nomenclature to communicate important information about device malfunction or failure of a device to perform according to specifications. Specific recommendations for changes in nomenclature include:

1. Eliminate the term “recall” in public communications regarding implanted devices.

The FDA has convened physicians on an ad hoc basis to review information regarding specific cardiac rhythm management devices that have been found to malfunction. These ad hoc groups have reviewed data and provided advice to FDA regarding potential actions that the agency was considering and language in advisories.

ISSUES/CONCERNS

Industry: The current system depends on industry to analyze data, determine, when possible, a root cause of any malfunctions identified, and to provide recommendations for action. In many cases, manufacturers are in the best position to evaluate their own devices because they know them best. However, a concern with this system is that the evaluation of the devices and the recommendations for action by those within the company involves an inherent conflict of interest that could affect the outcome of the analysis.

FDA: The FDA depends on industry to provide accurate and timely device performance information and analysis. The FDA provides oversight, assesses the validity of the conclusions reached by industry experts, and ultimately determines what actions should be taken. A valid concern is that members of FDA committees have relationships with industry that pose conflicts of interest. However, this is true of the pre-market process and that system has worked well. Also, some believe that the number and diversity of devices and the volume of data would be too great for a single committee. This could be addressed by establishing standing committees to address specific devices (pacemakers, ICDs, CRTs, and leads) and by including select experts on an ad hoc basis to evaluate specific problems.

ALTERNATIVES

An independent organization could be appointed to analyze all information and provide recommendations to the FDA. The Heart Rhythm Society does not endorse this approach. The Heart Rhythm Society believes that FDA, manufacturers, and physicians, working collaboratively are positioned best to analyze and evaluate device performance.

2. Change the term “Class I recall” to “Class I advisory notice or Class I safety alert.”
Class I advisory notices would be those in which device replacement should be considered because of the reasonable probability that the malfunction could result in death or significant harm.
3. Change Class II and III recalls (non life-threatening malfunctions or potential malfunctions) to “advisory notice or safety alerts.”

Threshold for action: The threshold for activation of an advisory notice may vary depending on the frequency of the device performance problem and the clinical implications of the malfunction. A single event, if it is associated with a significant risk for death or serious injury, is systematic, and for which there is reason to suspect that it could occur in other patients, merits notification of physicians and patients. In such a case, devices that are not implanted and in which the malfunction has not been corrected or addressed adequately should be retrieved from the sales force and hospital inventories. The Heart Rhythm Society considers it to be inadvisable to determine a fixed percentage of device malfunctions or attempt to classify all of the particular types of malfunction that would automatically trigger a notification or advisory. Rather, data should be reviewed on a regular basis by the committees identified in the previous section, in order to determine when a pattern of inadequate device performance exists.

CURRENT PRACTICE

In most instances, the manufacturer identifies first when a device malfunction merits notification of the FDA and the public. The decision by the manufacturer may be made in consultation with independent physicians and other experts. However, currently, no specific standards or guidelines exist to guide manufacturers to when the FDA and public should be notified of a device malfunction (17).

Manufacturers rarely use the term recall; rather manufacturers often use the terms “advisory” or “safety alert.” Table 3 lists the current terminology (30). Currently, the FDA may classify a malfunction as an advisory,

or a recall, or a safety alert. The FDA defines a recall as “an action taken to address a problem with a medical device that violates FDA law.” Recalls occur when a medical device is defective, when it could constitute a risk to health, or when it is both defective and a risk to health. Although the FDA evaluates all device abnormalities that are reported to it, the agency may choose not to comment publicly on device notifications that it does not classify as a recall.

ISSUES AND CONCERNS

The differences in terms used by manufacturers and the FDA (advisory and safety alert vs. recall) contribute to misunderstandings among physicians and patients regarding the actions that should be taken to mitigate a device malfunction. In addition, the term recall suggests to patients and physicians that a device should be removed when this may not be the case.

The absence of clear guidelines regarding the circumstances that trigger notification of physicians and patients of device malfunction creates uncertainty.

ALTERNATIVES

Alternative approaches to triggering notification of physicians and patients of device malfunction include:

1. Notify physicians of every device malfunction;
2. Establish a trigger based on a specific number of device malfunctions;
3. Establish a trigger based on the frequency or rate of events;
4. Provide information deemed by industry to be relevant to patient care decisions; and
5. Keep the old system (31).

Option one is sensitive but not specific and might very well inundate physicians with information that is clinically insignificant, potentially obfuscating information that is important to patient well-being. Likewise, options two and three do not recognize the clinical significance of a malfunction. Option four places responsibility for medical decisions with industry rather than with physicians and patients. Option five, the

current system has no trigger and has few if any proponents. Thus, the recommendations put forth here outline a trigger for notifying physicians and patients of device malfunctions that has significant advantages over alternative approaches.

TABLE 3

Class I recalls: “reasonable probability that the use of, or exposure to a violative product will cause serious adverse health consequences or death.”

Class II recalls: “the use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or in which the probability of serious adverse health consequences is remote.”

Class III recalls: “comprise situations in which the use of, or exposure to, a violative product is not likely to cause adverse health consequences.”

Safety alerts or Safety advisories: Linguistically equivalent, and are less significant than class III recalls.

COMMUNICATION AFTER DEVICE MALFUNCTION IS IDENTIFIED

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Recommendations

Industry: In addition to physician advisory notification letters, the Heart Rhythm Society supports the use of a standardized Physician Device Advisory Notification format for all manufacturer advisories to physicians regarding potential device malfunction. The Heart Rhythm Society recommends that industry use the Patient Device Advisory Notification letter format to communicate directly with patients.

Manufacturers should make a good faith effort to contact affected patients using the patient’s registration information obtained at the implant center at the time of the implant procedure. The definition of such an effort should be determined between the FDA and industry according to guidelines already in place for advisory communications. Whenever possible, physicians should be notified first and patients shortly thereafter. In addition to historical communication methods, physicians and patients could be notified by email to increase the timeliness of communication.

The Heart Rhythm Society recommends also that the standardized physician and patient notifications reside on the manufacturer’s website, and that they be linked to the Heart Rhythm Society website and to FDA enforcement reports and other notifications to facilitate easy access to all components of each individual device advisory. Product advisory notices could also appear in Heart Rhythm, the official journal of the Heart Rhythm Society. Updates to these notifications can be communicated in a similar manner and in the Product Performance Reports from each manufacturer.

Advisory notices should include general information regarding the potential clinical implications and appropriate clinical recommendations, and should acknowledge that management decisions are ultimately the decision of the patient in consultation with his or her doctor.

FDA: The Heart Rhythm Society supports a centralized, rather than the current regional system, for communication of device advisory notifications to promote a broader and more inclusive interpretation of the advisory issues. In addition, the unique and specialized nature of cardiac rhythm management device advisories requires a centralized rather than regional intake mechanism to enable accurate interpretation of data on an ongoing basis by key knowledgeable FDA staff and by the other parties such as a post-market physician advisory panel. The Heart Rhythm Society believes that a centralized system will facilitate timely FDA classifications and urges the FDA to classify all advisory notifications and include these data on the Physician Device Advisory Notification form within 30 days.

Congress: The Heart Rhythm Society recommends that Congress ensure that the FDA receives the resources and funding necessary to ensure that centralized notification and analysis of pacemaker, ICD, and lead malfunction notifications, as recommended in this section, is accomplished effectively.

Physicians: The Heart Rhythm Society urges physicians to utilize the standardized Physician Device Advisory Notification format to aid in the objective assessment and characterization of all device advisory communications. This format can be used to facilitate quick reference and identify key aspects of the advisory to help guide patient management decisions in an ongoing fashion.

CURRENT PRACTICE

The manufacturer is often the first to issue a public notification that a particular device has been found to malfunction. In the United States, physician notification of device malfunction occurs in the form of a letter, issued by the device manufacturer that may or may not include editorial input from the FDA (17).

Physician advisory letters are received by the FDA and often are classified regionally without a centralized intake mechanism. Not all manufacturer advisory information is communicated to a central FDA location. The FDA classification decision typically lags behind the manufacturer advisory letter. Not all manufacturer advisories receive a public FDA classification.

When the FDA is aware of an ongoing significant public health problem and believes that the clinical community may not otherwise have access to pertinent information about the problem, it may issue a Preliminary Public Health Notification, or a Public Health Notification if it believes all the relevant information regarding the problem is known by the agency.

If the FDA classifies a manufacturer device malfunction advisory as a Recall, it will be reported as part of a separate FDA notification, most often as an Enforcement Report (32). The FDA oversees the Recall to ensure that the actions the company takes are

adequate, and works with the company to obtain information about the problem, to correct the problem, and to conduct audits to make sure the corrective efforts are appropriate and effective.

ISSUES/CONCERNS

The lack of a standardized reporting format for device advisory notifications hinders physician and patient understanding of the key clinical issues at stake. The lack of a centralized mechanism designed to receive and interpret highly specific and specialized device advisory information by the FDA hinders an inclusive and adequate understanding of the issues and makes expert internal and external analysis of this information problematic. The lack of a standard mechanism for FDA classification of all advisories may lead to over or under emphasis on any particular advisory issue.

The physician and patient reporting and notification formats recommended by the Heart Rhythm Society will standardize the advisories, regardless of manufacturer, facilitate understanding, and inform appropriate action. However, there is a potential cost associated with standardizing advisory information for physician and patients that includes the possibility that key information will not be communicated. Standardization will also introduce complexity in the sense that industry and FDA communications will still be issued, increasing the total amount of material received with any single advisory. In addition, there may be legal implications to a standardized reporting format.

A centralized intake of implantable cardiac device advisory notifications will improve the quality and interpretation of advisory data and provide a second interpretation of these data other than that available from industry. However, this may require significant structural changes in procedures at the FDA, specific to implantable cardiac devices.

PHYSICIAN DEVICE ADVISORY NOTICE

Advisory Date:

Manufacturer(s)			
Product(s)	Trade Name	Model Number	
Manufactured on or before (Date)			
Performance Failure			
Root Cause (if known)			
Date Manufacturer Corrected Product Available (if known)			
Has all affected product been retrieved?	Yes	No	When?

FDA CLASSIFICATION STATUS

Advisory classification

Decision Pending

CLINICAL ACUITY

	(USA)	(Worldwide)
a) Total number of units currently implanted		
b) Estimated number of potentially affected devices of this mode worldwide		
c) Estimated incidences of this performance failure over the projected life of the device		
d) Total number with observed Performance Failure		
% of Performance Failures d/b x 100 =		
e) Mean age of product in implanted population		
f) Patient deaths reported	Yes	No
Number of deaths =		
g) Patient deaths with probable relationship to device failure	Yes	No
Number of deaths =		

* The data analysis provided in this report was generated by the manufacturer and may be subject to change

DEVICE COMPONENTS AT RISK OF PERFORMANCE FAILURE

Battery Failure	CRT (left ventricular pacing)
Diagnostic Data Failure	Lead Failure
Brady Therapies (lower rate pacing)	Hermiticity or internal component
Brady Therapies (runaway pacing)	EMI Susceptibility
Tachy Therapies (ATP)	Telemetry Failure
Tachy Therapies (shock)	Other (specify)

PATIENT MANAGEMENT RECOMMENDATIONS

Verify normal device function (at normal follow-up interval)	Yes	No
Verify normal device function (as soon as possible)	Yes	No
Specific measures to assess:		
Programming changes	Required	Recommended
If programming changes are required, specify changes:		
Accelerated device follow-up	Yes	No
Timeline - months:		

CONTACT

Industry Name
 Address1
 Address2
 City, State Zip
 Phone
 Fax
 Email
 Website

PATIENT NOTIFICATION LETTER

Dear (XX):

Our ongoing surveillance of the performance of (Manufacturer/Device Name/Model/Serial Number) has found that in some cases the (pacemaker, implantable cardioverter defibrillator, lead) might not be working as expected. Our records indicate you have this device implanted. Your (pacemaker, implantable cardioverter defibrillator) identification card will verify that this is your device model and serial number. (Describe the problem in lay terms).

Because every patient with a device is unique, appropriate medical decisions can only be made by you together with your physician, who knows you and your medical history. We are also sending a copy of this letter to the doctor who implanted the (pacemaker, implantable cardioverter defibrillator, lead) so that the two of you will have the information you need to decide what is in your best interest. If you have not heard from your doctor regarding this matter, we encourage you to contact him or her to follow up on this notice. We have also notified the Food and Drug Administration, the federal agency that oversees our company and implantable medical devices like yours.

Here are some sources for more information. Of course you are welcome to contact us with any questions:

Industry Name
 Industry Address

The Heart Rhythm Society is the professional medical organization with the most expertise on implantable devices like yours:

Heart Rhythm Society
 1400 K Street, N.W., Suite 500
 Washington D.C. 20005
<http://www.hrsonline.org/>

The branch of the U.S. Food and Drug Administration that oversees devices like yours is:

FDA - Center for Device and Radiological Health
 1350 Piccard Drive
 Rockville, MD 20850-4307
<http://www.fda.gov/cdrh/>

We genuinely care that our device performs properly and provides you the health benefits you and your doctor expect. Our surveillance is continuous, and if the rate of your device not performing as expected changes, we'll update you. Please let us know if we can be of further assistance.

Sincerely,
 (Authorized Industry Representative)

RECOMMENDATIONS FOR CLINICIANS MANAGING DEVICE ADVISORY NOTICES

CO-AUTHORS: E. PRYSTOWSKY, MD (CHAIR);
M. CAIN, MD; E. CHING, RN; D. ZIPES, MD

Recommendations

Physicians:

- The Heart Rhythm Society recommends that physicians and the facilities where ICDs and pacemakers are implanted should monitor local outcomes and adverse events associated with pacemaker and ICD system implantation and removal. Participation in the NCDR ICD Registry will facilitate obtaining this information.
- The Heart Rhythm Society recommends that physicians consider the risk of device removal and reimplantation when making clinical decisions and recommendations to patients who have a device that has or may have a malfunction.
- The Heart Rhythm Society recommends that physicians consider, when appropriate, alternatives to device explantation (reprogramming, enhanced monitoring, etc) that may mitigate the consequences of device malfunction and decrease patient risk.

Guidelines for Decisions on Device Recalls and Notifications

- Consider device/lead replacement if:
 - the mechanism of malfunction is known and is potentially recurrent,
 - the risk of malfunction is likely to lead to patient death or serious harm, and
 - The risk of replacement is less than or at least not substantially greater than the risk of device malfunction.
- Consider device/lead replacement in pacemaker-dependent patients for those:
 - patients with an ICD for secondary prevention of sudden death, and
 - Patients with an ICD for primary prevention of sudden death in whom appropriate therapy has been given when the risk of replacement is not substantially greater than the risk of device malfunction.

- Consider device replacement if the predicted end-of-life (EOL) is approaching.
- Consider conservative management with periodic non-invasive device monitoring in patients who are not pacemaker-dependent and those with an ICD for primary prevention of sudden death in whom there is a low probability of future ICD therapy, and the rate of device malfunction is low (<1/1000). Other patients may also be candidates for conservative management.
- Provide routine follow up for patients with a device malfunction that has been mitigated or corrected by reprogramming the software.
- Consider conservative management with periodic non-invasive device monitoring in patients where operative intervention risk is high or in patients who have other significant competing morbidities even when the risk of device malfunctions or patient harm is substantial.

Summary

Industry and FDA recalls or public health notifications regarding pacemakers, ICDs, or leads do not necessarily translate into an immediate need for physicians to replace the devices/leads in question. This must be individualized for each patient and device problem. Device replacement is associated with a risk for adverse events that is greater than 1%. This risk is greater than that associated with the initial device implant and is associated with the experience of the implanter. Replacement of the device/lead should be considered strongly if malfunction of the device/lead could result in patient death or serious harm, and if the risk of replacement is not substantially greater than the risk of device/lead failure. Alternatively, observation is recommended in situations of low patient risk.

Current Practice

Following notification of a device malfunction, physicians interpret the information provided by manufacturers and the FDA, communicate relevant information to their patients with the device in question, and with each patient, determine a course of action. The impact of a particular device malfunction may vary greatly among patients depending on individual clinical circumstances and it is

generally agreed that clinical decisions should rest ultimately with the patient and the physician. However, clinical practice and the percentage of devices replaced have varied widely following certain recalls suggesting that opportunities may exist to standardize and potentially improve care. A low threshold to explant devices may expose patients to unnecessary surgical risks; a high threshold may expose patients to a risk for device malfunction that exceeds the risk of device replacement.

It is very important for physicians and patients to recognize that the term recall as currently used by the FDA, does not mean necessarily that all of the devices/leads implicated need to be explanted. Several factors are important in deciding which patients can be safely observed versus those who likely need to have their device/lead replaced. One must balance the risk of explantation and reimplantation of the device, lead or both versus the risk of an alternative approach such as software reprogramming and/or close patient follow-up. This risk-benefit equation is dependent on the clinical situation and the expertise of the implanting physician.

Risk of ICD and Pacemaker Implantation/Explantation

Table 4 shows complications associated with PM and ICD implantation in a selection of studies. Overall, rates of infection ranged from 0.2 to 1.8% for pectoral implantations, and rates of lead dislodgement from 1.5 to 2.4%. Among acute complications, pneumothorax occurred at a rate of about 1% and perforation 0.5%.

Several patient-, device-, procedure-, and operator-related characteristics that increase the likelihood of peri-procedural complications have been identified. In younger patients, the risk of infection seems to increase from 5.5% (33) to 7.8% (34). Other patient factors have not been found to be significant. Among device-related factors, dual-chamber ICD implants carry a higher risk of complications than single-chamber. (35) Left ventricular lead insertion, for cardiac resynchronization, is associated with additional complications, including coronary sinus dissection and cardiac vein or coronary sinus perforation (4% and 2% respectively) in the MIRACLE study (36).

Several procedure-related factors have been shown to influence complication rates, such as absence of peri-procedure antibiotics (37). Importantly, complications are more frequent in patients having elective pacemaker replacements than initial implants, 6.5% versus 1.4%. (38) Subclavian insertion sites are associated with a higher risk for lead fracture than are cephalic (37). Older implant techniques, such as abdominal generator site (37) and the subcutaneous patch, (39) were associated with an increase in infections. Among operator characteristics, operators with lower implantation volume (40) and less experience (38) have higher rates of mechanical and infectious complications.

Lead extractions pose a substantial risk to the patient. Leads may need to be extracted due to a primary lead problem, an infected generator and lead system, or as a consequence of damage that occurs during an attempt to operate on the generator alone. In a study of 161 patients, ICD lead extraction was successful in 98% of cases. (41). Whereas one smaller study (42 patients) reported no serious morbidity or mortality (42), another (82 patients) reported major complications in 7.3% of patients, six experienced tamponade requiring emergency thoracotomy, and 2 (2.4%) died (43). Several studies have shown that operator experience correlates with outcome (40, 43, 44). In a multicenter study of pacemaker lead extractions, major complications occurred in only 0.97% of the more experienced physician group versus 1.8% in those with less experience (44).

The risk of primary or subsequent surgical intervention can be estimated by review of the literature and may be reduced by maintaining a high level of compliance with appropriate surgical technique. However, the available data indicate that complications associated with pacemaker and ICD implantation and removal are operator dependent and, with few exceptions, are not associated with individual patient characteristics. Importantly, the risk for complications at device replacement is greater than at the initial implant. Thus, each implanter and each facility should monitor, record, and report annually a summary of their procedure outcomes. The complications recorded should include at least the following elements: infection/erosion; lead dislodgement; tamponade; pneumothorax; hematoma and mortality. The NCDR ICD Registry operated by the American College

of Cardiology and the Heart Rhythm Society will be collecting this information on all implanting physicians and providing quarterly performance reports with benchmarking information to the hospitals (45). These data will aid the physician who must consider the risk of device removal and re-implantation when making clinical decisions and recommendations to patients who have a device that has or may have a malfunction.

Characterization of the level of patient risk due to device system malfunction and physician-patient communication

Not all device system malfunctions or problems have the same safety risk for the patient. Even a similar malfunction can have a very different risk profile for different patients. For example, a sudden loss of pacing function in a patient who is not pacemaker-dependent is not nearly as worrisome as it is for a pacemaker-dependent patient. It should be noted that it is not always easy to determine precisely when a patient is pacemaker dependent and that this determination may change over the course of follow-up. Thus, for any given Recall or Public Health Notification, it is important to consider the device problem on several levels, and then determine for each patient the risk-benefit of explanting the system or following the patient.

Device system problems can be categorized by considering the following questions:

- Will there be a sudden loss of function of either pacing or shock therapy?
- Does the probability of malfunction change with time?
- Can the problem be resolved or mitigated by reprogramming the device or altering the software?
- Have the component(s) responsible for the problem and the mechanism for the malfunction been identified?
- What is the predicted device malfunction rate, eg, 1 per 1000 or 1 per 5000?
- Will that predicted malfunction rate of a single component malfunction be magnified by a domino effect if other device functionality depends on the failed component?

Similar questions should be addressed with respect to patient risk if the device malfunctions.

- If the device in question is a pacemaker, will the patient have a subsidiary escape rhythm should the pacing function cease?
- For an ICD, was the indication primary or secondary prevention of sudden death?
- Has the patient received shock or antitachycardia pacing therapy and if so, how frequently and how recently?

Compiling the above data for each patient will provide the clinician a reasonable evaluation of a patient's risk if device malfunction occurs. These risks and the risks associated with device removal and reimplantation can be used to assess therapeutic alternatives and provide recommendations to the patient. The risk of a major complication explanting the ICD system (generator, lead or both) is at least 1%, and if the projected malfunction rate is 1 in 5000 (0.02%) then not explanting the ICD in a patient who is thought to be at lower risk to receive ICD therapy is reasonable. Likewise, a patient who is pacemaker-dependent and who has a pacemaker with a 1 in 200 (0.5%) malfunction rate would be a good candidate for a new device. Within this range of relatively straightforward patient decisions are many patients and the appropriate action may depend ultimately on the patient's willingness to accept short-term risk associated with an invasive procedure vs. potentially longer-term risk associated with a device that might malfunction.

Communication between the physician, allied health personnel and the patient is critical in these situations. If the potential malfunction is likely to occur and is potentially life-threatening, every effort should be made to contact the patient quickly to inform them of the facts, allay their fears, and plan a course of action. Face-to-face meetings are preferable if device replacement is contemplated, to review data and discuss therapeutic options. It is often useful for family members or friends to be present who can discuss the information with the patient at a later date. Anxiety is often high during such discussions, and it is not uncommon for the patient to forget important details needed to make a decision. In less urgent situations, much of the discussion can be done by phone or at the next scheduled office visit. Patients also have expressed the desire to learn about device malfunction, not just from their physician, but directly from the FDA and from the manufacturer.

TABLE 4

Study		N	f/u	Total		Lead	Lead		Other	PTX %		comment
Kron 2001, AVID (1, 37)	ICD		12	11.5	1†	4/1.5*	1.5	5/1**		1.1	0.4	*subclavian/cephalic **abd/pectoral †within 30 days, not all device-related
Gold 1996 (46)	ICD		>6		NR			0.2	2			
Rosenqvist 1998 (47)	ICD		4		0.8		2.4	0.7	3.5			
Kiviniemi 1999 (48)	PM		60	7.2	0		1.6	1.8		1.1	0.7	

NR, not reported. Not all complications were reported in every report.

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