

Recommendations from the Heart Rhythm Society Task Force on Lead Performance Policies and Guidelines

Developed in collaboration with the American College of Cardiology (ACC) and the American Heart Association (AHA)

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TABLE OF CONTENTS

INTRODUCTION	870
I. LEAD PERFORMANCE AND COMMUNICATION OF LEAD PERFORMANCE.....	870

II. PREMARKET EVALUATION OF PACEMAKER AND ICD LEADS	872
III. POSTMARKET SURVEILLANCE OF PACEMAKER AND ICD LEADS	875
IV. THRESHOLD FOR ACTIVATION OF LEAD ADVISORIES AND COMMUNICATION AFTER ABNORMAL PERFORMANCE IS IDENTIFIED....	878
V. RECOMMENDATIONS FOR CLINICIANS.....	879
TABLE 1. Lead Performance Definitions	871
TABLE 2. Factors to Consider When Determining Whether a Lead is “New”	874
TABLE 3. Methods of Postmarket Surveillance.....	875

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TABLE 4. Recommendations for Clinicians

Managing Lead Advisory Notices881

TABLE 5. Factors to Consider in the Risk–Benefit

Analysis When Managing Normally Functioning

Leads Subject to Advisory881

FIGURE 1.....873

REFERENCES882

APPENDIX.....884

Introduction

The clinical benefits of pacemakers and implantable cardioverter defibrillators (ICDs) have been well-established by numerous scientific studies.^{1–23} Millions of devices have been implanted worldwide resulting in improved quality of life and survival for many patients. While numerous patients have benefited from these important technologies, these device systems are complex and may occasionally malfunction. Timely detection, characterization, and communication of product specific performance issues are critical to patient safety. In October 2006, the Heart Rhythm Society (HRS) published the recommendations of the HRS Task Force on Device Performance Policies and Guidelines.²⁴ Since then, well-publicized performance concerns involving ICD leads, in addition to generators, have emphasized the importance of addressing how best to detect and react to reliability concerns involving pacemaker and ICD leads.

The Heart Rhythm Society is committed to patient safety and the delivery of quality care. Accordingly, it has long recognized the significance and challenge of monitoring device performance and the unique issues cardiac rhythm management devices present due to their life-saving nature, their life-long use, and their implantation in the body. In the 1990s, the North American Society of Pacing and Electrophysiology (subsequently Heart Rhythm Society) convened consensus conferences and published reports on postmarket surveillance and the management of cardiac device recalls.²⁵ Since the HRS Device Performance Policies and Guidelines were published in 2006, many of the Task Force recommendations have been enacted:

- greater transparency in postmarket analysis and reporting of data;
- improved industry product performance reports;
- the establishment of new systems of postmarket surveillance;
- standardized notification by industry when performance issues do arise; and
- the implementation of direct patient communication about important device performance issues.

The HRS Device Performance Task Force recognized that “physicians and patients need timely, accurate, and understandable information regarding device performance.”²⁴

However, while previous efforts have focused primarily on pacemaker and ICD generator malfunctions, monitoring lead performance poses unique challenges. The perfor-

mance expectations placed on pacemaker and ICD leads are substantial—a lead may experience more than 500,000,000 repetitive cardiac cycles during its lifetime. Many factors affect lead performance including lead design, manufacturing, physician technique, and patient characteristics. Differentiating abnormal lead performance from a procedural complication may also be difficult. In addition, while pacemaker and ICD generators may be explanted and returned to the manufacturer for analysis, malfunctioning leads are often abandoned; if they are removed, they may be damaged during explant. This makes assessment of lead performance rates difficult and makes analysis of lead failure mechanisms more challenging. Despite these challenges, recognition, accurate analysis, and transparent reporting of lead performance problems are crucial for patient safety and are foundational for informing clinical decisions, for establishing realistic expectations for patients and physicians, and for monitoring and improving product performance.

HRS believes that cooperation among industry, regulators, physicians, and patients is critical to maintaining confidence, trust, and transparency in the surveillance, analysis, and reporting of lead performance information. This expert task force was composed of HRS members and representatives from the American College of Cardiology and American Heart Association. Input was solicited from representatives of industry, the Food and Drug Administration (FDA), HRS members, and patient advocacy groups. This input was discussed by members of the task force and incorporated where appropriate by consensus. Each recommendation contained in this document was approved by greater than 90% of the Task Force by vote.

This document is the report of the task force’s findings, recommendations, and guidelines. Specific recommendations for industry, regulators, physicians, and others follow. The ultimate judgment, however, regarding the care of a particular patient must be made by the health care provider and patient taking into consideration the individual patient characteristics. The document is divided into 5 sections: I. Lead Performance and Communication of Lead Performance; II. Premarket Evaluation of Pacemaker and ICD Leads; III. Postmarket Surveillance of Pacemaker and ICD Leads; IV. Threshold for Activation of Lead Advisories and Communication after Abnormal Performance is Identified; and V. Recommendations for Clinicians. Each section contains a summary of recommendations followed by a discussion of relevant background information and rationale.

I. Lead Performance and Communication of Lead Performance Recommendations:

1. Manufacturers should provide lead and generator performance reports at least semiannually in a standardized, uniform format on a prespecified schedule. Reports should be accessible to health care providers, to regulators, to patients, and to the public at large.

- Manufacturers should report lead performance information in a logical and comprehensible manner that is usable by health care providers making clinical decisions and understandable to the public. Reports should include all information pertinent to patient care for each lead model. Details regarding returned product analysis, malfunction rates, results of prospective lead surveillance, data acquisition and analysis methodologies, and their limitations should be reported.
- Manufacturers should provide details regarding lead-related communications, including advisories, technical bulletins, and product updates both in the product performance report and on the manufacturer's website. Updates regarding the performance, confirmed clinical outcomes, and management recommendations of lead models subject to an advisory should also be included. Public posting of this important information on the manufacturer's website should be timely, and not await the next formal published report.

Lead Performance

Pacemaker and ICD leads must be able to reliably deliver life-sustaining therapy to the heart and convey electrical information back to the pulse generator while withstanding the hostile environment of the human body. Although substantial scientific and engineering efforts have been devoted to improving the performance of pacemaker and ICD leads, for a variety of reasons they occasionally fail to perform as intended.

Lead reliability measures the freedom of a lead from specific structural and electrical failures. It is typically expressed as the percentage of leads surviving at a given point in time (prevalence) or a failure rate per unit of time—for example, failure rate per month (incidence). Lead performance, on the other hand, is a comprehensive assessment of lead quality, usability, freedom from failure (malfunction), and conformance to applicable labeling (Table 1). Lead performance depends on a number of factors including lead design, materials, and manufacturing methods; implanting physician skill and technique; patient characteristics (e.g., age, anatomy, activity level); and the expertise of the caregivers providing post-implant care. A lead may be removed from service because it is malfunctioning or for reasons unrelated to its performance (e.g., patient death or device infection).

A malfunction occurs when an implanted lead fails to meet its performance specifications (including all claims in the labeling) or to otherwise perform as intended (Table 1). Ideally, the mechanism of a lead malfunction should be confirmed by direct bench laboratory analysis. Unfortunately, many such leads are not explanted due to the hazards associated with lead extraction or are damaged by the extraction process itself making analysis difficult. In addition, leads may fail to perform as expected in ways not identifiable by bench analysis; for example, a design flaw resulting in an increased risk of perforation or dislodgement may be difficult to distinguish from a complication due to a physi-

TABLE 1 Lead Performance Definitions

<p><u>Lead Malfunction:</u> Failure of a lead to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling for the lead. The intended performance of a lead refers to the intended use for which the lead is labeled or marketed (FDA Regulations 803.3(n)). Whenever possible, lead malfunction should be confirmed by laboratory analysis. Malfunctions do not include physician induced damage during the course of implanting, revising, or removing the lead. <i>Extrinsic malfunctions</i> are those caused by external factors (e.g., therapeutic radiation, excessive physical damage including subclavian crush and direct trauma to the device pocket, etc.) including, but not limited to, hazards that are listed in product labeling.</p> <p><u>Lead Performance:</u> A comprehensive assessment of lead quality, usability, freedom from failure (malfunction), and conformance to applicable labeling.</p> <p><u>Lead Reliability:</u> A measure of a lead to be free of specific structural and electrical failures, typically expressed at a given point in time or a failure rate per unit of time (e.g., failure rate per month).</p> <p><u>Lead Removed from Service Unrelated to Malfunction:</u> A lead that is removed from service (surgical abandonment, extraction, or programmed off) for reasons not related to failure: infection, device upgrade (pacemaker to ICD, for example), pacer/lead incompatibility, cardiac transplantation, mode change not due to lead failure, patient death unrelated to lead failure, etc.</p>
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cian's implant technique. Accurate and useful assessment of overall lead performance and malfunctions demands monitoring, analysis, and reporting not only of lead failures, but also of adverse clinical events when such events may be due to lead performance issues.

A review of past pacemaker and ICD lead performance provides context for interpretation of modern lead performance. Reported lead performance varies widely depending on study design, definitions, physician and patient characteristics, implant methodology, duration and method of follow-up, and lead models studied. These factors make comparisons of manufacturers and lead models difficult. Manufacturer product performance reports describe the performance of atrial, right ventricular, left ventricular, and high-voltage leads and demonstrate lead survival probabilities for most leads of 92%–99% at 5 years following initial implant.^{26–30} However, most of these lead survival estimates are significantly limited due to potential underreporting of device malfunctions, insufficient patient follow-up, lead surveillance based on voluntary reporting, and lack of uniform definitions of lead performance and malfunction. Some manufacturers have utilized prospective, multicenter lead studies in an effort to overcome these limitations. However, small sample sizes or slow enrollment can undermine the ability of these studies to accurately identify underperforming leads in a timely fashion. Additionally, they may fail to identify important differences in lead performance between models.

Other data sources also provide estimates of lead reliability. In Denmark, where all lead implantations are entered into a longitudinal registry, pacemaker lead reliability data are available from 1965 to 2006.³¹ Ten-year lead survival for unipolar and bipolar pacemaker leads implanted since 1993 was reported as 96.5% and 97.8%, respectively, and reliability has improved over time. Eckstein and associates evaluated ICD lead performance, including 38 different lead models, from 1993 to 2004, and reported a cumulative ICD lead survival probability of 97.5% at 5 years.³² Other reports have shown less favorable ICD lead survival probabilities of 91% to 99% at 2 years, 85% to 95% at 5 years, and 60% to 72% at 8 years,^{33–41} although some of these studies specifically included leads known to underperform or to be subject to an advisory.^{34–37}

Leads may malfunction early after implant or following a decade or more of reliable service. Mechanical or electrical abnormalities may develop in components such as insulation, conductors, the connector, the terminal pin, or the stimulation electrode. In addition to failure mechanisms that are intrinsic to the lead, extrinsic factors (lead damage due to trauma, mishandling, lead dislodgement, etc.) may cause pacemaker and ICD leads to provide insufficient therapy.

The clinical implications of a lead malfunction vary depending upon the type of malfunction and the individual patient's clinical condition. Notably, some structurally normal leads may provide insufficient therapy (e.g., lack of clinical improvement with cardiac resynchronization therapy), inappropriate therapy (e.g., shock delivery for rapid atrial fibrillation), or may need to be removed from service as a result of issues unrelated to the lead, such as the patient's underlying illness, physiology, implant technique, or device upgrade (e.g., from pacemaker to ICD). These circumstances are not considered to be lead malfunctions. Examples include leads removed due to infection, erosion, or lead dislodgement due to generator manipulation ("twiddler's syndrome"). A normally functioning lead that has been removed or abandoned prophylactically as a result of a manufacturer's safety alert or recall, and has been shown to be free of defects, also should not be considered to have malfunctioned. Some clinical observations, such as high pacing and defibrillation thresholds, dislodgement, and cardiac perforation, pose challenges both to clinical management and to performance classification.

A classification scheme for pacemaker and ICD leads removed from service is displayed in [Figure 1](#). The scheme incorporates clinical observations, structural diagnosis, methods used to confirm the abnormalities, and the clinical actions taken as a result of the findings. Although industry has proposed lead malfunction definitions,⁴² manufacturer Product Performance Reports should summarize the data for each lead model in tabular format based on the data elements in [Figure 1](#) and definitions in [Table 1](#). Reports should include the total number of leads implanted, the number that remain implanted, and a detailed accounting of the number and the reasons that leads were removed from service.

Malfunction-free survival and overall lead survival should be reported graphically, censoring leads removed from service for reasons unrelated to lead performance (infection, device upgrade, etc.).

Communication of Lead Performance

Manufacturers have historically provided detailed product performance information for marketed leads after a lead model has accumulated 200 lead implants and at least 10,000 implant months. Discontinued models are included until fewer than 500 leads are estimated to remain implanted. In recent years, manufacturers have enhanced the transparency and readability of their product performance reports, providing detailed information about each lead model.^{26–30}

Product performance reports should provide accurate, timely data regarding lead performance and reliability. This serves to set realistic performance expectations and enables physicians to make educated clinical decisions and recommendations to patients. A description of methodology should be provided so that readers may understand the report's strengths and weaknesses and data should be presented in a format that can generally be understood by the lay public including patients, their caregivers, and families. Reports should be available in multiple languages to facilitate accurate communication with health care providers and patients.

Graphic representation of performance data over time is useful and has historically been available in both paper and electronic form. Product performance reports should be formatted to provide lead and lead adapter performance data by model and should be published at least semiannually. Advisory notifications, field action letters, technical bulletins and updates, and other communications sent either by the manufacturer or FDA should be summarized and referenced. Updates regarding the performance, confirmed clinical outcomes, and management recommendations of lead models subject to an advisory should also be included. Public posting of important information on the manufacturer's website should be timely and not await the next formal published report.

II. Premarket Evaluation of Pacemaker and ICD Leads

Recommendations:

1. The amount and type of data required by a regulatory authority prior to a lead receiving marketing approval should vary depending on the nature and significance of the proposed lead modifications as well as the potential benefits and risks to patients.
2. Manufacturers should perform rigorous bench testing on all lead models prior to the first human implant.
3. Manufacturers may test leads with minor modifications by design verification studies, reliability analyses, electromechanical tests, and animal studies. Clinical studies

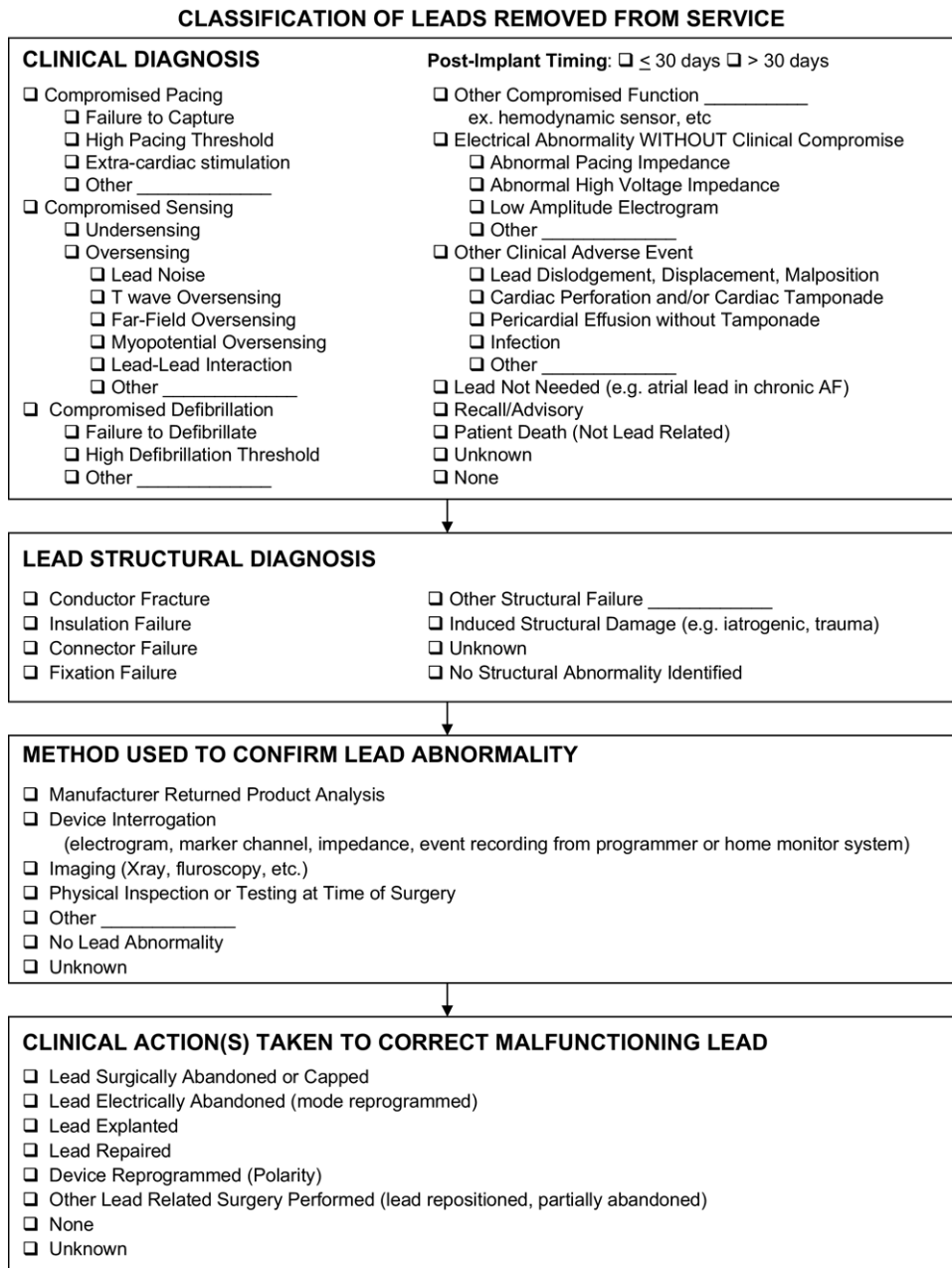


Figure 1 A classification scheme for leads removed from service is shown. A lead failure is a lead that does not perform its intended function as a result of a specific structural or electrical failure and that is removed from service because of clinical safety concerns associated with electrophysiologic or structural abnormalities. Manufacturer Product Performance Reports should summarize the data for each lead model in tabular format based on the data elements in this figure. In addition they should describe malfunction-free survival and overall lead survival, censoring leads removed from service for reasons unrelated to lead performance (infection, device upgrade, etc.).

- should not be required by regulatory authorities unless the modifications are significant.
4. Regulatory authorities should consider requiring additional supporting human clinical data for significant lead modifications including but not necessarily limited to a new fixation mechanism, a new connector, a new drug or steroid, a new clinical indication, a new patient population, or a new anatomical location.
 5. The FDA should convene a public meeting of its Circulatory System Medical Device Advisory Panel and enlist the input of clinicians, engineers, statisticians, patients,

- and industry representatives to define which lead modifications are “minor” and which are “significant.” Regulatory authorities should provide written guidance that clarifies the regulatory requirements for pacemaker and ICD leads and includes a description of the lead modifications that require premarket human clinical testing.
6. Efforts to evaluate and refine current standards and protocols for the preclinical testing of leads should be undertaken by industry, regulators, Heart Rhythm Society, and other appropriate professional organizations. Periodic reevaluation should be performed as additional data

from clinical trials and postmarket surveillance become available.

7. Manufacturers and regulatory authorities should track the long-term performance of all lead models to determine the predictive value of preclinical testing of new leads. The results of such studies may influence the design and conduct of clinical trials that assess the safety and effectiveness of new leads.
8. In the interest of transparency, manufacturers should report significant lead modifications in their product performance reports.

Premarket Evaluation of Pacemaker and ICD Leads

Premarket evaluation is intended to bring new and modified leads to market safely. The 2006 HRS Recommendations on Device Performance Policies and Guidelines did not directly address premarket evaluation. Because of the life-sustaining functions of pacemaker and ICD leads, rigorous scientific evaluation should be performed before leads are marketed to the public. Indeed, the goal of such premarket evaluation is to confirm the safety, quality, reliability, and clinical performance of the lead. Data to support lead safety and effectiveness may be drawn from multiple sources, including design verification studies, reliability analyses, bench and manufacturing tests, animal studies, and clinical trials.

Like many medical devices, leads undergo frequent design and manufacturing changes. Many proposed changes are brought about by the desire to improve lead clinical performance, reliability, or ease of manufacturing. Premarket evaluation typically involves 3 phases: bench testing, animal studies, and human trials. Bench testing has been used for decades to test pacing and defibrillation systems and manufacturers have developed and applied a variety of electromechanical tests to assess leads. Such tests are useful during lead development for identifying weaknesses, projecting long-term durability, and developing manufacturing techniques. The implementation of test methodology is specific to the lead design and may vary among manufacturers. While many bench tests are designed to satisfy and exceed international standards, bench testing alone cannot account for all patient attributes, physician techniques, or clinical scenarios and may not identify effects that only occur *in vivo*. Animal testing can complement bench testing by allowing the assessment of lead implant handling, low and high voltage electrical performance, and other *in vivo* performance (such as tissue reactions or insulation degradation). Bench and animal testing may occasionally identify underperforming leads that subsequently undergo modifications, although no published study has shown that the results of these tests accurately predict the long-term performance of pacemaker and ICD leads.⁴³

Clinical lead studies have historically been relatively small investigations intended to evaluate attributes such as lead handling, electrical performance (such as assessment of defibrillation threshold, pacing threshold, and intrinsic amplitude), and steroid elution. Small, short-term clinical stud-

TABLE 2 Factors to Consider When Determining Whether a Lead is “New”

Characteristic	Definition	Examples
Function	The purpose for which the lead is designed.	Pacing, defibrillation, hemodynamic monitoring, etc.
Design	The form and structure of the lead.	Size, shape, materials, construction, etc.
Method of Use	How the lead’s function is implemented or applied.	Transvenous, epicardial, myocardial, Subcutaneous Vascular access Delivery system Cardiac chamber Ultrasound energy Intracardiac pulse generators Wireless communication “Leadless” ICD (subcutaneous only)

ies may be useful for assessing acute or subacute lead performance but they are inadequate for assessing long-term lead performance as they are of insufficient size and are not designed to account for all implant, patient, and physician variables that can affect outcome. Premarket clinical testing is also not useful as a means of characterizing rare failures because sample sizes are too small.

The specific premarket requirements for a given lead depend on the nature and significance of the changes from previously approved leads. A typical lead model may undergo numerous changes during its market life—some may be viewed as “minor” changes, such as manufacturing changes to increase quality or improve yield during manufacturing. Although there is no generally accepted definition of what constitutes a “new” ICD or pacing lead (Table 2), a lead model that differs substantially in function, design, or method of use from a manufacturer’s legally marketed lead(s) would be expected to warrant a more thorough premarket evaluation. The challenge of lead premarket evaluation is to identify the changes that are substantial enough to warrant additional supporting clinical data. Supporting human clinical data should be considered for significant lead modifications including but not limited to a new lead fixation mechanism, a new connector, a new drug or steroid, a new clinical indication, a new patient population, or a new anatomical location. Even when clinical trials are performed, predicting long-term clinical lead performance remains difficult as problems may arise years after a lead is placed in clinical use. Minor modifications to existing marketed leads may be performed without necessarily requiring additional supporting clinical data.

Preclinical testing cannot simulate the full spectrum of stresses (patient, physician, biologic) to which a lead is exposed *in vivo* at implant or during years of use. These premarket pacemaker and ICD lead recommendations are

designed to ensure that patient safety and well-being are paramount without unnecessarily restraining beneficial innovations or quality improvements.

III. Postmarket Surveillance of Pacemaker and ICD Leads

Recommendations:

1. Pacemaker and ICD lead postmarket monitoring should be strengthened to provide accurate, objective, timely data on lead performance. The precise tools used to monitor lead performance will vary depending on the function and the novelty of the lead and the perceived risk to patients.
2. Regulatory authorities should require manufacturers to conduct prospective, active postmarket monitoring of each lead model. This may be accomplished via a manufacturer registry or other method that provides reliable, accurate data.
3. Manufacturers should further develop and adapt remote monitoring technology to monitor longitudinal lead performance. This technology has the potential to enhance patient safety and improve patient outcomes. Government agencies, insurers, industry, patient advocacy groups, and professional medical organizations should support modifications to existing regulations, such as the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, that currently limit the use of remote monitoring technology in this role.
4. The National Cardiovascular Data Registry (NCDR) ICD Registry should be adapted to permit better longi-

tudinal monitoring of lead performance. Congress should provide the resources necessary to enact such a modification to the Registry and to support its ongoing existence.

5. Health care providers should report all lead-related adverse events and lead performance issues to the manufacturer and regulatory authority. Whenever possible, explanted leads and lead fragments—even if damaged during removal—should be returned to the manufacturer for analysis.
6. Hospitals, cardiac catheterization laboratories, cardiac electrophysiology laboratories, and outpatient pacemaker and ICD clinics should train their personnel about reporting requirements. In these facilities, a protocol should be in place to facilitate adverse event and abnormal lead performance reporting and the return of explanted products.

Background and Current Practice

The goal of postmarket surveillance is to “enhance the public health by reducing the incidence of medical device adverse experiences.”⁴⁴ The current surveillance system relies on medical device manufacturers, regulators, health care providers, hospitals, other medical care facilities, and patients to report adverse events from medical devices. Historically, postmarket surveillance of pacemaker and ICD leads has been designed to identify uncommon, but potentially serious, adverse events. The ideal postmarket surveillance system would identify underperforming products, help elucidate lead failure modes, detect non-critical abnor-

TABLE 3 Methods of Postmarket Surveillance

Method	Definition	Advantages	Disadvantages
Returned Product Analysis	Study of leads removed from patients and returned to the manufacturer for analysis	Best opportunity for understanding actual failure mechanisms <i>in vivo</i>	Low return rate, damage during explantation, inability to assess lead failure rates
Complaints	Any communication received by the manufacturer that alleges deficiencies in performance of the lead after its market release	All-inclusive, sometimes offer opportunity to communicate directly with clinician	Reports often incomplete, unsubstantiated
Post-approval Clinical Studies	Prospective, multi-center studies	Provide actual lead survival estimates via accurate measurement of numerator and denominator	Expensive, time-consuming, slow to enroll patients
Registries	Observational study of leads	Relative independence from manufacturers, potential ability to compare manufacturers, target subgroups	Limited utility for determining failure mechanisms
Passive Reporting Systems	System that relies on individuals to report observed adverse events or performance issues An example is the FDA’s Manufacturer and User Device Experience (MAUDE) database	Useful for identifying rare, unusual lead-related adverse events	Limited by incomplete and inconsistent reporting; underestimates true incidence of lead failure

malities with the potential for serious adverse events, and inform health care providers and patients about device reliability and performance.

Monitoring the long-term performance of pacemaker and ICD leads is an important task for ensuring the delivery of quality patient care. A number of methods are currently utilized to monitor the performance of marketed leads (Table 3). No one method alone provides sufficient postmarket data on lead performance. Therefore, a comprehensive postmarket surveillance plan is required for each lead based on the lead's novelty and perceived risk to patients.

FDA-based postmarket surveillance: The FDA uses several different methods to conduct postmarket surveillance including spontaneous reporting systems, analysis of large health care databases, scientific studies, registries, and field inspection of facilities. Primarily, the FDA relies on a passive adverse event reporting system, depending on patients and the health care industry to identify and report adverse events including rare, serious occurrences. Although medical facilities and manufacturers are required to report lead-related failures that caused or could have caused death or serious injury, health care providers are not required to do so. In fact, only 8% of reports submitted via the FDA's MedWatch program (www.fda.gov/medwatch) are from physicians.⁴⁵ In addition, health care providers may fail to report abnormalities for a number of reasons: uncertainty about whether an adverse event is a true lead failure or an "expected" procedural complication (e.g., a cardiac perforation); belief that the failure is due to normal lead "wear and tear"; lack of understanding of reporting requirements; concerns about patient privacy and personal liability; and perceptions that data collection and reporting are unacceptably time consuming.⁴⁶ Additional underreporting may occur if a patient dies due to unrecognized device failure, although this is believed to be rare.⁴⁷

Data collected from submitted reports are entered into the FDA's publicly searchable Manufacturer and User Device Experience (MAUDE) database. From 2005–2007, approximately 8000 lead adverse event reports were received by the FDA.⁴³ While this database can potentially identify rare, unexpected events, it is significantly limited by incomplete and non-validated data, under-reporting of adverse events, reporting bias, the failure to update the database with results of manufacturer analyses, and the inability to determine the rate of lead malfunction due to the absence of denominator data.

Recognizing these shortcomings, the FDA has developed the Medical Product Surveillance Network (MedSun), a consortium of more than 350 medical facilities at which specially trained representatives actively search out and enter identified adverse events and product malfunctions into an internet-based, publicly searchable database.⁴⁸ For example, individual lead malfunctions reported in 2008 can be accessed.⁴⁹ The HeartNet subnetwork of MedSun focuses on identifying and solving problems related to medical devices used in electrophysiology laboratories.

The FDA may also utilize other methods of postmarket surveillance. For example, they 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 manufacturers to provide additional postmarket surveillance on any device when they deem it appropriate.

Industry-based postmarket surveillance: Manufacturers employ several methods to monitor the performance of their products following marketing approval including the analysis of complaints, returned products, and adverse event reports, and in some cases prospective registries and post-approval clinical studies (Table 3).

Returned product analysis (RPA) of leads removed (e.g., extracted) from patients is the best method for determining actual lead failure mechanisms *in vivo*.⁴³ Specifically, analysis of leads and lead segments provides a measure of lead hardware performance, shortens the time from problem identification to clinically useful communication, and contributes to subsequent lead redesign product improvements. RPA, however, is limited by the damage that occurs during explantation and by the low return rate which limits the ability to accurately assess lead failure rates.^{50,51}

There exists no uniform requirement for industry to perform longitudinal lead performance studies, although many companies have chosen to do so. Post-approval clinical studies are prospective, multicenter investigations of a product that can provide actual lead survival estimates via accurate measurement of the numerator and denominator. These descriptive, observational studies may occasionally be required by a regulatory authority, such as the FDA. Even when regulators, industry, and physicians are committed to assiduous follow-up, implementation of these studies can be challenging due to the large number of leads required, the long duration of study, the expense, and the limited value in determining actual lead failure mechanisms. In addition, the slow enrollment of patients limits the ability to rapidly identify lead performance issues.

Independent registries: Independent registries, including the Danish Pacemaker and ICD Registry, the United Kingdom Pacemaker and ICD Registry, and the Minneapolis Heart Institute Multicenter Registry can provide important long-term information about lead performance with a degree of clinical detail and verification not always available in other surveillance methods.⁴³ Their benefits include the relative independence from manufacturers, the potential ability to compare lead models and patient subgroups, and their documented utility for identifying underperforming products. In some cases, it remains difficult or impossible to determine the incidence of failure for a given lead model or class. These data collection methods may also be of limited utility for determining failure mechanisms.

In summary, despite the commitment of significant effort, time, and resources by regulators, industry, and physi-

cians to the postmarket monitoring of lead performance, significant limitations persist.

Emerging Modalities for Lead Surveillance

Remote monitoring: Transtelephonic monitoring was introduced in the early 1970s to monitor the basic function and longevity of pacemakers.⁵² Remote monitoring has evolved to include both pacemakers and ICDs, permit automated information retrieval and secure internet-based access to information, decrease the frequency of in-office visits, improve patient convenience, and reduce patient anxiety. In addition, the technical quality of the information transmitted via remote monitoring is superb and contains valuable information about lead performance. While the precise data provided by specific manufacturers and device models varies, detailed information about lead performance trends including but not limited to impedance, intrinsic electrical amplitude, and non-physiologic electrical signals that may be indicative of impending lead failure are typically provided. Some current systems perform automated daily checks and automated remote clinician notification of pre-specified “alerts,” including findings that may be indicative of lead performance abnormalities. Remote monitoring offers the potential to improve patient outcomes and prevent lead-associated adverse events by increasing the likelihood of early detection of abnormal lead performance and early therapeutic intervention.

Expanded utilization of remote monitoring offers the opportunity to enhance postmarket lead surveillance in the following ways⁵³:

- identifying abnormal lead behavior early;
- identifying predictors of lead failure;
- identifying safe management strategies to minimize inappropriate shocks and lead revisions;
- identifying important baseline clinical characteristics of patients who have lead defects;
- providing a mechanism for long-term data collection and prediction of long-term reliability of the lead;
- determining automatically and accurately the status of certain lead functions; and
- reducing the problem of underreporting of lead-related adverse events by providing the clinician with immediate 24-hour access to real-time device and patient data leading to greater transparency in postmarket surveillance, analysis, and reporting of information.

Although the clinical utility of remote monitoring to prevent adverse patient events has been reported, initial remote monitoring systems were not optimized for postmarket monitoring of lead performance.⁵⁴ Additional clinical information may be required to determine the clinical implications of certain findings and prevent false positive or false negative classification of lead performance. In some cases, the clinical implications of a finding may be uncertain (e.g., a transient increase in lead impedance without other findings). In addition, the short duration of time between detected lead abnormality and clinical events may in some

cases limit the ability to prevent lead-related adverse events such as inappropriate shocks.⁵⁵

Remote monitoring systems were initially designed primarily to promote the well-being of individual patients, not monitor lead performance population trends. Unlike remote monitoring, in-office visits permit device reprogramming and provocative testing that may sometimes facilitate assessment of lead performance. Current systems will require modifications and supplemental clinical data if a robust remote postmarket monitoring system is to be developed. In addition, the ability to perform comprehensive analysis of remote monitoring data to identify and evaluate underperforming leads may be limited by regulations, such as the HIPAA.⁵⁶ A recent Institute of Medicine report concluded that the HIPAA Privacy Rule significantly impedes research while inadequately safeguarding privacy.⁵⁷ A number of changes, including modifications to existing regulations, have been proposed.⁵⁸ These changes will be necessary if remote monitoring technology is to fully realize its potential to enhance patient safety, improve clinical outcomes, and reduce health care expenditures.

The NCDR ICD Registry: The American College of Cardiology and Heart Rhythm Society collaborated to develop the National Cardiovascular Data Registry (NCDR) ICD Registry, the only approved data repository for the Centers for Medicare and Medicaid Services (CMS) mandated data collection on primary prevention ICD implants. Although only primary prevention implant data are required, 76% of hospitals submit data on all their implants, and in total, more than 88% of all U.S. ICD implants are recorded. The Registry currently contains information from more than 330,000 implants from 1,500 participating hospitals.⁵⁹ Although in excess of 330,000 leads are currently included in the ICD Registry, detailed lead information is lacking. However, in 2010, the Registry will begin more comprehensive ICD lead data collection on atrial, ventricular, left ventricular, epicardial, and defibrillation leads used at the time of ICD implantation. Clinical data on lead performance will be collected at the time of initial implantation, replacement, and extraction. In addition, the NCDR ICD Registry is working with the Pediatric Arrhythmia and Congenital Electrophysiology Society to facilitate data acquisition in children to better assess lead performance in this important sub-population.⁶⁰

The NCDR ICD Registry offers great promise as a post-market surveillance tool. Because of the large number of leads in the Registry, it may be possible to identify infrequent but important lead performance issues, determine lead reliability rates, and compare the performance of various lead models. Even after incorporating expanded data collection on leads, the ICD Registry will have important limitations. Only malfunctions in leads undergoing revision or replacement will be identified and lead failure classification will be based on clinical data not detailed, independent lead structural analysis. Lead failures managed non-invasively and catastrophic failures leading to death will not be

captured. In addition, longitudinal patient follow-up is limited although a subset of Registry hospitals may provide such information in the future. Despite these limitations, the NCDR ICD Registry can be adapted to provide vital post-market performance data on ICD leads and would be even further enhanced by the eventual merger with manufacturer based remote monitoring systems.

In summary, postmarket surveillance of leads is necessary to evaluate their long-term performance and reliability and to identify underperforming products as early as possible. A comprehensive postmarket surveillance plan for individual leads should produce accurate, objective, timely data that tracks lead performance from market approval through the many years of expected device performance.

IV. Threshold for Activation of Lead Advisories and Communication after Abnormal Performance is Identified Recommendations:

1. Manufacturers evaluating a suspected lead performance issue should involve independent clinical advisory panels early in the process and utilize evidence-based decision making without regard to financial implications.
2. Standardized Physician Device Advisory Notification forms and Patient Device Advisory Notification letters should continue to be used for communicating lead performance concerns. Letters should be available in multiple languages to facilitate accurate communication with health care providers and patients.
3. Advisory notices should include general information regarding the potential clinical implications of the lead advisory and clinical recommendations for advisory lead management. Notices should acknowledge that management decisions ultimately should be made by the patient in consultation with his or her doctor.
4. Professional organizations, such as the Heart Rhythm Society, should be utilized in a consulting role to guide communication and provide clinical guidance even before formal public advisory communication.
5. The FDA should call a public meeting of its Risk Communication Advisory Committee to discuss the implications of the word “recall” and develop alternative terminology for implanted medical devices. In addition, regulatory authorities should outline the legal and regulatory barriers that prevent medical device manufacturers from using an alternative term to “recall,” such as “advisory notice” or “safety warning.” They should also provide guidance that explains when and how manufacturers can legally use terms other than “recall” in their product advisory notifications.
6. Regulatory authorities, patient advocacy groups, and other professional medical organizations should partner with Heart Rhythm Society to better educate clinicians and patients that the term “recall” is NOT synonymous with “device removal” or explant.
7. Regulatory authorities should classify all lead advisory notifications promptly. This information should be included in all subsequent manufacturer communications with physicians and patients and should be included in the Product Performance Report.
8. Arrhythmia clinical experts are encouraged to participate on industry “independent advisory panels.” In the interest of transparency, industry should publicly disclose the members of their clinician advisory boards.

Threshold for Activation of Lead Advisories

The decision of when to publicly communicate abnormal lead performance information is challenging. In order to determine the timing and method of communication that best serve the patients’ interests, the perspectives of each stakeholder—patient, health care provider, regulator, and industry—must be carefully considered. The appropriate threshold for notification of lead performance issues will vary depending on a number of factors, including the rate of abnormal lead performance and the clinical implications of the identified malfunction.

Lead performance issues and malfunction risks occur on a continuum and this concept is integral to the process of decision making and communication. Performance concerns fall into two main categories: (a) “emerging issues” where a manufacturer or regulatory authority may suspect there is a problem or may be aware of product failures but not know if they are “out of the ordinary,” and (b) “actual performance issues” where a clear problem has been identified. Determining where on the continuum an “emerging issue” becomes an “actual performance issue” is difficult.

A manufacturer’s structured process for evaluation of a suspected lead performance issue is critical to timely, thorough, and proper investigation. Such a plan should promote the acquisition of the necessary data as soon as possible, involve clinical specialists early in the process, and utilize evidence-based decision making without regard to financial implications. In some cases, a single report of a catastrophic failure may warrant further investigation. Independent physician advisory boards, consisting of knowledgeable clinical specialists, as recommended in the 2006 HRS Device Performance Recommendations,²⁴ should be consulted at an early stage in lead performance investigations.

Certain problems may warrant rapid communication with patients and health care providers while others may best be managed with further investigation in lieu of or prior to public notification. Pacemaker and ICD lead performance and the appropriate threshold for issuing an advisory is often very contextual, based on the performance of similar leads, patient characteristics, implant factors, precedent for prior communication, and the potential to mitigate patient risk. Thus, HRS considers it inadvisable to determine a fixed percentage or a particular type of lead malfunction that would automatically trigger a product notification, advisory, or public communication. Rather, data should be reviewed on a regular basis by the independent physician advisory committees in order to determine when a pattern of inad-

quate lead performance exists. A malfunction that (a) suggests an underlying systematic problem that may lead to recurrence of the observed malfunction in other patients and (b) is associated with a significant risk for death or serious injury merits early review by the manufacturer's advisory committee. Additional circumstances that warrant timely notification of the FDA include but are not limited to the following: (a) lead models whose performance falls outside of FDA-approved labeling or established performance standards, and (b) individual leads that fail to treat an arrhythmia, pace the heart, or provide adequate sensing that could delay or prevent delivery of potentially life-sustaining therapy.

While transparency and timely disclosure are paramount to ensure patient safety, premature notification of lead performance concerns can trigger unnecessary physician and patient anxiety and promote clinical overreaction.^{61,62} Unnecessary operations, lead extractions, and lead replacements may be the unintended consequences of premature or poorly communicated notifications about lead performance. The difficult decision for industry and regulators to embark on the process of public notification is made easier when the lead abnormality is understood, the rate of failure is high, and the clinical consequences of failure are severe. Most "real-life" examples, however, are not so straightforward.

Communication after Abnormal Lead Performance is Identified

The ultimate goal of communication is to promote patient safety and well-being. To achieve that goal, the avenues of communication must be explicitly defined and transparent. Communication must be organized, yet timely, so that neither patients nor physicians are needlessly alarmed nor driven to hasty, unsafe, and unwise reactions. Communication must not only identify the problem but also offer guidance, when possible, as to the clinical management and mitigation of patient risk. The 2006 HRS Device Performance Policies and Guidelines provide a standardized Physician Device Advisory Notification form and Patient Device Advisory Notification letter to ensure that all critical information regarding lead performance is communicated in an easily understood manner. These methods of communication have been successfully implemented. Manufacturers should make a good faith effort to contact patients affected by the lead advisory if they are in possession of the patient's contact information obtained at the time of initial device registration. Health care providers should contact their patients as soon as possible after advisory notification, as this can serve to minimize patient anxiety and promote evidence-based clinical management.

Changes in Nomenclature: Terminology should be commensurate with risk. HRS has previously recommended that the term "recall" not be used in reference to devices that do not require removal or explant, as it may foster miscommunication and lead to unnecessary and potentially harmful interventions.^{24,61–63} Research supports the concept that the specific wording chosen to warn patients has critical implications and that some words (urgent, danger, FDA) and

some phrases (FDA Public Safety Warning, Product Danger Alert, Public Safety Warning) are perceived as being just as important as phrases that include the word "recall."⁶⁴ The term "recall" has regulatory and legal implications that extend beyond cardiac rhythm management devices and substantial hurdles must be overcome to change the terminology. Nevertheless, the FDA is encouraged to explore the legal and regulatory alternatives to facilitate the establishment of a simple and intuitive nomenclature to publicly communicate important information about implanted medical device performance.

The recommendations in this section are offered to prevent misunderstandings, eliminate unwarranted patient anxiety and fear, and minimize inappropriate, unsafe responses to malfunctions that have low risks to patient safety.^{61,62}

V. Recommendations for Clinicians

Recommendations:

1. Lead and generator longevity expectations and the potential for lead failure should be reviewed with patients as part of the informed consent process prior to initial device implantation.
2. 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.
3. Physicians and other health care professionals should report documented or suspected lead failures to the manufacturer and regulatory authority. Leads and lead fragments explanted for performance issues should be returned to the manufacturer for analysis—even if damaged during removal.
4. Direct patient contact by a health care professional via telephone, letter, or in-person evaluation should be performed following the announcement of a relevant advisory or safety alert, particularly when a significant alteration of the patient's clinical management strategy is under consideration. Often, non-invasive management with close observation will be the lowest risk option. For patients in whom lead revision or replacement is recommended, patients should be thoroughly informed of the procedural risks.
5. Clinicians, manufacturers, regulators, and other stakeholders should collaborate to collect data and better characterize lead performance in specific high-risk populations, such as children and young adults.

Clinician Responsibilities: Informed Consent and Monitoring of Device Performance

Physicians who care for patients with cardiovascular implantable electronic devices (CIEDs) have several important clinical responsibilities. The informed consent process prior to initial device implantation should include a discussion about the potential for generator and lead performance abnormalities and should describe device and lead longevity and reliability expectations. Patients should be assured that contemporary ICD and pacemaker leads are very reliable

but should recognize that they may occasionally fail to perform as intended. Education and instruction on the proper response to a suspected device performance problem should also be provided. Easily understandable written materials should be available to all patients considering device implantation.

Routine, clinical monitoring of individual patient's lead performance is advisable, as no pacemaker or ICD lead model has achieved 100% reliability. The techniques, personnel, and frequency of the monitoring were delineated by expert consensus of the Heart Rhythm Society (HRS) and European Heart Rhythm Association (EHRA).⁵² However, the actual frequency and type of CIED follow-up are determined by many factors, including issues related to the patient, the device, and the underlying disease process. Remote interrogation, like an in-person evaluation, provides data about battery and lead performance, observed and treated tachyarrhythmias, frequency of delivered bradyarrhythmia support and, in some cases, patient activity, hemodynamics, and transthoracic impedance as a marker of lung fluid volume status. Remote monitoring, however, provides limited information about capture safety margin or patient dependency upon bradycardia support. Transtelephonic rhythm strip monitoring of pacemakers provides information about basic sensing, capture, and battery function only and is inferior to remote or in-person interrogation and monitoring.⁶⁵

Abnormal Lead Performance

The consequences of lead failure are related to the severity and type of abnormal lead performance, the patient's characteristics and personal medical history, and the clinical setting. Although there are many components to a pacing or defibrillation lead, there are three critical electrical functions that can fail in a lead system: sensing, low energy stimulation, and high energy shocks. If sensing is compromised then one or more of three activities can be affected: bradycardia stimulation, tachycardia detection, and discrimination of true ventricular arrhythmia from supraventricular arrhythmia, environmental interference, or lead-related noise events. Similarly, if low energy stimulation is compromised then antibradycardia stimulation, antitachycardia pacing, and cardiac resynchronization therapies can be impaired. Ineffective high energy shocks can fail to terminate an arrhythmia or may accelerate slower tachycardias to less tolerated rhythms such as fast ventricular tachycardia or ventricular fibrillation. Other lead deficiencies may predispose to an increased risk of perforation or dislodgement in the peri-implant period. Abnormalities of lead functions such as monitoring of the patient's hemodynamic or volume status are less critical, but may lead to adverse clinical events.

The clinical presentation of a patient with a lead performance abnormality depends on the nature of the lead problem, the type and programming of the device, and the patient's medical history. In many cases, abnormal lead performance may be asymptomatic while in others, patients

may present with potentially life-threatening symptoms. Factors that impact the patient's clinical presentation include the patient's underlying heart rhythm (for example, device dependency due to severe bradycardia), the severity of cardiac dysfunction and heart failure, the propensity for supraventricular arrhythmia (sinus tachycardia or rapid ventricular response rate during atrial fibrillation), and the frequency, type, and rate of ventricular arrhythmia.

Importantly, clinical presentation of abnormal lead performance is also affected by device programming. Tachycardia detection rate, required duration of arrhythmia prior to therapy delivery, and arrhythmia discriminators not only affect the frequency of appropriate therapies for true sustained ventricular arrhythmias, but also affect the frequency of therapies delivered for electrical noise due to conductor or insulation abnormalities. Many modern devices permit programming of automated diagnostics, audible or vibratory patient alarms, and automated, remote alerts with the potential to minimize or prevent unnecessary shocks by monitoring for lead performance abnormalities between in-office and remote device evaluations.⁵³

Clinical Management When Abnormal Lead Performance is Suspected

Patient Notification and Clinical Management Strategies: Communication with patients about device performance is a critically important role for clinicians, particularly when abnormal device performance is suspected. Direct patient contact by telephone, letter, or in-person evaluation by the patient's health care provider should be performed following the announcement of a relevant advisory or safety alert, especially when a significant alteration of the patient's clinical management strategy is under consideration. Individual patients may require face-to-face discussions with their physician or other qualified health care professional to address their concerns and create an appropriate treatment plan.

Historically, clinician management of pacemaker and ICD generator advisories has been widely disparate with some physicians recommending the replacement of all advisory devices, while others replace none or very few.⁶⁶ While the clinical consequences of lead abnormalities can be potentially catastrophic, so can the complications of prophylactic lead replacement. The clinical consequences of device replacement vary by procedure, operator, and patient characteristics. Generator replacement alone for advisory devices is associated with a measurable major complication rate of up to 5.8%.⁶¹ The risk of infection is higher for generator replacements than for initial implants.⁶⁷ The risks of lead extraction include the potential for catastrophic events such as cardiac tamponade, severe vascular injury, and death. Mortality associated with extraction of larger leads in experienced hands approaches 1%.^{43,68} Abandoning a non-functioning lead appears to be safe.⁶⁹

Because of the risks of extraction and the potential complications from adding additional leads, the decision of when to replace prophylactically an otherwise normally functioning advisory pacemaker or ICD lead is a difficult one.

Prophylactic removal of an advisory lead is not always the safest option. For example, extraction of the Teletronics Ac-cufix™ atrial J lead, which was prone to fracture, resulted in more deaths than the lead malfunction itself.⁷⁰ It is recommended that physicians know not only general risks associated with device replacement, but the specific risks at their own institution, as these may vary from center to center depending not only on physician skill but patient population. When appropriate, referral to another physician or institution with the required expertise should be provided to the patient.

Guidance for clinical management of pacemaker and ICD advisory leads is displayed in Table 4. Non-invasive management should be considered when the risk of advisory lead malfunction is low, particularly for patients who are not pacemaker dependent, and for primary prevention ICD patients with a low probability of future therapy. Clinicians should consider lead revision or replacement if, in their judgment, the risk of malfunction is likely to lead to patient death or serious harm, and the risk of revision or replacement is believed to be less than the risk of patient harm from lead malfunction. Because the risk of lead removal is greater than that for generator removal, because the risk of new lead placement is not inconsequential, and because remote monitoring offers the potential for close clinical follow-up, non-invasive management often offers the lowest risk management strategy.

These recommendations are intended to provide clinicians with guidance, but they cannot account for all clinical scenarios and they may not apply to individual implanters with higher failure rates or to individual high-risk patients. A number of factors should be considered when deciding whether an advisory lead should be replaced, revised, or followed non-invasively (Table 5). In all cases, the physician should communicate to the patient the risks and poten-

TABLE 4 Recommendations for Clinicians Managing Lead Advisory Notices

1. Conservative non-invasive management with periodic device monitoring (remote or in-person, as appropriate) should be strongly considered particularly for:
 - Patients who are not pacemaker dependent*
 - Patients with an ICD for primary prevention of sudden cardiac death who have not required device therapy for a ventricular arrhythmia
 - Patients whose operative risk is high or patients who have other significant competing morbidities even when the risk of lead malfunction or patient harm is substantial.
2. Lead revision or replacement should be considered if in the clinician's judgment:
 - The risk of malfunction is likely to lead to patient death or serious harm, and
 - The risk of revision or replacement is believed to be less than the risk of patient harm from the lead malfunction.
3. Reprogramming of the pacemaker or ICD should be performed when this can mitigate the risk of an adverse event from a lead malfunction.

*Pacemaker dependence refers to patients who have no hemodynamically stable underlying heart rhythm in the absence of pacing.

TABLE 5 Factors* to Consider in the Risk–Benefit Analysis When Managing Normally Functioning Leads Subject to Advisory

*All factors should be considered when formulating a clinical plan for individual patients. No single factor should determine the clinical management plan.

PATIENT

- Pacemaker dependence†
- Prior history of ventricular arrhythmia
- Patient prognosis
- Risk of future arrhythmia
- Surgical risk of revision/replacement procedure
- Patient anxiety about lead failure
- Impending battery depletion

LEAD

- Rate of abnormal performance (observed or projected) in Advisory Lead
- Lead failure rates
- Malfunction characteristics (gradual vs. sudden, predictable vs. unpredictable, etc.)
- Identified lead subset with higher failure rate (Serial numbers, vascular access, etc.)
- Malfunction mechanism known/understood
- Adverse clinical consequences of lead failure
- Availability of reprogramming to Mitigate Clinical Risk
- Availability of algorithms for early detection of lead abnormality

†Pacemaker dependence refers to patients who have no hemodynamically stable underlying heart rhythm in the absence of pacing.

tial benefits of available clinical management strategies, including revision or replacement of an existing lead, reprogramming the device to mitigate the risk of an adverse event from lead malfunction,⁷¹ and routine or intensified follow-up. Patient anxiety due to lead performance concerns should also be carefully considered when developing a management strategy. Patients should be provided updated lead performance information, particularly whenever such information may impact the clinical management strategy.

Special Considerations for Pediatric Patients

Certain subsets of pacemaker and ICD patients may be more likely to experience lead performance issues. This affects the clinical context in which advisory lead management decisions are made. For example, lead failure is more common in pediatric patients than their adult counterparts, most likely due to the rapid growth and active lifestyles of this unique patient population.^{72–74} In addition, novel pacing and ICD configurations necessitated by small body habitus and, in some cases, congenital anomalies increase the complexity and risk of managing lead failures and advisories. Meanwhile, the lifetime device risks and benefits are magnified by the long projected period of use. With current lead technology and performance, children who undergo pacemaker and ICD implantation can anticipate the need for repeat procedures to modify or replace leads and lead systems. When assessing the risks and benefits of prophylactic replacement of an advisory lead in the pediatric or congenital heart disease population, clinicians are reminded to consider the factors listed in Table 5.

Clinician Responsibilities for Reporting Suspected or Definite Lead Related Problems

Monitoring of lead performance and reporting of lead performance abnormalities are critical for the early identification of underperforming leads and for providing patients and physicians with realistic expectations about device performance. In the United States, the FDA has received thousands of pacemaker and ICD lead adverse event reports over the past several years, the vast majority submitted by manufacturers.⁴³ It is well recognized that physicians and other health care providers significantly underreport observed device abnormalities. This serves to delay and obscure the identification of potentially important lead performance issues. As such, physicians and other health care providers should report all observed lead related adverse events to the manufacturer and regulatory authority. Lead extraction centers, in particular, should, whenever possible, provide relevant clinical information and submit explanted leads and lead fragments for analysis—even if the lead is damaged during removal. Reports to FDA may be submitted via the internet at www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm. Post-mortem device interrogation should be strongly encouraged, particularly in cases of sudden or unexpected death.

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A relationship is considered to be "significant" if (a) the person receives \$10,000 or more during any 12-month period or 5% or more of the person's gross income;

or (b) the person owns 5% or more of the voting stock or share of the entity or owns \$10,000 or more of the fair market value of the entity.

A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Significant