

Medical Device Registries

Recommendations for Advancing Safety and Public Health

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The analysis included in this report is that of The Pew Charitable Trusts, the Blue Cross Blue Shield Association, and the Medical Device Epidemiology Network and does not necessarily reflect the views of outside reviewers. This report is intended for educational and informative purposes. References to specific policymakers, individuals, schools, policies, associations, or companies have been included solely to advance these purposes and do not constitute an endorsement, sponsorship, or recommendation.

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Overview

Medical devices in the United States are a pillar of a world-class system for medical care. These devices range from the infusion pumps that deliver medications to hospitalized patients to lifesaving cardiac valves to implanted devices that can restore hearing or vision. Patients rely on the Food and Drug Administration to ensure the safety and efficacy of new medical devices. However, recent high-profile failures of these technologies, including metal-on-metal hips and implantable cardiac defibrillators, are a reminder that this country lacks a robust system for assessing the safety and effectiveness of medical devices once they enter the market.

In 2012, FDA issued its report “Strengthening Our National System for Medical Device Postmarket Surveillance,” which outlines four key steps for creating a national surveillance system that would quickly identify poorly performing devices. The system would also generate real-world evidence of the benefits of such technologies of devices on the market and support future device development. The four steps are:

- Establish a unique device identification system and promote its incorporation into electronic health information.
- Encourage the development of national and international device registries* for selected products.
- Modernize adverse event reporting and analysis.
- Develop and use new methods for evidence generation, synthesis, and appraisal.¹

In order to inform the implementation of recommendations from FDA’s report, The Pew Charitable Trusts, the Blue Cross Blue Shield Association, and the Medical Device Epidemiological Network, or MDEpiNet, Science and Infrastructure Center at Weill Cornell Medical College worked together to develop recommendations on the use of registries that would improve the nation’s postmarket surveillance system. In the past year, a series of facilitated meetings[†] were convened in which diverse stakeholders (see Appendix A) discussed major objectives for optimizing the use of registries that can collect data over time on patients who are exposed to a specific medical device or type of device. Registries can support patient care decisions and improve outcomes by providing health care professionals with reliable information on the performance of a technology, and can highlight factors that affect the data collected, such as patient selection or operator experience. Registries can also go further than the premarket trials necessary for FDA approval by allowing for the evaluation of devices in wider populations and practice settings.

* The terms “registry” and “medical device registry” are used interchangeably in this document. They refer to patient registries that include medical device information.

† This report incorporates the participating stakeholders’ discussion but is not intended to represent a consensus of the participants.

Objectives and recommendations

This report looks at five objectives and makes recommendations for achieving them. Objectives 1 and 2 provide specific recommendations to advance registries for robust postmarket surveillance that could quickly be adopted by FDA, registry owners, and other stakeholders. Objectives 3, 4, and 5 approach optimizing the use of registries for device surveillance with a longer-term perspective.

Objective 1: Establish criteria for determining if a registry is the appropriate tool for postmarket surveillance.

- Many factors can influence whether the use of a registry is appropriate, and therefore each should be weighed by the public health value or effect on patient care that registry data can provide. In general, factors to consider include whether the device or type of device has characteristics that introduce uncertainty regarding long-term outcomes, substantial design variation within a class of devices, the potential for clinically significant variation in outcomes across populations, operator dependence in the use of the device, or high cost compared with the current therapy.
- A registry should be initiated only when the research questions cannot be answered by existing resources within the postmarket surveillance system or can be answered more efficiently by a registry.

Objectives 1 and 2 provide specific recommendations to advance registries for robust postmarket surveillance that can quickly be adopted by FDA, registry owners, and stakeholders. Objectives 3, 4, and 5 approach optimizing the use of registries for device surveillance with a longer-term perspective.

Objective 2: Deliver timely, actionable information from registries to all stakeholders, including the public.

- Findings and reports should be publicly released on a regular basis.
- The workings of the system—its governance, operations, and financing—should be made publicly available.
- Registries should provide a clear, reasonable, and responsive process for providing data to outside researchers.
- FDA, the Centers for Medicare & Medicaid Services, or CMS, and other stakeholders should encourage the preferential use of registries that meet the above criteria for public availability.

Objective 3: Streamline registry data collection through efficiencies that reduce the time and cost of reporting.

- The number of patients followed in a registry should reflect its underlying purpose.
- Registry data fields should be limited to the data most relevant to the purpose of the registry, and they must use standardized definitions.
- Registries should be coordinated with national efforts to improve quality measure reporting.



- Registries should maximize their use of existing data by incorporating unique device identifiers and linking to other electronic databases.

Objective 4: Gain additional value from device registries by using them to accelerate device innovation and to fulfill other regulatory responsibilities.

- FDA, manufacturers, patient advocates, and clinical societies should collaborate to develop guidance for the use of registries in the support of clinical trials for new products or to expand the uses of existing products.
- FDA should issue a guidance document describing how manufacturers could use registry participation to fulfill regulatory responsibilities other than postmarket surveillance.

Objective 5: Provide clarity for registry owners, providers, and patients by resolving varying legal interpretations of the Health Insurance Portability and Accountability Act, or HIPAA, privacy rule and the Federal Policy for the Protection of Human Subjects, known as the Common Rule, as they apply to registries.

- Stakeholder groups should work together to better understand and ultimately reduce unnecessary barriers to registry data collection and use.

A robust postmarketing surveillance system that expressly includes device registries can provide information to health care providers, payors, industry, and the public to improve patient safety and outcomes. This report will examine the elements needed to put such a system in place.

Introduction

When they first entered the market, metal-on-metal hip implants appeared to be the answer for younger patients needing a hip replacement. Physicians assumed that the hips would be more wear-resistant than the plastic and ceramic versions in use and that they would spare these patients repeated replacement over a lifetime. Ultimately, metal-on-metal hip implants failed at a rate two to four times higher than conventional hips² and posed a unique risk of adverse tissue reactions to the metal debris they shed. Unfortunately, the United States does not have a system in place to monitor the performance of many approved medical devices, so the metal-on-metal implants remained in the marketplace amid an emerging pattern of failure. One manufacturer, for example, used registry data from Australia and the United Kingdom as the basis for recalling its metal-on-metal implant. A strong system for assessing the postmarket performance of devices would have identified problems with the metal-on-metal implants in the United States more quickly.

With the purpose of furthering one of the goals put forward in FDA Center for Devices and Radiological Health's 2012 report "Strengthening Our National System for Medical Device Postmarket Surveillance"—promoting the development of national and international device registries for selected products—The Pew Charitable Trusts, the Blue Cross Blue Shield Association, the Medical Device Epidemiological Network Science and Infrastructure Center at Weill Cornell Medical College, and a diverse group of stakeholders convened to develop recommendations on the role of registries in improving the nation's postmarket device surveillance system.

About this report

Twenty-eight stakeholders representing practitioners, regulators, payors, industry, and patients met in 2013 to develop recommendations on the use of registries to improve the nation's postmarket device surveillance system. During this series of meetings—"Future Directions for Medical Device Registries: Advancing the State of Medical Device Registries for Postmarket Study" (see Appendix A for the participant list and Appendix B for the agendas)—participants were asked to provide insights and ideas, find ways to narrow differences on the subject, and highlight areas of agreement. They were not asked to reach consensus or to endorse the recommendations in the subsequent report.

The participants reviewed an initial draft of the report to confirm that the substance and conclusions of the group discussions were accurately represented. The draft was also reviewed by several health care policy experts who did not participate in the convenings.

The initial queries posed in the meetings addressed two key issues that are of immediate relevance to FDA's plan for using registries to strengthen device surveillance:

1. What are the research questions concerning medical devices that are most effectively and appropriately answered with registries?
2. Are there best practices related to the governance of registries and the dissemination of information that can support improved patient care and outcomes?

The consideration of these points informed the first two of five objectives in this report. Dialogue among the participants raised additional topics based on lessons learned by organizations that have started and maintained registries. Therefore, participants felt that matters pertaining to the long-term sustainability and value of registries should be addressed. The other three objectives reflect the longer-term view on optimizing the use of registries for device surveillance that came from these discussions.

The need to modernize

Manufacturers of high-risk medical devices¹ must receive premarket approval by FDA through an assessment of safety and effectiveness.³ The agency generally requires a combination of nonclinical laboratory studies and clinical data on the device's performance before it grants approval.

Clinical trials for high-risk devices such as cardiac stents or implantable defibrillators often involve a small number of patients and a limited amount of time. For example, one study found that premarket cardiovascular device trials follow, on average, 308 patients for a median of 365 days (cardiac stent patients were followed for a median of 180 days).⁴ After FDA approves a device, clinicians typically use marketed devices in a broader patient population and for longer periods than are entailed in premarket studies.

Recognizing that there may be problems with devices that were not identified through premarket review, FDA has the authority to collect postmarket evidence on the performance of medical devices in clinical use. The two main approaches are passive reporting of adverse events, which manufacturers and clinical facilities must do, and postmarket studies, which FDA can require of manufacturers. (See Appendix C.)

Recent high-profile device failures have raised concern about the current surveillance system. Examples such as the premature failure and metal debris complications of metal-on-metal hip implants and the successive episodes of defective leads for implantable cardioverter-defibrillators⁵ have highlighted the insufficiency of existing surveillance mechanisms for quickly detecting and addressing problems.

FDA and other stakeholders currently rely on passive systems—such as reporting of adverse events—to provide data on the performance of devices. When questions about an approved device arise, collection of the necessary data is hampered because few platforms exist to support investigation. Device registries, established as one of the four pillars of FDA's plan to strengthen the national postmarket surveillance system, are an important tool to fill this gap.⁶

The role of registries

The Agency for Healthcare Research and Quality defines a registry in general as an “organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes.”⁷

Similarly, FDA's National Medical Device Postmarket Surveillance Plan states that a registry is a “system that collects and maintains structured records on a specific disease, condition, procedure, or medical product for a specific time period and population.”⁸

* High-risk devices are categorized as Class III devices. FDA defines these as “those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury” to the patient.

Put more simply, registries collect data on a group of patients treated for a particular medical condition so that their outcomes can be assessed over time. They do not specify a treatment or study protocol, and they may be stand-alone entities or cover multiple areas. In general, data come in to registries in two ways: they are either entered directly or pulled from other electronic sources.

A registry for medical devices tracks patients whose care has involved a device such as an artificial hip or a cardiac stent and gathers data on patient outcomes. Because of the specifics of device and user interaction, registries generally need to capture information covering five domains:

1. Indications for the procedure.
2. Patient characteristics.
3. Procedure and sometimes physician details.
4. Device details.
5. Patient outcomes.

Registries can help track the experience of a broader patient population for a longer period than that which is studied in premarket clinical trials. Hip implants, for example, are expected to last 15 to 20 years⁹ but typically require only two years of clinical data for FDA approval.¹⁰

The use of registries internationally and in the United States has demonstrated that the system can provide actionable safety information about medical devices on the market. For example, the data from registries have been used to:

- Signal the problem with metal-on-metal hip prostheses.¹¹
- Evaluate concerns with clotting in left ventricular assist devices.¹²
- Demonstrate safety for implantable cardiac defibrillators in athletes.¹³
- Evaluate complications after cosmetic breast augmentation.¹⁴

Joint replacement registries in Australia and the United Kingdom provided the first alerts of high failure rates of metal-on-metal hip implants. The duration and size of these registries, which issue annual reports on device performance, provide a rich data source for clinical decision-making. The 2013 report of the Australian Orthopaedic Association's National Joint Replacement Registry tracked more than 799,000 procedures performed from September 1999 through December 2012.¹⁵ The most recent report of the National Joint Registry of England, Wales, and Northern Ireland¹⁶ included over 1.4 million hip, knee, ankle, shoulder, and elbow procedures from April 2003 through March 2013. Both registries report clinical outcomes such as implant revision rates.

In the United States, large, ongoing registries provide data to specific stakeholders (such as the American College of Cardiology's National Cardiovascular Data Registry, a group of seven established patient registries), but most do not deliver early and actionable information to the public. Reasons for this disparity include the fragmented nature of the U.S. health care system and the lack of a government entity with a specific mandate in this area. In addition, device registries are maintained for use by large health systems—the Department of Veterans Affairs or Kaiser Permanente—or by those with specific interests such as clinical specialty societies or manufacturers.

* The registry was known as the National Joint Registry of England and Wales until 2013, when Northern Ireland joined it.

Existing registries such as these, however, have the potential to become a solid pillar of the national surveillance system for devices because they have formed the foundation for data collection. (See Appendix C for more information on a selection of U.S. registries.)

In addition, the recent addition to the national surveillance system—the unique device identifier, or UDI—has the potential of being a primary source of data for a national device registry. Under the rule finalized by FDA in September 2013,¹⁷ every manufacturer must place a UDI on the product label for each device it sells. The UDI system, which will be phased in over several years, is expected to significantly improve medical device safety by providing faster identification of adverse events associated with devices and leading to more efficient recalls. The UDI could be used by FDA with its Sentinel surveillance system to proactively query databases—in particular, administrative and insurance claims databases—to locate potential safety issues. In addition, the UDI can strengthen the role of registries in postmarket surveillance.

How FDA plans to use registries

FDA's national surveillance strategy emphasizes the importance of medical device registries. However, the plan also makes it clear that the agency will not be running registries or mandating their existence: FDA can require postmarket studies in general but cannot specify the study design. Rather, "FDA envisions continuing to help facilitate the creation of registries."¹⁸ Private registries, such as the American College of Cardiology's National Cardiovascular Data Registry, will play a key role in this process.

FDA has announced the creation of a Medical Device Registry Task Force to operate under the Medical Device Epidemiological Network, or MDEpiNet, a public-private partnership launched by the agency in 2010 as a forum for addressing general issues that apply to the regulation of medical devices.¹⁹ Two of the charges of the task force are:

- "Identify priority medical device types for which the establishment of a longitudinal registry is of significant public health importance."
- "Define registry governance and data quality practices that promote rigorous design, conduct, analysis, and transparency to meet stakeholder needs."

This report is intended to inform the work of FDA's postmarket surveillance plan, MDEpiNet, and the affiliated registry task force.

The unique device identifier system, which will be phased in over several years, is expected to significantly improve medical device safety by providing faster identification of adverse events associated with devices and leading to more efficient recalls.

Objectives and recommendations for device registries in a national surveillance system

This report explores five objectives necessary to implement FDA's plan for using registries to strengthen device surveillance. The format of each section includes the objective, a brief discussion of the rationale for the policy decision, and recommendations for next steps. Objectives 1 and 2 have specific recommendations that can quickly be adopted by FDA, registry owners, and stakeholders to advance registries for robust postmarket surveillance. Objectives 3, 4, and 5 take a longer-term view on optimizing the use of registries.

Objective 1: Establish criteria for determining if a registry is the appropriate tool for postmarket surveillance.

The appropriate tool for postmarket surveillance of a device depends on the nature of the question and whether other available resources can address the issue.

For example, examining the long-term performance of a device could be accomplished by following the patients enrolled in the premarket trials for a longer period. In such a case, a registry might be appropriate if the premarket cohort is too small to detect adverse events of interest or for obtaining postmarket information in other populations that were excluded from the marketing approval trials, such as patients with comorbidities.

There is no fixed number of outstanding questions that constitute a threshold for establishing a registry. Rather, each question should be weighted by the public health value or effect on patient care that registry data can provide. In some cases, just one unanswered clinical question might justify the use of a registry, but the argument for a medical device registry becomes more compelling with each additional outstanding clinical question. Similar considerations inform the decision to end a registry; rarely will it be justifiable or affordable to maintain a registry in perpetuity.

Recommendation 1.1: Weigh the following criteria:

- The device utilizes new technology with characteristics for which the safety and effectiveness are not well understood.

Technological advances that result in innovative, first-of-a-kind devices may come to the market with higher uncertainty about long-term consequences than devices that represent incremental improvements. Postmarket surveillance is imperative when there is potential for unintended serious consequences. For example, the clinical trials for bronchial thermoplasty showed that the device lessened the frequency of asthma attacks by reducing airway smooth muscle with an acceptable level of safety, but the long-term effect of such ablation is not completely understood and can be fully delineated only with extended follow-up in larger numbers of patients.²⁰ In this case, a registry could be the appropriate tool.

Long-term observation of implanted devices is also a likely role for registries. Premarket studies typically assess the performance of an implanted device such as a cardiovascular stent or prosthetic joint for one to two years. However, some devices are implanted for a decade or more. A registry could be the mechanism for additional assessment.

- The device type has substantial design variation.

As illustrated by the example of metal-on-metal hip implants, significant variation in outcomes can emerge when there are many types of a device or changes in the design of a particular device occur over time. A registry

that captures the outcomes of these various devices would allow for a comparative assessment of performance. Robust evidence of outlier performance (good or bad) should inform clinical practice.

To assess the consequences of design variations, all devices should be reported in the same registry created specifically for the purpose of comparative analysis. Meaningful assessment depends on the registry having the data necessary to make adjustments to reflect use in similar populations. Maintenance of separate registries increases costs, causes logistical difficulties in combining data, and raises methodological uncertainties as to the comparability of the data collected.

- The performance of the device may have clinically significant variation across the population or in a significant subpopulation.

Registry data can identify subpopulations in which the benefit-risk profile differs. Procedural outcomes may vary among men and women or among older and younger patients. In general, women have higher bleeding rates and procedural morbidity and mortality than men. Although women may experience more risk and less benefit from medical devices, they are often underrepresented in clinical trials.²¹ Further, if a device is expected to have significant uptake among those over age 65, but older populations were not well-represented in the premarket studies, the registry can collect information on this large population.

The example of vascular closure devices, which are used to seal the puncture site in the artery left by catheters used in endovascular procedures, illustrates concerns about the ability to generalize trial results. Published evidence from large studies assessed the safety and effectiveness of the devices for cardiology procedures,²² but little data existed about the rate of complications in interventional radiology procedures, such as needle biopsies and radiofrequency ablation of tumors. When anecdotal reports of complications began to raise concern, the Cardiovascular and Interventional Radiological Society of Europe developed a registry to assess routine use of these devices for interventional radiology.²³ A total of 28 centers from 10 countries enrolled 1,107 patients (no inclusion or exclusion criteria) in eight months. Analyses of the registry data concluded that the use of closure devices in interventional radiology procedures was safe, with a low incidence of serious complications.

- The procedure's outcome is highly dependent on operator performance.

Patient outcomes with a device can be affected by operator skill, training, and experience. Therefore, data collected from a wide range of providers and facilities presents a more complete picture of overall device performance than can be gleaned in a small trial with a few highly trained investigators.

For example, the National Cardiovascular Data Registry-Implantable Cardioverter-Defibrillator Registry was used to study implantable cardioverter defibrillator, or ICD, implants performed by more than 4,000 physicians. Researchers examined the relationship between physicians' annual implantation volume and in-hospital complications. The study showed that physicians who implanted more ICDs had lower rates of procedural complications and in-hospital mortality, independent of hospital procedure volume, physician specialty, and ICD type.²⁴ Cases such as these illustrate that registry findings on operator dependence can be used to develop interventions to improve care. For example, use of a device might be restricted to high-volume centers, or existing training programs might be improved.

- The total cost of the device is substantially higher compared with current therapy.

When an expensive device enters the market, it invariably elicits concern as to whether the benefit is sufficient to justify the increased cost. Registry findings can inform decisions of payors and hospitals on the acquisition and utilization of expensive new devices.

Recommendation 1.2: A registry should be initiated only when the research questions cannot be answered by existing resources within the postmarket surveillance system or can be answered more efficiently by a registry.

A significant investment of resources is required to initiate and maintain registries. Thus a registry should be undertaken only when existing information sources, such as ongoing international trials or extended follow-up of the investigational cohort, are not capable of answering the outstanding postmarket questions.

Objective 2: Deliver timely, actionable information from registries to all stakeholders, including the public.

Currently, many registries in the United States are privately maintained, with access to data limited to the sponsoring organization. To improve public health and patient care, registry findings should be available to stakeholders, assuring that decision-makers—including regulators, clinicians, patients, and payors—have access to key information.

The Agency for Health Research and Quality states in its second edition of the registry handbook²⁵ that transparency will improve public and professional confidence in the validity of scientific data. To meet this goal, registries need to involve multiple stakeholders in all parts of registry operations, particularly data oversight, consideration of research requests, and analyses. For example, clinicians from professional societies could participate in a data safety monitoring board, and patients could be part of a committee reviewing research proposals.

Patients are often overlooked when considering how to use registry findings. Given the contribution that patients make in providing their data, an ethical obligation exists to ensure that they have access to registry information. For example, data from registries—written and presented at a lay level—should be available to patients to support informed choices about treatment.

One challenge to the goal of transparency comes in determining when adequate data have been collected and analyzed to permit meaningful conclusions. For example, one model of a device may fail at a higher rate than the industry norm three months after implantation but perform better than the norm at six months. Clinical experts and methodologists have a critical role in prespecifying analyses and interpreting registry findings. Thus, we strongly recommend providing access to raw data to researchers conducting independent analyses but do not recommend open access. Accordingly, registries should develop, implement, and communicate policies around which outside researchers can access registry data.

Recommendation 2.1: Device registries should regularly release findings and reports to all stakeholders, including the public, for use in making treatment decisions.

Summary reports on device performance should be released publicly on a regular schedule—preferably at least annually. Regular reports should begin as early as possible in the registry's life cycle and once a sufficient number of cases are compiled so that stakeholders are not misled by results from small data samples.

The reported outcomes should be prespecified and announced in advance. Further, the rationale for any decision to change the outcomes reported by the registry should be described in detail and made public.

Registries should compare the performance of the devices to each other where possible with comparable populations and appropriate risk-adjustment.

Determination should be made from the start regarding when or if findings will be released outside of the regularly scheduled reports—for example, if a device were found to fail at an unacceptably high rate—and the criteria for filing a report with FDA or making it public.

Recommendation 2.2: Medical device registries should make publicly available the following information about registry governance, operation, and finance:

- The original purpose of the registry and funding source.
- The governance structure of the registry, including members of the board of directors, or executive-steering committees.
- Scientific experts consulted by the registry.
- Members of external review and audit committees, advisory boards, or data safety monitoring boards used to provide external oversight and review of the data in the registry.
- Senior staff of the registry.
- The criteria used to identify conflicts of interest among those involved in the governance or operation of the registry and the names of those with a conflict of interest.
- Data elements, definitions, sources, and methods used for data extraction, input, or adjudicating the data.
- Information on the data quality program, including how data quality is evaluated and reported.
- Publications that have emerged from data in the registry, including abstracts presented at meetings or conferences.
- The status of the registry, including:
 - Number of patients and/or procedures.
 - Basic patient demographics.
 - Length of patient follow-up.
 - Rates of missing data.
 - Number of centers reporting data.
- A layperson’s version of the registry status and findings. While this may be difficult to accomplish in the short term, it should be a longer-term goal for registries.
- Registries should also participate in the Agency for Health Research and Quality’s Registry of Patient Registries to facilitate research collaborations and to reduce data collection redundancies.

Recommendation 2.3: Registries should provide a clear, reasonable, and responsive process for making data available to outside researchers.

Registries should be transparent about their data-sharing and research policies and procedures. For stakeholders to have confidence in registry findings, outside researchers need to be able to verify them and explore relevant new questions that may have important public health implications. The Yale University Open Data Access Project has pioneered data-sharing in which Yale has both coordinated external reviews of clinical trial data as well as made that data available to requesting investigators. The goal of this effort is to provide a means for rigorous and objective evaluation of clinical trial data to ensure that patients and practitioners possess necessary information about a drug or device when making treatment decisions.²⁶ These new methodologies may be applied to registry data as they are developed.

Recommendation 2.4: FDA, CMS, and other stakeholders should encourage the preferential use of registries that meet the above criteria for public availability.

Stakeholders need to have confidence in the information that comes from each registry, and public access to key information on the governance, operations, and financing of the entity is one of the most important ways to accomplish this goal. Registries (or stakeholders that control registry information) that do not make information available may address the needs of one specific stakeholder but do not contribute to the national postmarket surveillance infrastructure.

Accordingly, stakeholders such as FDA and CMS can encourage transparency in registries, including industry-operated registries, by specifying criteria that a registry should meet to comply with regulatory requirements. As previously noted, FDA does not have authority to mandate registry use but may encourage use of a particular registry. CMS can issue coverage decisions that require data collection in a registry with specific attributes.

Objective 3: Streamline registry data collection through efficiencies that reduce the time and cost of reporting.

Many registries function as stand-alone entities and are not integrated with other sources of information, such as electronic health records or insurance claims data. This structure introduces multiple inefficiencies for stakeholders.

- **Hospitals and clinicians.** Providers often must repeat the process of entering the same information for the electronic health record and the registry. Further, data elements are not often uniform or may reside in different databases within an institution, making data extraction difficult.
- **Manufacturers.** Establishing and running a study that collects its own data costs more than one that uses data from existing sources. Manufacturers bear the increased costs of registries as part of FDA-mandated postapproval studies that require direct data input compared with using existing data sources.
- **Patients.** Registries are typically designed to assess clinical outcomes over a period of time. Patients doing well after a procedure may consider additional visits to providers as an unnecessary obligation. If registries could pull in clinical information from other data sources, they might depend less on direct patient contact. Additionally, registries have not yet developed efficient mechanisms for collecting patient-reported outcomes data.^{*27}

Integrating information from other sources—in particular, electronic health records and insurance claim forms—could increase efficiency for all stakeholders. For example, patients with a new model of a prosthetic hip may be evaluated in a postapproval study that requires annual follow-up visits for 10 years after implant. Information from the patient’s records or claim forms could be monitored to provide information on the patient’s status (such as return visits for continuing pain or revision surgery), which would reduce the need for an office visit to assess device performance.

Integration would also help address the appropriate scope of the registry, which involves two competing and conflicting goals. On the one hand, registry data extraction can impose a significant time burden on clinical staff, and limiting the number of data fields can minimize that time. On the other hand, because many types of device

* Patient-reported outcomes refer to instruments in which responses are collected directly from the patient. Patient-reported outcomes are not interchangeable with “patient-centered outcomes”; patient-reported outcomes refer to a way of collecting data for the interest of the investigators, which may or may not be of interest to the patient.

Many institutions are have multiple data systems without the capacity to directly exchange information with each other. Registries can develop tools that enable hospitals and other providers to more easily extract needed data elements, such as software to convert data formats.

problems cannot be anticipated at the start of the trial, collecting “nice to have” data in addition to “must have” data can potentially answer unexpected questions. However, the option to pull data from other sources in the future allows registry designers to narrow the scope of initial data collection.

Claims data from CMS or other payors and electronic health records are the types of data sources that could be used by registries to answer subsequent questions about device performance without needing direct patient contact. Planning for this capability will maintain flexibility because new devices always have the potential for unexpected research questions.

Many institutions have multiple data systems without the capacity to directly exchange information with each other, otherwise known as noninteroperable systems. Registries can develop tools that enable hospitals and other providers to more easily extract needed data elements, such as software to convert data formats.

These concepts can be found at work in the Surveillance, Prevention, and Management of Diabetes Mellitus, or SUPREME-DM, project, which is a registry of patients with diabetes. Its primary purpose is to improve medication adherence and counseling by identifying and monitoring trends in patients with Type 1 and Type 2 diabetes mellitus, gestational diabetes mellitus, and prediabetes. The research project developed a registry using data from electronic health records across 11 integrated health care delivery systems.²⁸ The data are linked through a standardized unique patient identifier and allow for comparative effectiveness research, epidemiologic surveillance, and population-based care management for people with diabetes.²⁹ While the SUPREME-DM project is not a device registry, it does demonstrate that data from noncommunicating databases can be successfully integrated to provide important clinical information.

The unique device identifier system will address some of the issues with integrating information from different sources. A major barrier to using electronic health records and claims data for device assessment—whether as part of a registry or another surveillance effort—is the difficulty of identifying the specific device that was used. Including the UDI in these records will ameliorate this problem and enhance the ability of device registries to use existing data rather than collecting completely new information.

Of course, some clinical questions cannot be answered by relying solely on information from electronic health records, claims data, or other existing sources of information. Consider, for example, a question about the time needed for patients to become fully mobile after implantation of an orthopedic device. Claims data may show final outcomes such as whether the implant was removed or the patient died but not how well the patient was feeling or how well the implant was performing. In addition, patient-reported outcomes are not consistently captured in electronic health records.³⁰ In the case of a ventricular assist device study, infection rates could be inferred from the drugs prescribed and documented in the electronic health record, but it is unlikely that quality-

of-life information would be available in other databases. In these cases, registry-specific information will be needed to augment existing data.

The Transcatheter Valve Therapy, or TVT, Registry demonstrates the challenge of meeting the needs of multiple stakeholders while striving for efficiency. A panel of cardiologists, cardiac surgeons, industry representatives, FDA and CMS representatives, and other research-related groups chose the data elements for inclusion in the registry. However, these stakeholders all sought to include data elements that would benefit their own constituencies—often with the goal of creating data collection consistencies across databases to facilitate comparisons—resulting in several hundred data fields for each patient. The time required for data extraction and input placed a substantial burden—on average, four hours per patient at the time of implant—on the clinical facility. This example demonstrates that the amount of data collected should balance stakeholder interests with the workload placed on those who collect the data.

If stakeholders conclude that one of the questions for which the registry was initiated has been addressed, the data collection specific to that purpose can end. For example, CMS was instrumental in establishing the Interagency Registry for Mechanically Assisted Circulatory Support, or INTERMACS, in 2005 by requiring collection of long-term data for left ventricular assist and other circulatory support devices in a registry. The agency ended the requirement for participation in the registry after it concluded that sufficient evidence had been obtained.³¹

Recommendation 3.1: The underlying purpose of a registry should inform the number of patients included in it.

For registries intended to answer specific research questions, the number of patients included will depend on the necessary statistical sample size. In some cases, all of the patients treated with the device of interest may need to be followed. The appropriate number of patients must be determined early to ensure that the registry is cost-efficient. Planning becomes more difficult if the registry has multiple purposes.

Registry overseers should periodically evaluate the registry analyses to determine whether the questions have been adequately addressed and the registry can be discontinued. However, some of the questions—such as assessing the comparative performance of devices in a class that regularly has new products—will require continued data collection and do not have a foreseeable end.

Recommendation 3.2: Registry data fields should use standardized definitions and be limited to the data most relevant to the purpose of the registry.

Registries should not collect more data than necessary to answer the specific question or questions for which it was established. This is also one of the key tactics behind the recent development of large, simple clinical trials.³²

It may be tempting for researchers to cast a wide net in anticipation of unforeseen questions. Instead, linking registries with insurance claims data and electronic health records could answer future research questions without collecting data superfluous to current issues.

Accordingly, all stakeholders involved in initiating registries, including FDA, CMS, and professional societies, should strive to limit the size and scope to minimize the time and cost of data collection and should work to create registries that can interact with other electronic sources of data if unexpected questions arise.

Recommendation 3.3: Device registries should be coordinated with national efforts to improve quality measure reporting.

While some data collected for quality improvement are different from those for postmarket surveillance, integrating the two can increase the value of a registry to stakeholders. The mechanism to accomplish this would vary. For example, payors could identify incentives—such as inclusion in preferred networks—to reward hospitals or clinicians who use registries to assess the performance of devices. Additionally, opportunities exist to encourage the use of device registries through efforts such as CMS' Physician Quality Reporting System,³³ which uses a combination of incentive payments and adjustments to promote reporting of quality information. Clinicians may qualify to earn such an incentive by reporting quality measures data to a participating registry.

Clinical societies can include information on medical devices in their efforts to assess the performance of clinicians and hospitals. Such an approach could prove to be successful, especially in subspecialties such as cardiology or orthopedic surgery because the outcomes of many procedures depend on the performance of both the clinician and the device.

Finally, consumer groups can include device registries as part of their endeavor to raise awareness among patients. *Consumer Reports* and the Society of Thoracic Surgeons, for example, have collaborated to disseminate information on surgeon performance to magazine subscribers. Similar efforts could be designed to raise awareness of the participation of hospitals and providers in various registries.

Recommendation 3.4: Registries should incorporate unique device identifiers and link to other electronic databases to maximize the use of existing data.

The UDI could potentially be used to search electronic health records to identify patients who have received a specific device, confirm the identity of the device to be studied, avoid duplicative effort, and reduce errors in data entry.

The Office of the National Coordinator for Health Information Technology should update the standards for electronic health records to include a field for capturing the UDI of implanted devices. CMS should then provide financial incentives, through the Medicare Electronic Health Care Record Incentive Program, for hospitals to utilize this new field. Additionally, payors, hospitals, and other stakeholders should consider whether and how the claim can be updated to capture the UDI for implanted devices. Although the specific device identity is not currently required for procedure reimbursement, the overall cost of including the UDI in claim forms might eventually be offset by avoiding unsafe devices or value-based purchasing of high-performing devices.

The UDI could potentially be used to search electronic health records to identify patients who have received a specific device, confirm the identity of the device to be studied, avoid duplication, and reduce errors in data entry.

Objective 4: Gain additional value from device registries by using them to accelerate device innovation and to fulfill other regulatory responsibilities.

Registries have shown the potential to provide value to stakeholders beyond postmarket surveillance. Two promising areas involve using registries to accelerate device innovation and fulfill regulatory obligations.

Registries can promote device innovation in three ways. First, they can collect outcomes data that can be used as a contemporaneous control for other devices in that class. FDA did just that when it used data from a ventricular assist device registry³⁴ to approve a new device in that class.³⁵

Second, registries can serve as an existing foundation for studying the performance of an approved device for a new indication, which can be cheaper than a conventional clinical trial because existing registries are already collecting the clinical data necessary to answer the needed research questions.³⁶ This use of registries occurred recently with the TVT Registry. The first transcatheter valve received initial approval for device delivery through the femoral artery. Further study conducted through the registry demonstrated the safety and efficacy of a transapical approach.³⁷ This evidence was used to garner FDA approval for the expanded indication. Using registry data to support approval of a next-generation device model or to expand device indications would be a cost-effective incentive to engage manufacturers.

Third, a new randomized study can use an existing registry infrastructure to enroll large numbers of patients and reduce costs by leveraging data already collected for other uses. Doing so retains most of the benefits of a randomized trial while adding the benefits of a large observational registry.³⁸

As an example, the Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction, or TASTE, trial was a multicenter, prospective, randomized, and controlled open-label clinical trial, with enrollment of patients from the national comprehensive Swedish Coronary Angiography and Angioplasty Registry and data collected from other national registries. The registry enrolled over 7,000 patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention and found that the treatment group had no significant benefit in comparison to the control group; no patients were lost to follow-up.³⁹ The authors estimate that the registry-based trial reduces costs to 1 percent or less of a conventional randomized trial.

Registries have also been used to allow patient access to new devices while additional data are collected to support reimbursement. If CMS cannot make a determination that a device is medically necessary with the available information, it may decide to cover the device conditionally to collect outcomes data that will answer questions specific to the risks and benefits in the Medicare population. This program, known as Coverage with Evidence Development, has stimulated the development of some device registries.⁴⁰

For example, CMS used this program to cover transcatheter aortic valve replacement in 2012. Under the terms, the agency would pay for the procedure only if hospitals enrolled the patients in the national TVT Registry.⁴¹ (See Appendix D.)

In addition to these innovation benefits, FDA could allow the use of registries to fulfill some other regulatory obligations. For manufacturers, this would help to balance the cost of registries, which would serve as another incentive to participate. For example, summary data from a registry could substitute for much of the required annual reporting for new premarket approval devices, or registries could provide adverse event reporting services for the manufacturer. Ultimately, FDA will need to provide clarity to stakeholders on how these regulatory benefits can be realized.

Registries can support cheaper and more efficient clinical trials... with the decentralized approach to registries and the electronic collection of data in the United States, realizing the potential of registries will take a focused effort by many stakeholders.

Recommendation 4.1: FDA, manufacturers, patient advocates, and clinical societies should work together to develop guidance regarding the use of registries in clinical trials for new products or expanded uses of existing products.

Registries can support cheaper and more-efficient clinical trials, as demonstrated with the TASTE trial. With the decentralized approach to registries and the electronic collection of data in the United States, realizing the potential of registries will take a focused effort by many stakeholders. As a start, manufacturers, FDA, and clinical societies should begin discussions on what advances in infrastructure and methodology can position U.S. device registries to reduce the costs of clinical trials while still producing high-quality data.

Given the current varied state of registries in the United States, these conversations should be sector-specific, with the cardiac, orthopedic, and ophthalmologic sectors taking the lead. Manufacturers and professional societies in these areas have extensive experience with international registries and are in a position to move the field forward.

Recommendation 4.2: FDA should issue a guidance document describing how manufacturers could use registry participation to fulfill regulatory responsibilities other than postmarket surveillance.

FDA has suggested that some stakeholder regulatory requirements might be met through registry participation. Specific examples of the possible incentives would encourage manufacturer support of registries.

Objective 5: Provide clarity for registry owners, providers, and patients by resolving varying legal interpretations of the Health Insurance Portability and Accountability Act, or HIPAA, privacy rule and the Federal Policy for the Protection of Human Subjects, known as the Common Rule, as they apply to registries.

Interpretations by hospitals of the Federal Policy for the Protection of Human Subjects (also known as the Common Rule) and the Health Insurance Portability and Accountability Act, or HIPAA, often make it difficult to include data from these institutions in the registries. A recent report by the Government Accountability Office stated that there is widespread concern among physicians that submission of data to a registry violates HIPAA.⁴²

Hospitals and other health care facilities typically apply the Common Rule to all research involving human subjects at those institutions. The rule requires prospective review and approval of research by an institutional review board and the informed consent (usually written) of each of the human subjects involved in the research, unless the board expressly grants a waiver of informed consent requirements.

HIPAA, among other things, requires the protection and confidential handling of protected health information for research and other purposes.⁴³ It covers the permitted uses and disclosures of individually identifiable health information.⁴⁴

Some areas of disagreement among agencies, registries, and hospitals are:

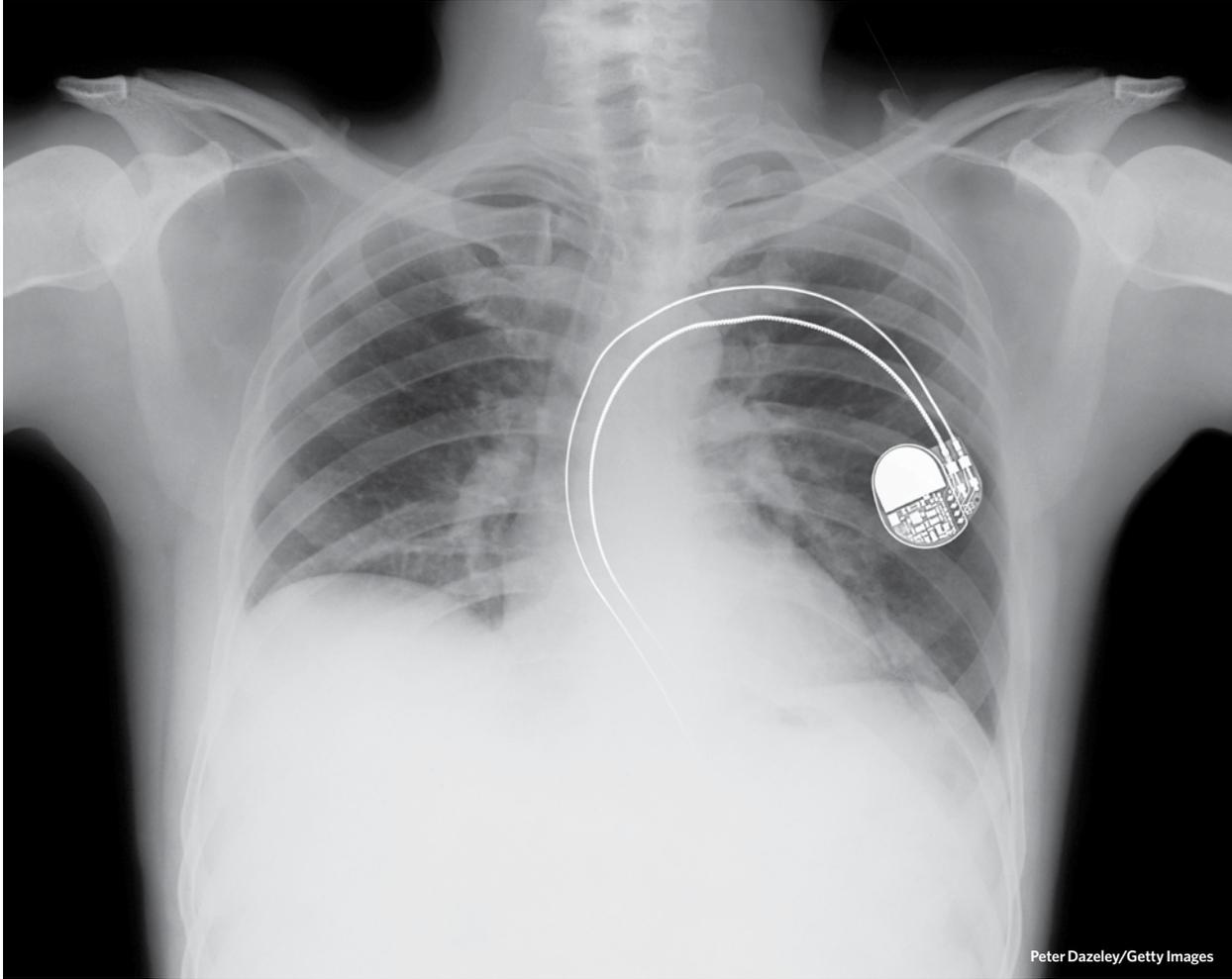
- Whether a registry using data collected for nonresearch reasons, such as patient information from an electronic health record, constitutes human subject research under the Common Rule.
- When a protocol review and waiver of informed consent from a central review board can be accepted by an institution's local board and when a separate review is necessary.
- Whether registries can be exempted from Common Rule requirements if they comply with more stringent HIPAA requirements.
- What registry data are considered protected health information under HIPAA requirements.

The Physician Clinical Registry Coalition, a group of 20 clinical data registries advocating for policy changes related to registries, wrote a Sept. 23, 2013, letter to the Department of Health and Human Services' Office of Human Research Protections stating that barriers to development "could be alleviated by the clarification of several issues that would help reduce confusion about whether the Common Rule applies to clinical data registries or the individuals or entities submitting data to registries."⁴⁵

The Agency for Healthcare Research and Quality manual on registries includes a detailed discussion of the legal considerations and frequently recommends consulting legal counsel on each issue, which substantially adds to costs. Such complexity and inconsistency has the potential to result in prohibitively expensive delays. An official agreement among federal agencies on the privacy, consent, and data ownership requirements for registries would be a significant advancement. All clinical registries are potentially subject to these legal requirements, and resolving the conflicting interpretations would reduce time and cost barriers for registry developers.

Recommendation 5.1: Work across stakeholder groups to better understand and ultimately reduce unnecessary barriers to registry data collection and use.

While registries should maintain high standards for human subject protection, legal barriers that are unnecessary for patient protection can be reduced. At the core of the question is whether registries are conducting human subjects research; very different standards apply with regard to institutional review boards and patient consent if this is the case. Given these issues, FDA, registries, and the federal HHS Office of Human Research Protections and Office for Civil Rights should work together on guidance to establish the boundary between quality improvement efforts and research activities for registries, and when requirements of HIPAA and the Common Rule do and do not apply.



Conclusion

The FDA-sponsored MDEpiNet Medical Device Registry Task Force and all U.S. registries should implement these recommendations to better understand the safety and effectiveness of medical devices. Only then will registries play a central role in a robust national surveillance system that quickly identifies poorly performing devices, provides information to patients and clinicians for shared decision-making, and supports device innovation.

Appendix A: Participant lists

Meeting facilitation

Abby Dilley, RESOLVE

Tim Sandusky, RESOLVE

Chrissie Juliano, RESOLVE

Meeting participants

- **Naomi Aronson, Ph.D.**, the Blue Cross Blue Shield Association
- **Peter Berger, M.D.**, Geisinger Health System
- **Elise Berliner, Ph.D.**, Agency for Healthcare Research and Quality
- **Shamiram Feinglass, M.D.**, Feinglass & Associates
- **Tadashi Funahashi, M.D.**, Kaiser Permanente
- **Richard Gliklich, M.D.**, Quintiles Outcome
- **Thomas Gross, M.D.**, Center for Devices and Radiological Health, Food and Drug Administration
- **Louis Jacques, M.D.**, Centers for Medicare & Medicaid Services
- **Les Levin, M.D.**, Health Quality Ontario
- **David Lewallen, M.D.**, Mayo Clinic, American Joint Replacement Registry
- **Barry Liden**, Edwards Lifesciences
- **Michael Mack, M.D.**, Baylor Health Care System
- **William Maisel, M.D.**, Center for Devices and Radiological Health, Food and Drug Administration
- **Aran Maree, M.D.**, Johnson & Johnson
- **Danica Marinac-Dabic, M.D., Ph.D.**, Center for Devices and Radiological Health, Food and Drug Administration
- **Kristi Mitchell, M.P.H.**, Avalere Health
- **Michael Mussallem**, Edwards Lifesciences
- **Kirsten Paulson**, The Pew Charitable Trusts
- **Elizabeth Paxton**, Kaiser Permanente
- **Pamela Plouhar, Ph.D.**, DePuy Orthopaedics Inc.
- **Leigh Purvis**, AARP Inc.
- **Rita Redberg, M.D.**, University of California, San Francisco
- **William Rich III, M.D. F.A.C.S.**, American Academy of Ophthalmologists
- **Josh Rising, M.D.**, The Pew Charitable Trusts
- **Joe Ross, M.D.**, Yale University
- **John Rumsfeld, M.D., Ph.D.**, Veterans Health Administration and National Cardiovascular Data Registry
- **Lewis Sandy, M.D.**, UnitedHealth Group
- **John Santa, M.D.**, Consumer Reports Health Rating Center
- **Jeff Secunda**, AdvaMed
- **Art Sedrakyan, M.D., Ph.D.**, Medical Device Epidemiology Network, Science and Infrastructure Center, Weill Cornell Medical College
- **Jeff Shuren, M.D., J.D.**, Center for Devices and Radiological Health, Food and Drug Administration
- **Tamara Syrek Jensen, J.D.**, Centers for Medicare & Medicaid Services
- **Stephanie Teleki, Ph.D.**, California Healthcare Foundation
- **Janet Trunzo**, AdvaMed
- **Ryan Wilson**, AARP Inc.
- **Chantal Worzala**, American Hospital Association

Appendix B: Meeting agendas

Future Directions for Medical Device Registries: Advancing the State of Medical Device Registries for Postmarket Study

April 30, 2013

The Pew Charitable Trusts

Philadelphia Room (5th Floor)

Agenda

Meeting Goals

- Come to a common understanding of FDA's postmarketing surveillance legal authorities over medical devices and the agency's use of those authorities.
- Obtain feedback on scientific questions that would be best answered by medical device registries.
- Compile a list of what standards are needed for registries that support FDA-mandated studies.
- Refine the work plan going forward.

Outcomes

- A summary of the deliberations, key themes, and any identified next steps.
- Identification of any work groups, and associated charges, objectives, members, and work plan between now and the next meeting.

8 a.m. **Coffee and Light Breakfast**

8:15 a.m. **Welcome, Introductions, and Overview of the Project and this Meeting**

- Josh Rising, Director, Medical Devices Initiative, The Pew Charitable Trusts
- Naomi Aronson, Executive Director, Blue Cross Blue Shield Association Technology Evaluation Center
- Art Sedrakyan, Director, Medical Device Epidemiological Network Science and Infrastructure Center
- Abby Dilley, RESOLVE

9:15 a.m. **The FDA's Legislative Authority**

Objectives: Review and establish a common understanding of FDA's authorities, history of oversight, and use of medical device registries for FDA-mandated postapproval studies

Presentation and Discussion

FDA's Legislative Authority and Its Use to Date

- Danica Marinac-Dabic, Director, Division of Epidemiology, Center for Devices and Radiological Health, FDA

FDA's use of post-approval studies since 2005

- Josh Rising, Director, Medical Device Initiative, The Pew Charitable Trusts

10:15 a.m. **Break**

10:30 a.m. **Defining "Medical Device Registry," Scope, and Rationale**

Objectives: Establish a working definition for the deliberations; clarity on the project scope, including the focus of purpose and standards of medical device registries; and rationale for advancing their effective use

Discussion

- **Working definition**

- Art Sedrakyan, Director, Medical Device Epidemiological Network Science and Infrastructure Center

- **Capabilities and limitations of registries**

- What questions can registries answer?
- Other roles of medical device registries
- Limitations of registries

- **Rationale for advancing their effective use and the scope of the deliberations (scientific questions to be answered by a registry, and standards for registries)**

11:30 a.m. **Case Studies: Transcatheter Valve Registry and Orthopedic Studies**

Objectives: Through the use of two case studies, understand what postmarket scientific questions the FDA asked concerning recently approved devices and the methodology used to answer those questions

Presentations and Discussion

12:30 p.m. **Lunch (provided)**

1p.m. **What Scientific Questions Are Answered by a Medical Device Registry?**

Objective: Articulate the postmarket scientific questions that are appropriately answered by a registry

Presentation and Discussion

2:15 p.m. **Break**

2:30 p.m. **What Are Possible Key Standards for the Effective Function of FDA-Mandated Medical Device Registries?**

Objective: Identify areas of registry design and operation where standards should be developed

Discussion

3:45 p.m.

Work Plan Review and Development and Wrap-Up

Objective: Determine a work plan for advancement of the deliberations between this and the next meeting; if work groups are established, determine scopes of work

- In addition to a revised work plan, what summary document(s) might be most useful to produce? Highlighting what themes?
- Any additional next steps?

4 p.m.

Adjourn

Future Directions for Medical Device Registries: Advancing the State of Medical Device Registries for Postmarket Study

June 26, 2013

The Pew Charitable Trusts
Carolinas Room (10th Floor)

Agenda

Meeting Goals

- Review, discuss, and refine the work group-proposed framework for which medical devices should be followed in registries that assess patient outcomes.
- Discuss how device registries that assess patient outcomes can maximize value for multiple stakeholders.
- Assess models of transparency and governance that are appropriate for medical device registries and identify other structural elements where best practices exist to meet stakeholder needs.
- Refine the work plan going forward.

Outcomes:

- A summary of the deliberations, key themes, and any identified next steps.
- Identification of work group(s) charges, objectives, members, and work plan between this and the next meeting in September.

8 a.m. **Coffee and Light Breakfast**

8:45 a.m. **Welcome, Round of Introduction, Update of Activities Since April Meeting, and Review of Goals and Agenda for This Meeting**

- Rebecca Rimel, President and CEO, The Pew Charitable Trusts
- Josh Rising, Director, Medical Devices, The Pew Charitable Trusts
- Abby Dilley, RESOLVE

9:15 a.m. **Scope of These Deliberations and Their Relationship to FDA's Efforts**

Objectives: Review the proposed scope and framework of the meetings. Discuss and reach a general understanding of the broad landscape in which device registries function as a critical, integrated component.

- Josh Rising

9:45 a.m. **For Which Devices Are Additional Data Most Needed, Why, and for Which Should Registry Development Be Prioritized?**

Objective: Understand which types of medical devices generate questions that should be studied through registries and the associated data elements that should be collected.

Which Devices Should Be Followed in Registries-Work Group Discussion

- John Rumsfeld

Additional Proposed Questions for Discussion

- Naomi Aronson
 - Should different approaches apply to assessing the postmarket performance of first-of-a-kind devices vs. devices in a class that is well-established?
 - How important is it to assess the relative performance of devices in the same class?
 - For which types of devices are operator characteristics particularly important to assess?
 - What are the device characteristics for which performance among different patient populations is particularly important to assess?

Break as Needed

11:15 a.m.

When Are Registries the Right Tool for Assessing Medical Device Performance?

Objective: Define the data needs best addressed with a post-market patient registry.

- Art Sedrakyan

12 p.m.

Lunch (provided)

12:45 p.m.

The Value Proposition: How Can Registries Involving Devices Have Value for Multiple Stakeholders?

Objective: Continue to link the development of medical device registries into the broader, evolving landscape of an active surveillance system.

- Shami Feinglass
 - How Can Registries Be Structured to Minimize the Burden on Participants?
 - How Can Registries Be Structured to Maximize the Value to All Stakeholders?
 - What Trends—Such as the Implementation of a UDI System for Devices—Will Shape the Future of Developing These Registries?

1:45 p.m.

Transparency in Medical Device Registries

Objective: Identify guiding principles for establishing transparency for patient registries involving medical devices.

- John Santa
 - What is the right level of transparency around raw data, organized data, data analysis and presentation of the data?
 - Does the right level of transparency differ based upon the registry model (registries run by clinical societies vs. manufacturers)?
 - Does the source of the data make a difference (i.e., what if the data come from a “patient” source)?
 - When and how frequently should information from registries be communicated to manufacturers, clinicians and patients?

- Should manufacturers have an opportunity to respond to findings from the registry before they are released?
- Can unintended consequences be avoided? Are unintended consequences occurring in the present “system”?
- Are there best practices to learn from?
- Are there other registry areas where transparency should be addressed?

2:30 p.m. **Break**

2:45 p.m. **Governance in FDA-Mandated Medical Device Registries**

Objective: Identify components of registry governance that are critical for effective registries.

- David Lewallen
 - What governance models exist, and are there identifiable best practices?
 - What is the role for patients, consumers, clinicians, manufacturers/sponsor and other stakeholders in the governance of registries?
 - Does the governance model affect other key registry elements, for example external data verification and analysis?

3:30 p.m. **Work Plan Review and Development and Wrap-up**

Objective: Determine a work plan for advancement of the deliberations between this and the next meeting; if work groups are established, determine scopes of work.

- In addition to a revised work plan, what summary document(s) might be most useful to produce? Highlight themes?
- Any additional next steps?

4 p.m. **Adjourn**

Future Directions for Medical Device Registries: Advancing the State of Medical Device Registries for Postmarket Study

Sept. 18, 2013

The Pew Charitable Trusts
Carolinas Room (10th Floor)

Agenda

Meeting Goals

- Review, discuss, and refine the policy findings and/or recommendations presented by the project partners.
- Discuss additional key questions regarding the effective and efficient use of registries to establish an active surveillance system for medical devices, including possible funding mechanisms for building and sustaining medical device registries, how to initiate registries, etc.
- Ideas for actions that could be taken regarding specific devices, based on the proposed criteria, decision-making process, and overall move toward a more active surveillance system.
- Discuss the overall work plan and, ultimately, the dissemination of a white paper the partners are drafting and next steps for the group participants.

Outcomes:

- Refined and further developed key findings/recommendations.
- Additional ideas for shaping the role of registries, including preparation and release of the white paper by the partners within the context of the broader landscape of efforts on medical devices.
- Clarity on next steps for engagement of this group and other related activities.

8:15 a.m. **Coffee and Light Breakfast**

8:45 a.m. **Welcome, Introductions, and Review of Goals and Agenda for this Meeting**

- Josh Rising, Director, Medical Devices, The Pew Charitable Trusts
- Abby Dilley, RESOLVE

9 a.m. **Development of Recommendations and White Paper in the Broader Context**

Objective: Provide an overview of the development of a white paper, including the work thus far, outreach for additional input, timeline and avenues for publications, and collective and individual activities of the partners.

- Josh Rising, Director, Medical Devices, The Pew Charitable Trusts
- Naomi Aronson, Executive Director, Blue Cross Blue Shield Association Technology Evaluation Center
- Art Sedrakyan, Director, Medical Device Epidemiological Network Science and Infrastructure Center, Weill Cornell Medical College

9:15 a.m. **Transparency and Release of Information**

Objectives: Review, discuss, further develop and revise the draft recommendations pertaining to transparency and information availability.

10:15 a.m.

Decision-making for the Establishment of a Registry

Objective: Further discuss the criteria to determine when a device should be followed in a registry and develop the decision-making process.

In Full Group: Brief Review of Document

- Questions of safety and effectiveness
- Other questions

Break (15 minutes) and Reconvene Into Three Work Groups to Discuss Case Examples

- For each case:
 - Do the criteria help clarify whether the medical device is a strong candidate for a registry?
 - Did other questions or criteria come up? If so, which ones and why?
 - For criteria that indicated the medical device could benefit from a registry, are they amenable to long- or short-term data collection efforts?
 - Are there any insights for initiation of a registry (i.e., how steps can be taken to initiate and by whom)?
- Reconvene in full group to share small group discussions/insights and address the following questions:
 - Do the recommendations contain the right level of clarity and specificity?
 - Do the recommendations help shape how to think most effectively about registries? In other words, are the recommendations actionable?

12:30 p.m.

Lunch (provided)

1:15 p.m.

Initiating, Building, and Sustaining Medical Device Registries

Objective: Discuss how—for devices that meet the established criteria—the initiation of registries can be accomplished and their sustainability can be ensured. Identify top priorities for devices registries.

- Building on case study discussions, are there other insights on how registries are initiated and by whom?
- What is the sustainability model for registries with long-term data collection needs?
- What incentives can be highlighted or added to maintain engagement over time?
- When is it time to sunset?

3 p.m.

Break

3:15 p.m.

Other Recommendations and Insights

Objective: Thinking back over the day—what else needs to be said?

3:30 p.m.

Next Steps, Wrapping Up This Process, and Discussion of Plan Moving Forward

Objective: Discuss next steps for partners and group participants.

- Process regarding white paper drafting, review, and finalization.
- Additional outreach and input.
- Role of participants moving forward, in paper dissemination, etc.

4 p.m.

Adjourn

Appendix C: Reporting of adverse events and postmarket studies

Reporting of adverse events. Manufacturers and health care facilities, such as hospitals and nursing homes, must file reports to FDA when device malfunctions, serious injuries, or deaths associated with medical devices occur. Additionally, consumers and clinicians are encouraged to voluntarily report problems with devices. FDA receives “several hundred thousand”⁴⁶ medical device reports, or MDRs, of suspected device-associated deaths, serious injuries, and malfunctions each year. The agency uses the MDRs to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessments of these products.

Although the MDRs are an important source of information, this passive surveillance system has well-known limitations.⁴⁷ Reports may be incomplete, inaccurate, or biased. In addition, the occurrence rate of an event cannot be determined because of potential underreporting of events and lack of information about the frequency of device use (so-called denominator data). FDA often has difficulty in determining the model of a device referenced in an MDR.

Postmarket studies. FDA can require the manufacturers of some devices to conduct additional studies on their products in the postmarket setting. As one example, the agency directed the manufacturer of a cervical disc prosthesis to follow 330 patients from the premarket study for seven years following implant and submit information on patient outcomes in annual reports.⁴⁸ In another instance, FDA mandated manufacturers of metal-on-metal hips to further study the performance of their devices after they were found to have a high failure rate. Postmarket studies can be designed as registries if only observational data are needed. However, establishing a new registry may not be practical for small postmarket studies.

Postmarket studies have limitations as well. For example, more than three-quarters of the metal-on-metal hip studies required by FDA had no approved study protocol one year after they were ordered.⁴⁹ Studies may take a significant amount of time to enroll patients, in part because there is no national infrastructure in which to embed the research. In studies that enroll only a small number of patients, it is difficult to reach definitive conclusions owing to the lack of statistical power or ability to detect rare events in smaller populations.⁵⁰ When the studies are completed and reported to FDA, the results are posted on its website.⁵¹

Appendix D: Examples of registries in the United States

The following list gives examples of some of device registries that exist in the United States, organized by the groups that established them:

Medical professional societies. Medical societies often run registries that are primarily designed to assess physician and hospital performance. Some of these registries also collect information on devices that are used in procedures conducted by members of the societies.

The National Cardiovascular Data Registry, or NCDR, is the American College of Cardiology's group of seven registries, including those for procedures involving implantable cardioverter defibrillators and leads, diagnostic cardiac catheterization, and percutaneous coronary intervention.⁵²

The most recent addition to the NCDR is the TVT Registry, which was initiated in June 2012 to track real-world outcomes related to the new transcatheter aortic valve replacement procedure. FDA ordered the manufacturer of this innovative device to conduct postmarket studies, as did CMS through Coverage with Evidence Development. Ultimately, FDA, CMS, the Society of Thoracic Surgeons, the American College of Cardiology, and the manufacturer developed the TVT Registry through a collaborative process. As of December 2013, only one type of transcatheter valve has been approved for sale in the United States. The TVT Registry recently published its first report on the performance of the device.⁵³

FDA has used data from the NCDR to investigate the performance of cardiac devices when potential problems have been identified.⁵⁴ One limitation of the NCDR is that it does not typically release information to the public about the performance of specific devices or routinely perform analyses on specific devices.

The American Academy of Ophthalmology recently initiated the Intelligent Research in Sight, or IRIS, Registry, an eye disease clinical registry, with the goal of quality of care and outcome improvement. IRIS intends to include device assessment as part of the registry's work.

Manufacturers. Manufacturers have started and operated their own registries to study outcomes related to their products. They can sometimes use these registries to fulfill FDA postmarket obligations. For example, Medtronic has registries for several of its devices, including a Product Surveillance Registry for Medtronic neurostimulation systems.⁵⁵ Medtronic's website includes annual product performance reports with study characteristics such as the number of patients, primary treatment indication, product performance events, number of patients with an adverse event, and number of deaths. All of the data analysis is done within Medtronic; while its device performance reports present data by model, they do not include any comparison to devices outside of Medtronic.⁵⁶ Manufacturer registries are limited because—due to data protection—they do not compare similar devices across different companies. Additionally, these registries are often limited by the fact that not all manufacturers make findings from their registries public.

Clinical systems. A number of health systems have established registries to learn about various aspects of care. One of the most notable examples is Kaiser Permanente, which developed implant registries to understand how patient demographics, surgical techniques, and specific implants are associated with patient outcomes. Kaiser currently runs registries for patients with replacement heart valves, total joint replacements, cardiac implantable devices (pacemakers, implantable cardiac defibrillators, and stents), spine implants, and anterior cruciate ligament reconstruction implants.⁵⁷ However, like manufacturer registries, those run by clinical systems do not always make their findings publicly available. Additionally, clinical systems may not use all of the devices on the market, so their conclusions may be limited.

Other

- The American Joint Replacement Registry, or AJRR, was launched in 2009 as a collaborative effort by many stakeholders, including orthopedic surgeons, manufacturers, and payors. Currently, over 270 hospitals are members of the AJRR. The most recent registry report was released in fall 2013.⁵⁸
- The California Joint Replacement Registry, or CJRR, is funded by a grant from the California HealthCare Foundation, managed by the Pacific Business Group on Health, and supported by the California Orthopaedic Association. The registry collects information on hip and knee replacement surgeries performed in the state.⁵⁹ It incorporates clinical information and direct feedback from patients to develop postsurgery outcome information and when needed, generates safety alerts on devices whose short-term results provoke concern. As of spring 2012, the CJRR reported that 10 hospital sites were members, representing about 18 percent of annual hip and knee replacements in California; the CJRR aims to capture about 30 percent of such procedures in the state.⁶⁰ Further information regarding the data is not publicly available.
- The Department of Veterans Affairs Cardiovascular Assessment, Reporting, and Tracking, or CART, system is a surveillance program specific to cardiovascular disease. It is integrated into the VA's electronic health records system and is used for quality management, patient-safety surveillance, and research. A key piece of CART's success is the department's specific electronic health record system: the Computerized Patient Record System.⁶¹ Annual results are not made public.⁶²
- The Interagency Registry for Mechanically Assisted Circulatory Support, or INTERMACS, was established in 2005 to collect long-term data for left ventricular assist devices and other circulatory support devices such as total artificial hearts. INTERMACS was established jointly by the National Institutes of Health's National Heart, Lung, and Blood Institute, CMS, and FDA. FDA accepts data collected through the registry to meet postapproval regulatory requirements, and CMS required hospitals to participate in the registry as a condition for receiving payment for a procedure.⁶³ Over 12,000 patients at more than 150 sites are enrolled in the registry.⁶⁴

FDA approved the HeartWare ventricular assist system in November 2012. The premarket clinical trial compared outcomes from 137 advanced heart failure participants using the system with those from similar patients followed by INTERMACS. According to an FDA news release, it was the first time the agency approved a left ventricular assist device using registry data as the control arm of a study.⁶⁵ In November 2013, INTERMACS registry data were used to investigate concerns of elevated thrombosis rates for a newer HeartMate model. Researchers observed an increasing occurrence of pump thrombosis, which is associated with morbidity and mortality, with the use of this device.⁶⁶

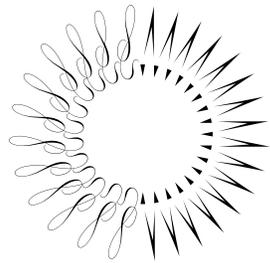
Endnotes

- 1 Food and Drug Administration, Center for Devices and Radiological Health, "Strengthening Our National System for Medical Device Postmarket Surveillance" (2012), 4, accessed Feb. 19, 2014, <http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/UCM301924.pdf>.
- 2 A.J. Smith et al., "Failure Rates of Stemmed Metal-on-Metal Hip Replacements: Analysis of Data From the National Joint Registry of England and Wales," *Lancet* 379, no. 9822 (2012): 1199–204, accessed May 28, 2014, <http://www.ncbi.nlm.nih.gov/pubmed/22417410>.
- 3 Food and Drug Administration, "Premarket Approval" (2012), accessed Feb. 19, 2014, <http://www.fda.gov/Medicaldevices/Deviceregulationandguidance/Howtomarketyourdevice/Premarketsubmissions/Premarketapprovalpma/Default.Htm>.
- 4 S.S. Dhruva, L.A. Bero, and R.F. Redberg, "Strength of Study Evidence Examined by the FDA in Premarket Approval of Cardiovascular Devices," *Journal of the American Medical Association* 302, no. 24 (2009): 2679–85, <http://jama.jamanetwork.com/article.aspx?articleid=185124>.
- 5 R.G. Hauser, D. McGriff, and L.K. Retel, "Riata Implantable Cardioverter-Defibrillator Lead Failure: Analysis of Explanted Leads With a Unique Insulation Defect," *Heart Rhythm* 9, no. 5 (2012): 742–9, doi:10.1016/j.hrthm.2011.12.019.
- 6 J.S. Rumsfeld and E.D. Peterson, "Achieving Meaningful Device Surveillance: From Reaction to Proaction," *Journal of the American Medical Association* 304, no. 18 (2010): 2065–6, doi: 10.1001/jama.2010.1648.
- 7 R.E. Gliklich and N.A. Dreyer, eds., *Registries for Evaluating Patient Outcomes: A User's Guide*, 2nd ed. (Rockville, MD: Agency for Healthcare Research and Quality, 2010).
- 8 Food and Drug Administration, "Strengthening Our National System for Medical Device Postmarket Surveillance" (2012), 1, <http://www.effectivehealthcare.ahrq.gov/ehc/products/74/531/Registries%202nd%20ed%20final%20to%20Eisenberg%209-15-10.pdf>.
- 9 National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases, "Questions and Answers About Hip Replacement," accessed April 1, 2014, http://www.niams.nih.gov/health_info/Hip_Replacement.
- 10 American Academy of Orthopaedic Surgeons, "FDA Orders Postmarket Studies on MOM Hip Implants" (2011), accessed Feb. 14, 2014, <http://www.aaos.org/news/aaosnow/jun11/clinical1.asp>.
- 11 S.E. Graves et al., "A Multinational Assessment of Metal-on-Metal Bearings in Hip Replacement," *Journal of Bone and Joint Surgery* 93, Suppl. 3 (2011): 43–7, doi:10.2106/JBJS.K.01220.
- 12 R.C. Starling et al., "Unexpected Abrupt Increase in Left Ventricular Assist Device Thrombosis," *New England Journal of Medicine* 370, no. 1 (2014): 33–40, doi:10.1056/NEJMoa1313385.
- 13 R. Lampert et al., "Safety of Sports for Athletes With Implantable Cardioverter-Defibrillators: Results of a Prospective, Multinational Registry," *Circulation* 127, no. 20 (2013): 2021–30, doi:10.1161/CIRCULATIONAHA.112.000447.
- 14 G.B. Hvilsom et al., "Local Complications After Cosmetic Breast Augmentation: Results From the Danish Registry for Plastic Surgery of the Breast," *Plastic and Reconstructive Surgery* 30, no. 3 (2010): 172–9, doi:10.1097/PRS.0b013e3181b0389e.
- 15 Australian Orthopaedic Association, National Joint Registry, "Lay Summary 2013 Annual Report: Hip and Knee Replacement—Supplementary Report" (2013), accessed May 13, 2014, <https://aoanjrr.dmac.adelaide.edu.au/documents/10180/127369/Lay%20Summary%202013%20Annual%20Report%20Hip%20and%20Knee%20Replacement>.
- 16 National Joint Registry Editorial Board, "National Joint Registry for England, Wales and Northern Ireland: 10th Annual Report" (2013), 14, accessed May 13, 2014, http://www.njrcentre.org.uk/njrcentre/Portals/0/Documents/England/Reports/10th_annual_report/NJR%2010th%20Annual%20Report%202013%20B.pdf.
- 17 Food and Drug Administration, "Unique Device Identification System, Final Rule," *Federal Register* 78, no. 185 (Sept. 24, 2013), accessed March 11, 2014, <http://www.gpo.gov/fdsys/pkg/FR-2013-09-24/pdf/2013-23059.pdf>.
- 18 Food and Drug Administration, Center for Devices and Radiological Health, "Strengthening Our National System" (2012).
- 19 Food and Drug Administration, Center for Devices and Radiological Health, "Strengthening Our National System for Medical Device Postmarket Surveillance: Update and Next Steps" (2013), <http://www.fda.gov/downloads/MedicalDevices/Safety/CDRHPostmarketSurveillance/UCM348845.pdf>.
- 20 Food and Drug Administration, "Approval Letter: P080032 Alair Bronchial Thermoplasty System" (April 27, 2010), accessed Dec. 20, 2013, http://www.accessdata.fda.gov/cdrh_docs/pdf8/p080032a.pdf.

- 21 S.S. Dhruva and R. F. Redberg, "Evaluating Sex Differences in Medical Device Clinical Trials: Time for Action," *Journal of the American Medical Association* 307, no. 11 (2012): 1145-6, doi:10.1001/jama.2012.254.
- 22 B.G. Schwartz et al., "Review of Vascular Closure Devices," *Journal of Invasive Cardiology* 22, no. 12 (2010): 599-607, <http://www.invasivecardiology.com/content/review-vascular-closure-devices>.
- 23 J.A. Reekers et al., "CIRSE Vascular Closure Device Registry," *Cardiovascular and Interventional Radiology* 34 (2011): 50-3, doi:10.1007/s00270-010-0004-y.
- 24 J.V. Freeman et al., "Physician Procedure Volume and Complications of Cardioverter-Defibrillator Implantation," *Circulation* 125, no. 1 (2012): 57-64, doi:10.1161/CIRCULATIONAHA.111.046995.
- 25 Gliklich and Dreyer, *Registries for Evaluating Patient Outcomes*, 189.
- 26 H.M. Krumholz et al., "A Historic Moment for Open Science: The Yale University Open Data Access Project and Medtronic," *Annals of Internal Medicine* 158, no. 12 (2013): 910-1, doi:10.7326/0003-4819-158-12-201306180-00009.
- 27 P.D. Franklin, L. Harrold, and D.C. Ayers, "Incorporating Patient-Reported Outcomes in Total Joint Arthroplasty Registries: Challenges and Opportunities," *Clinical Orthopaedics and Related Research* 471, no. 11 (2013): 3482-8, doi:10.1007/s11999-013-3193-2.
- 28 Kaiser Permanente, "Surveillance, Prevention, and Management of Diabetes Mellitus (SUPREME-DM)" (2012), accessed Feb. 19, 2014, <http://www.supreme-dm.org/Cores.html>.
- 29 G.A. Nichols et al., "Construction of a Multisite DataLink Using Electronic Health Records for the Identification, Surveillance, Prevention, and Management of Diabetes Mellitus: The Supreme-DM Project," *Preventing Chronic Disease* 9 (2012): E110, doi:10.5888/pcd9.110311.
- 30 J.A. Schreiber, "Electronic Health Records: Current Issues in Oncology," *Oncology Nursing Forum* 40, no. 1 (2013): 14-6, doi:10.1188/13.ONF.14-16.
- 31 Centers for Medicare & Medicaid Services, "Decision Memo for Ventricular Assist Devices as Destination Therapy (CAG-00432R)" (2013), accessed May 13, 2014, <http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=268&NcaName=Ventricular+Assist+Devices+for+Bridge-to-Transplant+and+Destination+Therapy&NCDId=246&IsPopUp=y&bc=AAAAAAACAAAA%3d%3d&>.
- 32 Clinical Trials Transformation Initiative, "Large Simple Trials: Summary" (2013), accessed Dec. 17, 2013, <http://www.ctti-clinicaltrials.org/what-we-do/investigational-plan/large-simple-trials>.
- 33 Centers for Medicare & Medicaid Services, "Physician Quality Reporting System" (2014), accessed Dec. 20, 2013, <http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/PQRS>.
- 34 Centers for Medicare & Medicaid Services, "Decision Memo for Ventricular Assist Devices as Destination Therapy (CAG-00119R)" (2007), accessed Dec. 11, 2013, <http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=187&NCDId=246&ncdver=5&NcaName=Ventricular+Assist+Devices+as+Destination+Therapy>.
- 35 Food and Drug Administration, "Summary of Safety and Effectiveness Data: HeartWare Ventricular Assist System P100047" (2012), accessed Feb. 19, 2014, http://www.accessdata.fda.gov/cdrh_docs/pdf10/P100047b.pdf.
- 36 S.H. Jain, P.H. Conway, and D.M. Berwick, "A Public-Private Strategy to Advance the Use of Clinical Registries," *Anesthesiology* 117, no. 2 (2012): 227-9, doi:10.1097/ALN.0b013e318259a9ed.
- 37 Food and Drug Administration, "FDA Approval Expands Access to Artificial Heart Valve for Inoperable Patients" (Sept. 23, 2013), accessed Feb. 19, 2014, <http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm369510.htm>.
- 38 M.S. Lauer and R.B. D'Agostino, "The Randomized Registry Trial—The Next Disruptive Technology in Clinical Research?" *New England Journal of Medicine* 369, no. 17 (2013): 1579-81, doi:10.1056/NEJMp1310102.
- 39 O. Fröbert et al., "Thrombus Aspiration During ST-Segment Elevation Myocardial Infarction," *New England Journal of Medicine* 369, no. 17 (2013): 1587-97, doi:10.1056/NEJMoa1308789.
- 40 Centers for Medicare & Medicaid Services, "Coverage With Evidence Development" (2013), accessed Dec. 11, 2013, <http://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/index.html>.
- 41 Centers for Medicare & Medicaid Services, "Decision Memo for Transcatheter Aortic Valve Replacement (TAVR) (CAG-00430N)" (2012), accessed Dec. 6, 2013, <http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=257&ver=4&NcaName=Transcatheter>.

- 42 Government Accountability Office, *Clinical Data Registries: HHS Could Improve Medicare Quality and Efficiency Through Key Requirements and Oversight*, Report No. GAO-14-75 (2013), accessed Feb. 19, 2014, <http://www.gao.gov/assets/660/659701.pdf>.
- 43 45 CFR § 160; 45 CFR § 164.
- 44 45 CFR § 160.103.
- 45 R.M. Portman, letter to Jerry A. Menikoff at Health and Human Services' Office for Human Research Protections, Sept. 23, 2013, accessed Feb. 20, 2014, <http://www.sts.org/sites/default/files/documents/Registry%20Coalition%20-%20Letter%20to%20J%20Menikoff%20OHRP%20Sept%20%202013.pdf>.
- 46 Food and Drug Administration, "MAUDE—Manufacturer and User Facility Device Experience" (2014), accessed Oct. 20, 2013, <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/textsearch.cfm>.
- 47 Institute of Medicine, "Medical Devices and the Public's Health: The FDA 510(k) Clearance Process at 35 Years" (National Academies Press: Washington, July 29, 2011), accessed Feb. 19, 2014, <http://www.iom.edu/Reports/2011/Medical-Devices-and-the-Publics-Health-the-FDA-510k-Clearance-Process-at-35-Years.aspx>.
- 48 Food and Drug Administration, Center for Devices and Radiological Health, "Approval Letter: P110009 Mobi-C Cervical Disc Prosthesis" (Aug. 23, 2013), accessed Nov. 19, 2013, http://www.accessdata.fda.gov/cdrh_docs/pdf11/P110009a.pdf.
- 49 J.P. Rising, I.S. Reynolds, and A. Sedrakyan, "Delays and Difficulties in Assessing Metal-on-Metal Hip Implants," *New England Journal of Medicine* 367, no. 1 (2012), e1, <http://www.nejm.org/doi/full/10.1056/NEJMp1206794>.
- 50 Food and Drug Administration, "Post-approval Studies: P020018 S010. 2014," accessed Feb. 19, 2014, http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?c_id=151&t_id=371805; and Food and Drug Administration, "Post-approval Studies: P050033," accessed Feb. 19, 2014, http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?c_id=151&t_id=371805.
- 51 Food and Drug Administration, "Post-approval Studies," accessed Feb. 19, 2014, http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm.
- 52 F.A. Masoudi et al., "Cardiovascular Care Facts: A Report From the National Cardiovascular Data Registry: 2011," *Journal of the American College of Cardiology* 62, no. 21 (2013): 1931–47, doi:10.1016/j.jacc.2013.05.099; and J.S. Rumsfeld, G.J. Dehmer, and R.G. Brindis, "The National Cardiovascular Data Registry: Its Role in Benchmarking and Improving Quality," *U.S. Cardiology* 6 (2009): 11–5, accessed May 28, 2014, <http://www.radcliffecardiology.com/articles/national-cardiovascular-data-registry-its-role-benchmarking-and-improving-quality>.
- 53 M.J. Mack et al., "Outcomes Following Transcatheter Aortic Valve Replacement in the United States," *Journal of the American Medical Association* 310, no. 19 (2013): 2069–77, <http://jama.jamanetwork.com/data/Journals/JAMA/929168/joi130093.pdf?resultClick=3>.
- 54 D.R. Tavis et al., "Risk of Local Adverse Events by Gender Following Cardiac Catheterization," *Pharmacoepidemiology and Drug Safety* 16, no. 2 (2007): 125–31, doi:10.1002/pds.1307.
- 55 Medtronic International Trading Sàrl, "Product Surveillance Registry—Deep Brain Stimulation for Epilepsy (MORE)" (May 15, 2014), accessed May 28, 2014, <http://clinicaltrials.gov/ct2/show/NCT01521754>.
- 56 Medtronic Inc., "Medtronic Product Performance Report" (March 31, 2014) 36–7, accessed May 13, 2014, http://professional.medtronic.com/wcm/groups/mdtcom_sg/@mdt/@neuro/documents/documents/2013-ppr-report.pdf.
- 57 Kaiser Permanente, "National Implant Registries" (2008), accessed May 13, 2014, <http://www.kpimplantregistries.org>.
- 58 American Joint Replacement Registry, "American Joint Replacement Registry: Fall 2013 Update" (2013), accessed May 13, 2014, http://teamwork.aaos.org/ajrr/AJRR%20Documents/AJRR%20Fall%202013_F11062013.pdf.
- 59 California Joint Replacement Registry website, accessed March 17, 2013, <http://www.caljrr.org>.
- 60 Pacific Business Group on Health, "Improving the Value of Specialty Care With a Focus on Joint Replacements: Action Steps for Purchasers," California Joint Replacement Registry Issue Brief (2012), accessed April 28, 2014, http://www.pbgh.org/storage/documents/CJRR_IssueBrief_11.pdf.
- 61 Institute of Medicine, "Medical Devices and the Public's Health."
- 62 T.T. Tsai et al., "Feasibility of Proactive Medical Device Surveillance: The VA Clinical Assessment Reporting and Tracking (CART) Program," *Medical Care* 51, no. 3, Suppl. 1 (2013): S57–61, doi:10.1097/MLR.0b013e31827da819.

- 63 Centers for Medicare & Medicaid Services, "Decision Memo for Ventricular Assist Devices."
- 64 University of Alabama School of Medicine, "Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS)," accessed Dec. 10, 2013, <http://www.uab.edu/medicine/intermacs>.
- 65 Food and Drug Administration, "FDA Approves Pump for Heart Failure Patients Awaiting Heart Transplant" (Nov. 20, 2012), accessed Dec. 11, 2013, <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm328818.htm>.
- 66 Starling et al., "Unexpected Abrupt Increase," 33-40.



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