

IMDRF International Medical
Device Regulators Forum

Final Document

International Medical Device Regulators Forum

**Title: Principles of International System of Registries Linked to
Other Data Sources and Tools**

Authoring Group: IMDRF Patient Registries Working Group

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A handwritten signature in black ink, appearing to read 'Fabio P. Quintino', enclosed within a large, loopy oval shape.

Fabio P. Quintino, IMDRF Chair

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Preface

The document herein was produced by the International Medical Device Regulators Forum (IMDRF), a voluntary group of medical device regulators from around the world. The document has been subject to consultation throughout its development.

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1.0 Introduction

The International Medical Device Regulators Forum (IMDRF) Registry Working Group was created with the purpose of developing:

- (1) Essential principles for linking electronic patient, device and outcome registries and/or related data repositories or identifiers such as Unique Device Identifiers (UDIs), including the principles behind data access, security, informatics formats, governance and other key areas related to global regulatory applications for medical device evaluation; and
- (2) Essential principles related to optimal methodologies for analysis of heterogeneous data sources applied to medical device safety, signal detection, performance and reliability.

This report focuses on the task described in (1).

2.0 Scope

This document provides information and guidance on:

- Vision for international system of registries linked to other relevant data sources and tools that would add value to multiple stakeholders including regulators
- Definition and qualifiers that define the impact, value and sustainability of registries
- Successes in building national registries and international collaborations
- Data features and quality requirements for participating registries
- Desirable dimensions of data for assuring analysis validity when linking registries with other relevant data sources and tools

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4.0 Vision for International System of Registries Linked to other Data Sources and Tools.

4.1 Vision and Purpose

- I. We envision international collaboration in medical device evidence generation, synthesis and appraisal. Robust registries and collaborative registry consortia are key pillars of international enterprise.
- II. The international collaboration will harness the global strength of international experience with devices, and leverage individual country strengths in cardiac, vascular and orthopedic areas. While not all countries will contribute data to every device evaluation, all countries will benefit from the global collaborative.
- III. Worldwide, regulators will initiate early engagement with their respective registries and other relevant data sources to (a) commence multi-stakeholder communication of their needs, (b) establish a value proposition for implementation/strengthening of device registries within existing registry systems and (c) promote the usage of unique device identification.
- IV. The international collaboration will establish a forum and a set of priority questions related to devices in collaboration with registry leaders and other stakeholders.
- V. The priority questions related to devices in cardiac, vascular, orthopedic, and other clinical areas will be sufficiently broad to facilitate registry creation/collaboration but also sufficiently specific to inform actionable processes.
 - a. Priority questions related to devices will be dynamic, changing over time as current ones are answered and as new questions emerge. As treatment outcomes are influenced by many factors, including device performance and non-device related factors such as patient selection/number of patients, clinician experience and skills, and hospital settings (e.g. geographic scope such as national and/or regional territories and their local practices), consideration of all relevant factors will ensure the data gathered by the registry provides valuable, meaningful results.
 - b. Continuous (e.g. semi- annual) analyses by registry consortia (e.g. ICOR, ICVR, ICCR) will be undertaken in order to keep stakeholders informed about consistent or changing risk posed by devices.

4.2 Definition of Medical Device Registry

For the purpose of the development of the IMDRF registry essential principles document the medical device registry is defined as:

Organized system with a primary aim to increase the knowledge on medical devices contributing to improve the quality of patient care that continuously collects relevant data, evaluates meaningful outcomes and comprehensively covers the population defined by exposure to particular device(s) at a reasonably generalizable scale (e.g. international, national, regional, and health system)". We think that such revised definition might better reflect the use of medical devices registry data to increase the quality of medical care.

Additionally, the following qualifiers define the impact, value and sustainability of the medical device registry:

1. **DEVICE:** The registry contains sufficient information to uniquely identify the device. Ideally, the unique device identifier would be included, but when the UDI is not available, the registry would include a combination of identifiers (catalog, number, manufacturer, description) that, in combination, will assist in uniquely identifying the device.
2. **QUALITY IMPROVEMENT SYSTEM:** The registry is part of a health care delivery quality improvement system or evolving into one as device technologies are diffused into practice and need continuing evaluation (including outlier identification).
3. **BENEFICIAL CHANGE:** The registry has established mechanisms to bring about beneficial change in health care delivery through stakeholder participation, ownership and integration into the relevant health care systems.
4. **EFFICIENCY:** The registry is embedded in the health care delivery system so that data collection occurs as part of care delivery (i.e., not overly burdensome, not highly complicated, not overly costly, etc.) and integrated with work flow of clinical teams.
5. **ACTIONABLE DATA:** The registry provides actionable information in a relevant and timely manner to decision makers.
6. **TRANSPARENCY:** The governance structure, data access, and analytical processes of the registry are transparent
7. **LINKABILITY:** Information in the registry can be linked with other data sources for enhancement including adequate follow up achievement.
8. **TOTAL DEVICE LIFE-CYCLE:** The registry can serve as infrastructure for seamless integration of evidence throughout the device life cycle.

5.0 What can we learn from the Existing Efforts in the Orthopedic, Vascular and Cardiac Fields?

5.1 Example Registries

Several registries currently exist that fully or partially meet the registry definition and desirable elements. The descriptions below illustrate the strengths and limitations of these registries for regulatory process and global post-market surveillance system creation. Additional aim of this description is to encourage dialogue between regulators and registries for establishment of value proposition for implementation and strengthening of device registry within these existing registry systems (see vision and purpose).

5.1.1 Orthopedic

The National Joint Registry (NJR) of England, Wales and Northern Ireland

The National Joint Registry (NJR) was established by the Department of Health and Welsh Government in April 2003 to collect information on and to monitor the performance of joint replacement implants. Northern Ireland joined the NJR in 2013. The registry includes data on all hip, knee, ankle, elbow, and shoulder joint replacements across the National Health System (NHS) and the independent healthcare sector, and is the largest joint replacement registry in the world – currently the registry includes approximately 2 million records. The data from the NJR are used to monitor clinical outcomes data (rates of mortality) following surgery and also implant survivorship (measured as the time between procedures), at the level of hospital, surgeon and implant, tracking and linking information on primary and revision procedures.

The NJR is managed by the Health Quality Improvement Partnership (HQIP) on behalf of the Department of Health and the Governments of Wales and Northern Ireland. Day-to-day operations of the Registry is subcontracted to Northgate Public Services, a software and outsourcing business that manages collection and reporting of the data. Since April 2014 the NJR is funded through subscriptions charged to hospitals (on a cost per procedure basis) and to industry (for data and reporting services). The NJR reports in excess of 95% coverage nationally,

NJR of England, Wales, and Northern Ireland

- **DEVICE:** Has detailed information on each device component
 - **QUALITY IMPROVEMENT SYSTEM:** Regularly monitors surgeon and device performance and has “surgeon outlier” and “implant scrutiny” groups.
 - **BENEFICIAL CHANGE:** Informs professionals, regulators and manufacturers about device use, choices and performance. Number of documented outlier devices was no longer used as a result.
 - **EFFICIENCY:** Data collection is not being embedded in the delivery of care in some delivery sites, is extensive but easy to complete. Submission is mandatory for NHS. Data capture is electronic including bar code scanning but the majority of the data are collected on paper first.
 - **ACTIONABLE DATA:** Reports back to each participating hospitals to compare against others. Device and surgeon outcome analysis is done twice yearly and is reviewed by a designated panel. Device outliers are reported to manufacturers and competent authorities.
 - **TRANSPARENCY:** Has a formal governance system overseen by a steering committee. The NJR publishes annual detailed report. Provides manufacturers, clinicians and the UK regulator has “real-time” electronic access to relevant information to conduct their own analyses.
 - **LINKABILITY:** Linkages are carried out with hospital episode statistics. UK regulators can cross-correlate NJR data on implants with manufacturer vigilance reports.
 - **TOTAL LIFE-CYCLE:** NJR can be used to collect data on joint replacement performance for both pre-market and post-market phases. It is also used to collect/analyse data for post-market clinical follow-up.
-

and is currently undertaking Data Quality Audit to validate underlying data quality. The registry publishes an in-depth annual report in September of each year and provided regular updates about device performance to manufacturers and competent authorities and about surgeon performance to clinicians and hospitals.

Canadian Orthopedic Registry

→ **DEVICE:** Contains device information including both product number and lot number.

→ **QUALITY IMPROVEMENT SYSTEM:** Does not perform quality assurance analysis but provides data to provincial and territorial ministries of health who may engage in quality activities.

→ **BENEFICIAL CHANGE:** Produces general annual reports and 'Analyses in Brief' on relevant clinical and administrative topics. Topics are based on CIHI's consultation with stakeholders and advisory committee.

→ **EFFICIENCY:** The data comes from surgeons, Facilities, regions and Provincial ministries of health. Reporting is mandatory in Ontario, British Columbia and Manitoba. The registry is currently transitioning from paper to electronic forms including bar code scans. In process of integration into care delivery system with major success in British Columbia.

→ **ACTIONABLE DATA:** Data is provided back upon request. Occasionally perform an analysis on component type related topics, such as 2013's Analysis in Brief on early revisions and bearing surfaces and fixation method.

→ **TRANSPARENCY:** Guided by Advisory Committee that includes representative from each province and key arthroplasty stakeholder groups. Customized data are also available upon request in a privacy appropriate manner to researchers and health system managers. The CJRR does not currently release manufacturer information to third parties but has capability to reports by manufacturer

→ **LINKABILITY:** Data is linked with the Hospital Morbidity Database (HMDB) and the Discharge Abstract Database, using patient's Health Care Number. The CJRR data can be linked to CIHI's other data holdings as well

→ **TOTAL LIFE-CYCLE:** Occasional device analyses are performed. No clinical trial infrastructure yet developed for pre-market assessments.

Canadian Joint Replacement Registry

The Canadian Joint Replacement Registry (CJRR) was launched in May 2001 by the Canadian Institute of Health Information (CIHI) as a voluntary registry and has now been mandated by some provinces. It was developed to provide a rich set of additional patient-level clinical, surgical and prosthesis information beyond what is captured in the Hospital Morbidity Database and the Discharge Abstract Database, allowing for more in-depth analysis of hip and knee replacement procedures. The CJRR is now mandated in three provinces and voluntary in others. CJRR currently covers approximately 70% of all hip and knee replacement procedures in Canada.

The CJRR produces annual reports to characterize the epidemiology of hip and knee replacement procedures (including elective and urgent cases) performed in Canada. Customized data cuts are also available upon request in a privacy appropriate manner to researchers and health system managers. As of 2012–2013, CJRR implemented a new minimum data set (MDS) based on data elements recommended by the International

Society of Arthroplasty Registries such as i) Surgeon and patients demographics, and ii) General procedure information (Type of procedure, Diagnostic grouping and Reason for revision and Prosthesis Information.

Kaiser Permanente Total Joint Replacement Registry

Kaiser Permanente (KP) is one of the largest - integrated healthcare systems in the United States with 10 million members in Southern and Northern California, Northwest, Hawaii, Colorado, Ohio, Mid-Atlantic States, and Georgia. In 2001, KP implemented the first inter-regional and the

largest US population-based Total Joint Replacement Registry (TJRR). Using an integrated electronic health record (EHR), additional orthopedic (Hip fracture, Spine, Shoulder, ACL), cardiology, and vascular implant registries were also established. All surgeries are captured in the registry. Currently there are over 150,000 cases recorded over time with the follow up data available for more than 90% of patients.

Australian National Joint Registry

The Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) was established in September 1999. It was implemented in a staged manner and achieved full national implementation by mid-2002 with 100% surgeon and hospital coverage. It is currently monitoring the outcome of over one million of these procedures. In 2007 it also commenced data collection on primary, revision and re-operations of shoulder, elbow, wrist, and ankle arthroplasty as well as spinal disc replacement. The AOANJRR shoulder registry is currently the largest shoulder registry globally. The AOANJRR is owned and controlled by the Australian Orthopaedic Association (AOA) and funded by government. The AOA subcontracts an academic institution to manage data collection and undertake independent analysis.

Registry produces annual reports and almost 300 different ad hoc reports at the request of surgeons, academic institutions, researchers, government, regulatory bodies and industry each year. Over 120 outlier hip knee and shoulder prostheses have been identified and most been

removed from the market. The impact of the AOANJRR in Australia and globally has been significant. It is recognized as one of the best quality arthroplasty registries globally and within Australia since its implementation there has been a major decrease in the revision burden for joint arthroplasty and increased utilization of best practice identified by the AOANJRR.

Dutch Arthroplasty Register

The Dutch Arthroplasty Register (LROI) is a real-time online, digital quality arthroplasty registry in the Netherlands, initiated in 2007 by the Netherlands Orthopaedic Association. The completeness of the LROI is over 96%. All hospitals in the Netherlands participate in the

Australian National Joint Registry

→ **DEVICE:** Has detailed device information including attributes and major contributor to global device library.

→ **QUALITY IMPROVEMENT SYSTEM:** is national/federal Quality Assurance activity. Well integrated into the health care system within Australia.

→ **BENEFICIAL CHANGE:** used extensively by Australian Therapeutics Good's Administration (TGA) and Federal Departments of Health of each state. Used for reimbursement and procurement.

→ **EFFICIENCY:** has a paper based and electronic system for data entry. The paper based system is most efficient and in each hospital dedicated registry coordinators ensures completeness and delivery of data which is monitored weekly by registry.

→ **ACTIONABLE DATA:** contracted to inform TGA about any outlier device before the annual report is published. Surgeons and hospitals receive individualized information about their outcomes compared to national average. Data updated every 6 weeks.

→ **TRANSPARENCY:** The registry reports to AOA Board and publications including the annual report are reviewed by independent editorial board. The Federal Government chairs an oversight committee that includes industry and consumers. Information regarding specific products is provided to industry, researchers, and a wide range of stakeholders.

→ **LINKABILITY:** linked with major administrative data sets and a range of large cohort studies. Recently linked to cancer registries and applied to link to national drug prescription data.

→ **TOTAL LIFE-CYCLE:** Tracks every device and it's iteration in the post market area. To enhance premarket assessment it has developed the capacity to undertake clinical trials more efficiently and cost effectively.

registry. As of 2014 also shoulder-, ankle, elbow, wrist implants and revision surgeries are registered as well as patient reported outcomes for primary hip- and knee implants. As of August 2015, 244,108 hip implants and 186,813 knee implants are captured. Annually about 24,000 knee and 26,000 hip implants are performed in a Dutch population of 18 million. The LROI provides mirror information on a real-time web-based dashboard on the types of implants, operation techniques, and patient variables. As a result, orthopaedic departments can improve their performance by comparing their own data with national data. A second important aim of the LROI is to ensure that all joint implants are traceable at a national level. In case of a recall, all registered implants (i.e. article and lot numbers) de-encryption of the Unique Identification Number (BSN) of the patient is possible at the hospital level. In 2015, the Government of The Netherlands will also establish, according to EU regulations, a national implant registry, where all data from existing implanted medical devices will be uploaded with a unique identification code which can be traced back to the hospital. This registry is financed by a surcharge by health insurers on the hospitals DRG for hip and knee arthroplasty surgery. The registry recently had an impact on use of more evidence based implants. Overall there are about 95 different hips and 90 acetabular cups used in Netherlands.

Brazilian National Implants Registry

The first approach to implement Orthopedic Registry was started by Brazilian Society of Orthopedics (SBOT) in 2007. In 2008, the SBOT initiated data collection using paper based questionnaires and faced several challenges such as data collection complexity and informatics. The SBOT contacted ANVISA (Brazilian National Health Surveillance Agency) to initiate a comprehensive registry creation. In 2010 ANVISA started a Project to develop registry. In a first step, a data collection tool with the most important questions about surgery and implant details was developed. This questionnaire was pilot tested in the electronic patient records of a public hospital specializing in Orthopedics in Porto Alegre. A larger, second pilot was conducted in 15 hospitals of Curitiba, a city of two million people. All hip and knee arthroplasty surgery data were collected in these hospitals. Based on these experiences, ANVISA is currently developing a software platform that will be implemented nationwide with possible expansion to other implants (e.g. cardiology). The new platform, called RNI (National Implants Registry), will (a) identify

Brazilian National Implants Registry

Scope: aiming to be national and the platform to be used is in developmental stage.

→ **DEVICE:** It will have detailed device information. ANVISA is working on regulations to guarantee the appropriate labels. As part of IMDRF, the Agency will work to implement in the future UDI.

→ **QUALITY IMPROVEMENT SYSTEM:** It is not a quality assurance system, but information could be used to insert data for quality systems.

→ **BENEFICIAL CHANGE:** In the future, sufficient information to guide actions and decisions to improve Health Care System is anticipated.

→ **EFFICIENCY:** It is a database that will be incorporated by public hospitals and it will be available for private hospitals. Regarding device information, a bar code/data matrix on the product labels is requested of SBOT and hospital teams in order to make data input into the system easier and avoid typing errors.

→ **ACTIONABLE DATA:** In order to achieve this, qualified data is important and some features on system to provide data validation is foreseen. Reports and alerts will be available and they are in development stage.

→ **TRANSPARENCY:** ANVISA will manage access to stakeholders with proper scope to enable participation of different stakeholders. Guidelines will be elaborated.

→ **LINKABILITY:** It will be linked with some data sources.

→ **TOTAL LIFE-CYCLE:** It is intended to use data for post market and it could be linked to some laboratory tests on products to provide information for premarket.

demographic and clinical characteristics of patients, (b) collect patient outcomes, and (c) correlate outcomes with implanted products to provide enough data to hospitals, manufactures, and surgeons for quality improvement. A pilot version will be tested in Brazilian hospitals in the second half of 2016 and probably it will be ready in the first half of 2017. The RNI will be managed by ANVISA and data access will be available for different stakeholders (on a relevant level) to enable participation of different stakeholders. The entire project is a joint effort of ANVISA with different institutions such as the Health Ministry, Universities, Hospitals and professional associations.

5.1.2 Vascular

Vascular Quality Initiative

- **DEVICE:** Limited device information
 - **QUALITY IMPROVEMENT SYSTEM:** It is registered as a patient safety organization with the goal of quality improvement.
 - **BENEFICIAL CHANGE:** The registry has been established by Society of vascular surgeons and is gradually engaging multiple stakeholders such as regulators and manufacturers to bring about beneficial change in improving outcomes of vascular surgery. No specific findings of the registry impact on overall outcome improvement in vascular surgery are known.
 - **EFFICIENCY:** Data collection is based on web based data entry and is not yet embedded in care delivery. However, surgeons are very enthusiastically supportive within participating centers.
 - **ACTIONABLE DATA:** Provides reports back to each participating sites. Each center can compare their data against other participating centers in their regional group.
 - **TRANSPARENCY:** Analytic process is described. Data access is through specific requests. Regulator does not have direct access to data.
 - **LINKABILITY:** Can be linked with CMS claims and potentially commercial claims to enhance the data and obtain long-term outcomes. However, all linkages have to be probabilistic as it does not have a process to share identifiable patient information with claims data owners.
 - **TOTAL LIFE-CYCLE:** The registry is in a process of working with number of manufacturers to nest clinical trials.
-

Vascular Quality Initiative (VQI)

The United States Vascular Quality Initiative (VQI) is the national data registry and quality improvement vehicle for the nation's largest group of physicians that provide vascular care, the Society for Vascular Surgery. It has both centralized and decentralized management as a collaborative of regional quality groups collecting and analyzing data in an effort to improve patient care. Since 2002, the VQI has collected data from its members – currently 356 hospitals and practices in 46 states with more than 1300 physicians – for outcomes analysis, benchmarking, and quality improvement. The Vascular Quality Initiative reached maturity in 2010 and has its origins in the Vascular Study Group of Northern New England. These data include more than 120 descriptive variables describing the patient's vascular conditions, the precise details of the operative procedure and devices (stents, atherectomies, endografts, filters, dialysis access, other) utilized during the procedure, as well as detailed peri-operative and long-term outcomes. Participation and reporting is voluntary. VQI records procedures at a

rate of 7,000-8,000 procedures per month and as of July, 2015, more than 215,000 procedures had been recorded. The 1-year results are reported as part of national quality improvement registry and longer follow up requires linking with claims which are started with Medicare data. The impact of the VQI is tremendous; VQI data have informed about length of stay and compliance with evidence-based therapies – since its initiation, length of hospital stay has been reduced, a much higher compliance with evidence based therapies such as use of pre-operative

beta blockers, statins and use of patching after carotid procedures have been observed, and the costs of admission for certain procedures reduced.

Australian Vascular Audit

The Australasian Vascular Audit (AVA) is a binational vascular audit encompassing all vascular surgery performed in Australia and New Zealand, under the auspices of the Australian and New Zealand Society for Vascular Surgery (ANZSVS). The audit involves all open and endovascular aortic procedures; open and endovascular carotid procedures; infrainguinal bypass procedures and AV fistula procedures for hemodialysis. Data collection begins January, 2010 and is used to provide risk-adjusted analysis of mortality, Stroke/death, and patency for each of these 4 index operations. Apart from these index procedures, all other vascular procedures are captured on a voluntary basis. Annual reports are produced and the audit is protected by Commonwealth quality assurance protection legislation. Participation is compulsory in order to retain membership of the ANZSVS but the audit is available to non-members. Internal and external validation of Australian data is performed using Medicare (for private patients) and Australian Institute of Health and Welfare data (for all procedures). After 5 years, 65% of data has been captured compared with these external data sources in Australia. Follow up is limited to in-hospital stay only.

UK National Vascular Registry

The National Vascular Registry (NVR) is commissioned by the UK Government to measure the quality and outcomes of care for patients who undergo major vascular surgery in National Health System (NHS) hospitals in England and Wales. It aims to provide comparative information on the performance of NHS hospitals and thereby support local quality improvement as well as inform patients about the care delivered in the NHS. The NVR includes repair of Abdominal Aortic Aneurysm (AAA), Carotid endarterectomy, Lower limb angioplasty/stenting, Lower limb bypass, and Lower limb amputation for Peripheral Arterial Disease (PAD). The NVR was formed in January 2013 by the amalgamation of the National Vascular Database UK Carotid Interventions Audit projects.

The Clinical Effectiveness Unit of the Royal College of Surgeons of England is engaged in the analyses, in partnership with Northgate Public Services who manage the data collection system and data. The NVR is overseen by a project board chaired by a representative from the Royal College of Surgeons of England, and representatives from the Vascular Society of Great Britain and Ireland, the British Society of Interventional Radiology, HQIP and Northgate Public Services. In 2014 information for elective infrarenal Abdominal Aortic Aneurysm (AAA) repair and carotid endarterectomy procedures was made available for all UK NHS trusts that currently perform them. For English NHS trusts, the same information was published online for individual consultants, as part of NHS England's transparency initiative.

Japanese Registry of Endovascular Aneurysm Repair (Abdominal and Thoracic)

The Japanese Registry of Endovascular Aneurysm Repair for abdominal and thoracic aneurysm was established in 2007 when the first commercial device was approved in Japan. Since then, the Japanese Committee for Stentgraft Management (JCSM) has qualified the institution and the physicians who can perform endovascular repairs of aortic aneurysms. The JCSM has run the registry which is a Web-based Data Entry System. It is mandatory for qualified physicians to enter the data for all consecutive cases into the registry. The registry contains data elements

which include brief patient background data, anatomical morphology of aneurysm, procedure information, and short-term outcomes. While device information is collected, devices are not uniquely identifiable. It is also designed to collect 5-year follow-up data. The brief summary of procedure is released by Web page. Device companies are not allowed to access data of their own devices. There is no systematic approach for data audit.

5.1.3 Cardiac

The US Cath-PCI Registry

The NCDR® is the American College of Cardiology's suite of cardiovascular data registries helping hospitals and private practices measure and improve the quality of care they provide. The NCDR consists of five hospital based registries, one outpatient registry and two multispecialty registries. The oldest registry of the NCDR portfolio is the CathPCI (Cardiac Catheterization and Percutaneous Coronary Intervention) Registry. Created in 1998, the Cath PCI registry contains over 18,000,000 records. Approximately 95% of US hospitals participate in the CathPCI registry, and worldwide a total of 1692 sites contribute data to the registry. Device-specific capture (stents) is 100% per the CathPCI database dictionary, and the CathPCI registry is positioned to incorporate UDI once UDI is available. The CathPCI registry has been extensively analyzed, with over 200 original manuscripts authored describing key analyses of the CathPCI registry. For example, The CathPCI registry, augmented by data from a subset of voluntary hospital participants, was used to demonstrate that the VasoSeal closure device was associated with a significantly higher risk of adverse outcomes after angiography than other vascular hemostasis devices.

The US Trans-Catheter Valve Therapies (TVT) Registry

The US TVT registry started in early 2011 as the FDA initiated the framework in concert with the American College of Cardiology National Cardiovascular Device Registry (ACC/NCDR), Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database, industry, Center for Medicare Services (CMS), National Institutes of Health (NIH), and patients. The process is based on CMS National Coverage Decision (NCD) and the NCD defined CMS reimbursement strategy for transcatheter valve replacement procedures. Since that time, the number of TVT procedures performed in the USA captured in the TVT Registry has increased substantially. Currently over 54,000 patient records representing virtually all patients treated

The Japan PCI

- **DEVICE:** It has been already functioning as a national registry.
- **QUALITY IMPROVEMENT SYSTEM:** Random auditing is performed on monthly basis.
- **BENEFICIAL CHANGE:** It was established by domestic interventional professional society (Japanese Association of Cardiovascular Intervention and Therapeutics: CVIT)
- **EFFICIENCY:** It reflects both quality improvement and research priorities, identify key data elements and metrics to assess the quality of care for a specified patient population.
- **ACTIONABLE DATA:** At present, annual report is prepared by the CVIT Scientific Committee and distributed to professional members who include only interventional cardiologists and does not include distributors or manufacturers. The CVIT Scientific Committee of CVIT is currently working to develop real-time feedback system on short-term outcomes for each operator and sites (e.g. dashboard).
- **TRANSPARENCY:** Data is available upon approval by scientific committee members, and is open for use to professional members.
- **LINKABILITY:** Its format and definition is in sync with uniform electrical charting system such as SS-MIX, and could serve as a basic dataset for various clinical studies.
- **TOTAL LIFE-CYCLE:** The committee is also working towards collaborating with various manufactures to perform post-marketing survey, but has not been formally implemented as of June 2015.

in the U.S have been entered into the TVT Registry.

The Japan PCI (J-PCI) Registry

J-PCI is the national data registry that was established by Japanese Association of Cardiovascular Intervention and Therapeutics (CVIT) in 2008. Since then, the J-PCI has provided benchmarking reports to the members of the society. Its primary aim is to optimize the management and outcomes of patients with cardiovascular disease by collecting and reporting data to improve the quality and safety of care through the provision of outcomes. The J-PCI also provides data for individual board certification (for interventional cardiologists) as well as for site certification system. In concordance with other Japanese national registries, its infrastructure is built-in on the NCD. In 2013, over 220,000 coronary procedures were registered from over 500 hospitals. In addition to J-PCI, J-EVT/SHD has also been developed for registration of endovascular and structural interventions. At present, annual report is prepared by the scientific committee and distributed to professional members. The professional members include only interventional cardiologists and do not include distributors or manufacturers. The included variables are considered universal among the participating hospitals; committees of experts from multiple disciplines, reflecting both quality improvement and research priorities, identify key data elements and metrics to assess the quality of care for a specified patient population. Its format and definition is in sync with uniform electronic charting system, and could serve as a basic dataset for various clinical studies. The scientific committee of CVIT is currently working to develop real-time feedback system on short-term outcomes for each operator and sites (e.g. dashboard). Data are available upon approval by scientific committee members, and is open for use to professional members. The committee is also working towards collaborating with various manufactures to perform post-marketing survey, but this has not been formally implemented as of June 2015.

The Japanese Trans-Catheter Valve Therapy (TVT) Registry

This registry was established by the Japanese Consortium of Four Academic Societies in May 2014. The database itself is managed by the NCD, which is a national surgical database platform and provides a web-based platform for data entry system. The registry contains data elements which includes patient background data, procedure information and short-term outcomes. It is also designed to collect 5 year follow-up data. Any pre-specified adverse events need to be entered within 30-days of occurrence. In addition, the registry has a function that alarming e-mails are to be sent to device companies when an adverse event is input by the medical professionals. Device companies are allowed to access dataset of its own devices, with approval from the Consortium. Quality of data is validated through site visit (site audit).

The Japan Adult Cardiovascular Surgery Database

Japan Adult Cardiovascular Surgery Database (JACVSD) was established in 1999 as a registry of cardiovascular surgical procedure. It is not a device specific database but includes procedures which require the device such as prosthetic heart valve. JACVSD is Web based data entry system regarding the data of cardiovascular surgical procedure, which include patient background data, procedure information and early outcomes within 30 days after surgery. However no follow-up data is available. Device companies are not allowed to access dataset of its own devices. The quality of data is validated through site visits (site audit).

5.2 Current Major International Collaborations

5.2.1 ICOR

The International Consortium of Orthopedic Registries (ICOR) initiative was launched in 2011 to develop international infrastructure for addressing the evidence gaps in orthopedic implants safety and effectiveness (www.icor-initiative.org). The inaugural conference was held on May 9-10 at the headquarters of the Food and Drug Administration in Silver Spring, Maryland. Over 70 stakeholders and more than 30 orthopedic joint registries (total joint replacement) representing 14 nations are currently part of the network.

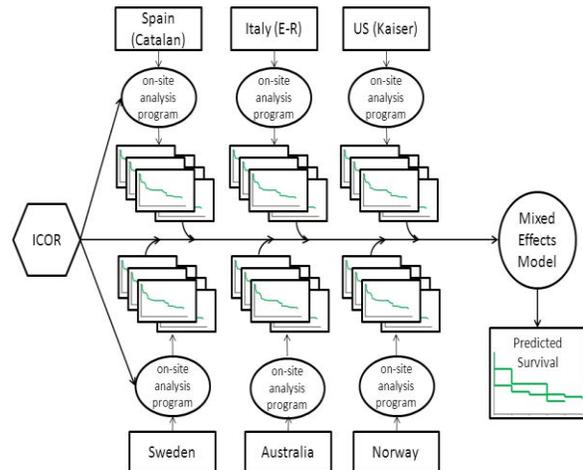


Figure 1. ICOR distributed research network & analytics

Since September 2012, the ICOR has been working on the implementation of worldwide surveillance system and meaningful use of unique device identification in orthopedics through contract with the FDA. The ICOR focused on two goals:

1. Major demonstration projects of research and surveillance for hip and knee implants
2. Harmonization of worldwide implant data through creation of implant library

Major Comparative Studies of Hip and Knee Implants:

The ICOR established a distributed data system where standardized data extraction is implemented by the ICOR coordinating center and distributed to participating registries (Figure 1). Each registry completes the analyses and then completely de-identified detailed data summaries that include all subgroup effects and interactions are shared with the coordinating center. The data is combined using multivariable hierarchical models. The main outcomes is all cause revision after surgery which reflects the patients experience and indicates failure of the implant as well the pain and suffering that necessitates second surgery.

Multinational investigations:

The expert consensus defines the priorities, the inclusion/exclusion criteria and a control group for all investigations. Over 30 projects are completed and published. Examples include:

1. International comparative evaluation of knee replacement with fixed vs mobile non-posterior stabilized implants.
2. International comparative evaluation of knee replacement with fixed vs mobile posterior stabilized implants
3. International comparative evaluation of fixed cruciate retaining versus fixed posterior cruciate substituting total knee replacement.
4. Evaluation of head size on outcomes of hip replacement in a combined analysis of six international registries: focusing on metal on Highly cross-linked polyethylene bearings
5. Comparative Effectiveness of Ceramic on Ceramic Implants in Stemmed Hip Replacement: Multinational Study of Six International Registries.

6. Distributed analysis of hip implants using six National and regional registries: comparing metal on metal to metal on Highly cross-linked polyethylene bearings in uncemented Total hip arthroplasty in young patients.
7. Total hip arthroplasty risk of revision: Metal on conventional versus metal on crosslinked results from six international registries
8. Multinational Comprehensive Evaluation of Fixation Method Used in Hip Replacement: Interaction with Age in Context.

Creating Implant Library for Orthopedic Implants: The Role of Registries

The creation of an orthopedic implant library and relevant nomenclature for device attributes and characteristics is the critical link with clinical and research community interested in devices from post market surveillance and research perspective when using registries. In orthopedics, large registries or networks of registries capture device information on very detailed level and can become particularly important for active surveillance and post-market evaluation. The registries can also provide denominator data for specific devices implants and facilitate comparative studies. This is especially the case in settings where participation to the registry is mandatory or the registries have over 90% of the exposed population coverage.

The FDA UDI rule mandates that manufacturers must label medical devices with a UDI identifier to populate the Global Unique Device Identification Database (GUDID), a public hub of standardized UDI data intended to integrate with billing, inventory, and electronic. The ICOR contribution to this process and the ICOR implant library of clinical attributes and characteristics is as an adjunct database to GUDID. Once the device identifier is included in the ICOR data library, the linkage should be by Device Identifier.

In order to monitor and evaluate total joint arthroplasty procedures, the specific devices must be accurately identified and classified. The ICOR facilitated standardized processes that enabled the development of a universal implant library that all registries could use for consistency of reporting and enhanced inter-registry collaboration.

5.3.2 International Consortium of Cardiovascular Registries

Building from the success of ICOR, in May 2013, the FDA and the MDEpiNet's Science and Infrastructure Center initiated the creation of the International Consortium of Cardiovascular Registries (ICCR) as a pioneering effort focusing on implantable valves and transcatheter valve technology. As surgical treatment options for valve disease are replaced by newer, less invasive procedures such as transcatheter valve replacement, questions about specific device performance, safety, and effectiveness remain unanswered in real-world settings. The ICTVR established a collaborative global network among transcatheter valve registries to conduct analytical projects within this consortium. The governance model and research projects build from the experience gained from ICOR. The registries participating in this network identify gaps in evidence, harmonize relevant data and create innovative methodologies to analyze data using distributed research methods :

1. To develop a multi-national distributive TAVR research network, including a governance structure whose leadership will oversee the creation of new methodological approaches for research and the establishment of public-private partnerships to address stakeholder's needs and sustainability.
2. To align the TAVR registry rare endpoint and other key variable definitions that support distributive research by reviewing current data fields in registries; summarizing, defining, and prioritizing data elements in order to reach consensus on those definitions among registry leads around the world.
3. To conduct analytic ICTVR projects using distributive research methods through the description of the international variations in , the evaluation of the association between specific patient and procedural characteristics and rare procedure-related adverse outcomes, and determine the association between specific device attributes and in-hospital and mid-term outcomes.

5.3.3. International Consortium of Vascular Registries

The mission of the International Consortium of Vascular Registries (ICVR) is to provide a collaborative platform through which registries and other stakeholders around the world can share data to improve vascular health care. The ICVR was launched in November 2014 at Cornell University as another collaboration of FDA and the MDEpiNet's Science and Infrastructure Center with participation of over 12 national registries, manufacturers and other stakeholders. The goal is to more rapidly generate evidence through worldwide registries related to vascular devices and procedures. An important component is working with manufacturers and regulators to improve the safety and effectiveness of vascular devices, to define optimal patient and pathology selection for devices, and to identify potential device problems as soon as possible.

In order to create this collaborative platform, the ICVR is leveraging existing national registries, including the Society for Vascular Surgery Vascular Quality Initiative (VQI) and a history of collaboration in Vascunet, a "sub-committee of the European Society of Vascular Surgery which aims to increase knowledge and understanding of vascular disease, and to promote excellence in vascular surgery, by means of international vascular audit". The primary focus of ICVR is related to vascular device evaluation and several prospective projects are launched including a registry of infrarenal AAA treatment, pararenal AAA treatment, and TEVAR treatment of aortic dissection. There are two main work streams developed simultaneously: (1) registry of EVAR devices used for treatment of AAAs. The registry will involve long term (up to 5 year) follow-up of limited outcomes (death, re-intervention), and would be compared with open surgical treatment during the same time period for comparable populations, (2) analytic projects to understand international variation in device use in different patient subgroups using existing data. Combine the information whenever relevant using distributed analysis methodology

5.3 Other Collaborations with the Potential to Address Devices

5.3.1 Vascunet

Vascunet is a sub-committee of the European Society of Vascular Surgery which aims to increase knowledge and understanding of vascular disease, and to promote excellence in vascular surgery, by means of international vascular audit. The Vascunet Committee currently includes members from UK, Denmark, Sweden, Germany, Switzerland, Australia, New Zealand, Hungary, Finland, Norway, Italy, Netherlands and Spain, but other countries are welcome to join the group. Vascunet began in 1997 at the ESVS annual meeting in Lisbon. It was agreed that there should be a common European minimal dataset for vascular registries and an organising committee was convened to organise a session at the meeting for presentation of national vascular registries. In 2006 in Prague a common European dataset was defined and funding was agreed by the ESVS to allow the production of an international comparison report. In Madrid 2007 the first Vascunet Database Report was published on aortic aneurysm repair. This report demonstrated that international data merging was possible and acted as a stimulus for further national registries to become involved. In Nice 2008 the second Vascunet Database report was published, concentrating on AAA repair and carotid surgery. There is a reported on data from 10 Registries, 8 national and 2 regional. Over 100,000 cases were submitted and outcome data helped provide a better benchmark for AAA mortality and combined stroke and death in carotid surgery. As an example, the report highlighted a high mortality rate following elective AAA repair in the UK when compared with other countries which lead to a national quality improvement programme development in the UK. Since 2009 the Vascunet group has published 8 original articles.

5.3.2 Cross Border Patient Registries Initiative (PARENT)

PARENT is a Joint Action supported by the EU-Commission. The overall objective of the PARENT Joint Action is to support the EU Member States in developing comparable and interoperable patient registries in fields of identified importance (e.g. chronic diseases, medical technology) with the aim to rationalize the development and governance of patient registries, thus enabling analyses of secondary data for public health and research purposes in cross-border settings.

The PARENT initiative (<http://patientregistries.eu>) has a key general guidance to determine if data within the registry (population) differs from the target population with respect to characteristics that influence the outcome variable(s) of interest. Having large numbers of patients in a registry to assure statistical power is of course valuable, but external and internal validity of the registry can not be ignored. In some instances, when an all-inclusive registry is unrealistic, random sampling of hospitals/patients is a reasonable strategy for registry development. However, the sample should be large enough to capture the universe of different medical devices and have sufficient power for safety and effectiveness assessments. In these instances it is critically important to ensure a very high rate of follow up of over 80% through direct contact with patients or robust systems of data linkage.

Additional to the focus on methodology by setting up guidelines and a comprehensive literature review on the topic PARENT created a database to provide web service to obtain reliable and up-

to-date information about patient registry metadata (Register of Registries). The tool will provide a search function in order to identify potentially relevant data providers in Europe on a specific topic.

5.3.3 Nordic Arthroplasty Register Association (NARA)

The Nordic Arthroplasty Register Association (NARA) was established in 2007 by Sweden, Norway, and Denmark with the main target to further improve Nordic implant surgery research. By conducting multinational registry studies it is possible to obtain high number of patients. A NARA minimal dataset was created to contain data that all registries could deliver. After Finland joined NARA in 2010, the total population of the countries involved is 25.5 million. Selection and transformation of the respective data sets and de-identification of the patients, including deletion of the national civil registration numbers, are performed within national registers of each country. NARA aims to perform analyses of the patient demographics of the participating countries, outcomes of joint replacement operations in general, results of specific implant types and surgical methods, as well as tries to construct a standardized “case-mix indicator” to be used in comparisons. NARA aims at preventing large scale use of unproven implants.

6.0 Quality and Robustness of Registry Data Needed for Regulatory Decision Making

6.1 Data Quality

To support its use in regulatory decision making, the quality and robustness of registry data used must be understood. The extent to which the data must achieve certain parameters (i.e. must have 95% or more case ascertainment) will depend upon the use of the data. However, before a regulatory authority is able to make a decision based upon registry data, the authority will require assessment of the registry data across a number of dimensions:

- **Coverage** – completeness of participation for targeted data collection (e.g. out of a targeted group of 100 hospitals providing care, how many participate and what percent of cases are recorded within registry). This can be measured by comparing registry data with a verified external data source, to assess the extent to which all records are recorded within the registry. Collaboration with NDI, SSDI (US) or other relevant external data source must be anticipated for the collection of patient outcomes data including mortality. The independent external data source should also have 100% coverage of collected data. An example is the use of insurance reimbursement data on medical procedures, if insurance covers 100% of all procedures in a country.
- **Completeness** - the extent to which data items used within analyses are consistently captured within the registry. Mandatory fields will be populated in all cases (where electronic data capture is used). Optional fields or paper-based capture will reduce the proportion of cases for which a data item is recorded. For example, if capturing details of the device is not mandatory this will significantly reduce the extent to which a regulator is able to draw conclusions from the data.

- **Accuracy** – the extent to which data recorded in the registry is an accurate reflection of the healthcare event – e.g., correct patient age, correct device, and correct procedure type. Assessment of the accuracy may be difficult to measure but as with case ascertainment is reliant upon validation against external data sources, or completion of external audit and review to compare registry data with local records.
- **Consistency** – the uniformity to which registry coordinators follow the same processes and procedures for data capture, including harmonized data definitions and relative stability in Case Report Form versioning.
- **Integrity** – for regulatory use, it is essential that medical devices are uniquely identified within the registry, and that the unique identifiers are consistently recorded – such that all procedures using a device can be identified and analyzed.
- **Reliability** – the extent to which data elements are reproducible. For example, if the New York Heart Association Functional Class differs by informant for the same patient, the data element would be considered unreliable.

In addition to principles discussed above it is important to adhere to STROBE criteria (www.strobe-statement.org) for methodological quality and minimum requirements.

6.2 Example Best Practices for the Total Product Life Cycle (TPLC): UK Beyond Compliance and US Transcatheter Valve Therapy (TVT) Case Study

For emerging registries important issues are to identify the „best practices“ for collaboration between the regulatory authority and registry boards (e.g. NJR, Netherlands Implant Registry). Different models of registry ownership exist, including those established by (1) government, (2) professional societies (e.g. AJRR, NCDR etc), and (3) independent entities (e.g. Swedish Knee etc). In all models, requirements for collaborations between regulators and healthcare professionals as well as manufacturers should be defined. Good collaboration between regulators, registries and manufacturers is beneficial for all involved parties and most importantly, the patient and also the “future“ patient will benefit the most. In this respect the UK “Beyond Compliance“ (<http://www.beyondcompliance.org.uk/>) initiative is a good example of the advantages of collaboration between registries, manufacturers and orthopedic surgeons. This initiative is designed to stimulate innovation while optimizing patient safety. Ultimately “Beyond Compliance“ can become a bridge between pre-market and post-market as total product life cycle evaluation (TPLC) for the medical device and related medical procedures.

In the USA, the FDA worked in concert with the American College of Cardiology National Cardiovascular Device Registry (ACC/NCDR) and Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database, other medical societies, industry partners, Center for Medicare Services (CMS), National Institutes of Health (NIH), and patients to collaboratively build the Transcatheter Valve Therapies (TVT) Registry. Roles of the SVT registry include serving as the platform for National Coverage Decision (NCD) for TVT devices (<https://www.ncdr.com/TVT/Home/Default.aspx>), to being the data sources for comprehensive, registry-based surveillance. The TVT Registry has replaced traditional “one off” post-approval studies FDA traditionally requires at the time of device approval. The registry is monitoring the

diffusion of technology while also nesting clinical trials of new devices in pre-market evaluations. The TVT registry is one of several ongoing initiatives to establish Strategically Coordinated Registry Networks (CRNs) for specific high-impact treatments and disease states that may serve as models to accelerate the evolution towards a modern electronic clinical and device evaluation infrastructure. Building on FDA-spearheaded development of the International Consortium of Orthopedic Registries (ICOR) via the Medical Device Epidemiology Network Initiative (MDEpiNet), FDA leads the development of the International Consortium of Cardiovascular Registries (ICCR) in the field of transcatheter valve therapy. FDA continues to promote the development of international efforts under its plan to strengthen postmarket surveillance for medical devices.

7.0 Assuring Analysis Validity when Linking Data Sources

Evaluation of medical devices is best accomplished using the totality of the evidence. The information framework that potentially contributes data to medical device evaluation includes and sometimes extends beyond the scope of registries. All parts of this information framework must act in synchrony to assure the validity of analyses derived from the data. The information framework includes the following desirable dimensions:

1. Controlled vocabularies. The use of standardized common data elements that accomplish syntactic and semantic interoperability of the data among computer systems is a requisite condition. This includes standardized data elements representing clinical, technical, procedural, and administrative concepts, along with the structured documents thereof to transport data from one system to another. The IMDRF Common Data Elements group has identified a list of device-related common data elements for use in regulatory submissions (<http://www.imdrf.org/docs/imdrf/final/consultations/imdrf-cons-cde-mdi-150708-2.pdf>.) Phase 2 of this work will be evaluating the fitness for use of data exchange messages with these CDEs.
2. Structured and semi-structured data capture at the point of care. The multi-stakeholder dialogue should lead to development of processes that capture registry data. This includes specifying information that should be collected as data, integrating clinical workflows with the process of data acquisition, utilizing all members of the healthcare team in capturing data, transitioning from a paper-based paradigm of transaction-based reports to an informatics-based paradigm that enables “collect once, use many times”, and even recommending that a common data model be used as the architecture in the respective IT systems.
3. Data quality assurance and supplementation. “Cleaning” of the data, is an important step to addressing data quality limitations of data collected via routine clinical processes, particularly when that data will be analyzed for evaluating quality assessment, process improvement, and outcomes determinations.
4. Data packaging and upload of data to registries. The submission of “clean”, packaged data per registry schemas often requires some degree of conversion from clinical

representations in health records and ancillary systems to formats consistent with the technical requirements of the recipient registries.

5. Registry informatics. Registries are uniquely positioned to serve as the data hub to provide a systematic perspective of device performance. One of the keys to registry activities is having a common data model for the information framework. Of specific note: the common data model explicitly requires unique identification of patients as single individuals wherever included in a registry, and also requires identification of devices on a detailed level, particularly with respect to longitudinal follow-up and outcomes assessment.
6. Unique device identification. The device identifier of the UDI is a great example of a unique key that could be used to link data. Until the device identifier of the UDI is more completely integrated into device registries, it will be necessary to identify several keys that could be used to pull and link data. For example, standardizing hashes that can act as a surrogate key for a patient identifier, NPIs, or other unique identifiers that can work across data sources should be explored. Most common data models identify the common structure in which to store and retrieve data but do not explicitly define the values that are to be used as index keys.
7. Analytics. Whether individual data are aggregated into a physical or virtual (distributed data) environment for analyses, or data are kept separate and analyses conducted via a distributed analysis model, the linking of the resulting analyses, coupled with advanced analytics and information visualization, promises to be a tenable solution particularly for high priority, high cost, high utilization, and otherwise high interest areas. In order for analytics to provide correct interpretations of the data, the preceding components of the information framework must all be in place and contributing appropriately to the device innovation ecosystem.
8. Reproducibility. Because of the sequential steps required to extract data from registries, the use of a flexible system to produce dynamic reports is critical. For example, systems such as *SWeave* or *knitr* enhance reproducibility of findings by generating a file that includes narrative and analysis, graphics, code, and the results of computations.

While the above describes the information framework for device data, there are additional aspects including governance and management, ownership and stewardship, usability and optimization, privacy and security, and implementation and operations that are described elsewhere in this document and in other guidance (see useful references). The focus of subsections 7.1-7.5 are data principles and best practices to enable national, regional, health care enterprise, society, and other registries, combined with additional data sources, to be integrated into a “system of systems”. It is envisioned that this “system of systems” will provide the largest platform for accelerating the delivery and availability of high quality device information for purposes of device innovation and surveillance.

7.1 Key Recommendations of the IMDRF Registry Workgroup.

The recommendations in Table 1 represent desirable characteristics and properties of registries to best position those registries to contribute to a global network of networks. Adherence to these criteria enables a registry to act as a node in a data network, including the receipt of data of patients in the registry, the compilation and forwarding of key data to an analysis center, and the linkage of data across sources external to the registry. These criteria also position a registry to participate as an analysis contributor in a distributed analysis network. In the distributed analysis model, data remain in their respective secure environments, rather than being consolidated into one database. An analysis coordinating center develops computer code so that each registry can evaluate the query within the confines of the registry computational systems, returning the aggregate results to the analysis coordinating center. Finally, these same characteristics and properties are the principles and best practices that position registries to act as the core of embedded observational and randomized controlled clinical trials. Specifically, while data from registries that do not conform to the proposed requirements may still be incorporated into decision making, those data would likely not be able to be included in all analyses.

Procedure documentation captured at the time of device implant, particularly when accomplished using a structured reporting approach, typically includes a wealth of clinical, technical, operator, device and administrative data. By linking to unique device identification key attributes filed as part of regulatory processes can be downloaded from reference databases (e.g., FDA GUDID database). Additional data necessary for analyses that are not filed in regulatory systems can also be expected to be available in supplemental reference database systems (e.g. (ICOR library). Unique device identification also permits improved linkage of data across disparate sources when using regulatory reporting systems such as US FDA MedWatch. UDI will also have the potential to be collected in US EHRs by 2018 for implantable devices so the link to UDI is not limited to registry databases. Other countries are requiring UDI to be added to their EHR

Other potential sources of data include clinical and billing documentation captured during routine transactions of healthcare, particularly the electronic health record, healthcare claims and other payer data, and medication prescription databases. Linkage across registries, particularly between registries focused primarily on devices and those focused on longitudinal follow-up of disease (e.g., American College of Cardiology National Cardiovascular Data Registry (ACC NCDR) CathPCI registry for cardiac catheterization and the ACC NCDR PINNACLE registry for the follow-up of coronary artery disease and other cardiovascular disease), or even across registry classes (cardiology linked to oncology) should also be considered.

Table 1. Five key registry characteristics and properties to assure cross-registry analysis validity

	Component	Desirable Characteristics
1.	Use of controlled vocabularies (standardized data dictionaries)	<p>Predefined standard data elements, preferably characterized per the ISO/IEC 11179 metadata standard (http://metadata-standards.org/11179)</p> <p>Inclusive of all classes of data in the registry (patient demographics, clinical characteristics, procedure details, operator information, device data, clinical outcomes, administrative information)</p>

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		Baseline clinical characteristics and definitions consistent across jurisdictions (e.g., published as a clinical data standard in the medical literature, or a published registry data dictionary)
		Specific attention to the use of consistent and standardized clinical outcome definitions across jurisdictions, both short-term and long-term
		Use of common data elements in medical device identification developed by the IMDRF RPS workgroup
		Demonstrated syntactic and semantic interoperability via standard data exchange mechanisms (e.g., source data available in an HL7 Fast Healthcare Interoperable Resource,
2.	Use of a common data model (e.g., Observational Medical Outcomes Partnership Common Data Model, at: http://omop.org/CDM)	Standardized organization, format and content of observational data, at a minimum organizing person, conditions, drug, device, procedure and visit information in discrete tables, rather than a transaction-oriented organization of the data
		Enables use of standardized applications, tools and methods to be applied to the data
		Explicit requirement of unique patient identification at the individual patient level, specifically managing the patient as a single entity throughout the registry and enabling deterministic matching across data streams external to the registry
		Facilitates the linking of long-term observational information to the individual patient
3.	Inclusion of device-related performance and device outcomes information	Registry specification to require prompting at the point of care for device-related information whenever a device is implanted, adjusted / altered, or explanted. This assumes the ability to track patient and device- related events across time and health delivery systems. (In the US, this is a significant challenge. FORCE-TJR – an orthopedic registry -has documented that 1 in 4 readmissions, for example, following TJR is to a non-surgical hospital. While the insurer and FORCE-TJR have complete data, the surgical hospital database does not.) Reference attached.
		Data collection embedded in clinical device structured reporting processes (e.g., US Veteran Administration Clinical Assessment, Reporting, and Tracking System for Cardiac Catheterization Laboratories program [CART CL – at: http://www.hsr.d.research.va.gov/for_managers/stories/cart-cl.cfm], US FDA Automated Adverse Event Reporting Systems.
4.	Implementation of a data quality plan for the evaluation and assurance of the quality and provenance of the data	Inclusive of components of monitoring, auditing, and validation. The patient must be tracked across time and healthcare systems.
		Consistent with the requirements of regulatory bodies to accept and processes registry data
5.	Governance that anticipates the conduct of analyses across different types of analysis frameworks	Parsimonious approach to identifying the volume and variety of data to be collected, to be based primarily on anticipated analyses
		Registry capacity to function as the analysis center, wherein analyses are conducted of data managed primarily or solely within the registry
		Registry positioned to participate in a distributed data environment, wherein analyses are conducted at an analysis center of source data that is linked (via patient and / or device identifiers) across different data sources

		Registry positioned to participate in a distributed analysis environment, wherein an analysis center requests a derived analytic output to be aggregated with those of other data centers (e.g., US FDA Sentinel Initiative – at: http://www.fda.gov/Safety/FDAsSentinelInitiative/ucm2007250.htm)
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7.2 Registries and Unique Device and Patient Identification

7.2.1 Registries and Unique Device Identification

The IMDRF Registry Workgroup recommends the inclusion of unique device identification. Specifically, registries should incorporate unique device identification such as the device identifier of the Unique Device Identifier (IMDRF UDI Guidance www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-131209-udi-guidance-140901.pdf). The assignment of DIs for products sold in the US is currently centrally managed by the FDA. The assignment of Dis for products sold in other countries will be managed under the regulatory authority of that country and is intended to be linked. The intention of the UDI rule and the recommendations of the UDI IMDRF Guidance are to use the AIDC (automated identification data capture) component of the UDI to scan and separate the device identifier and five production identifiers of the UDI into key structured data that can uniquely identify a device and provide valuable production information to be used in device surveillance and evaluation.

7.2.2 Registries and Unique Patient Identification

Compliance with applicable national privacy laws is expected. Matching of patients across data sources can be either deterministic or probabilistic. In deterministic matching, either unique identifiers for each record are compared to determine the presence of a match, or an exact match of a selected set of fields is used for linking of patient data between data sources. Unique identifiers can include national IDs, system IDs, or another value type that is uniquely associated with one, and only one patient. Deterministic matching is not completely reliable for several reasons, including the frequent situation where no single identifier provides a reliable match between records from two data sources, and because unique patient identifiers themselves are not 100% reliably associated with one and only one individual. In addition, the very presence of a unique patient identifier in databases has been a concern of some from the perspective of patient privacy. This is where probabilistic matching may be of utility. In probabilistic matching, several field values are compared between two records and each field is assigned a weight that indicates how closely the two field values match. The sum of the weights of the individual fields indicates the strength of the match between records from different data sources, with a specific strength of match selected as representing a valid linkage.

Even with the inherent limitations of both deterministic and probabilistic matching, the IMDRF Registry Workgroup recommends that where available a country (or region) specific unique patient identifier be associated with every record in a registry, as this is a foundational enabler of deterministic matching across multiple data sources that use the same unique patient identifier. In lieu of a unique patient identifier, a sufficient amount of patient-level protected health information (e.g., surname, first name, date of birth, date of procedure, postal code, sex)

sufficient to accomplish high performance probabilistic matching is to be included in each registry.

A technical approach to record matching that reduces exposure and transfer of protected health information while accomplishing deterministic matching is the application of one-way hash algorithms that assign a unique identifier via the hash without exposing the protected health information from which the hash is derived. Provided that the data sources all use the same hashing algorithm, linkage of records can occur that result in transfer of minimum datasets for analytic purposes by using the hash as the linkage index. Whatever the technical approach, a modest amount of protected, patient-identifiable data must be maintained internal to registries to enable registries to contribute to a longitudinal picture of patient and device outcomes that fully inform the device evaluation ecosystem.

7.3 Registry Governance to Encourage Data Linkage

The critical role of registry governance in facilitating the participation and contribution of registries to a medical device evaluation “system of systems” cannot be over-emphasized. Registries should anticipate, and therefore have in place, policies and principles for handling data relevant to device evaluation. The dimensions that must be encompassed include policies and processes for assuring data transparency and integrity while maintaining provenance and traceability; processes for the review, acceptance, and control of data release; and processes for the review, acceptance, and control of data analysis requests.

Specific to data release, regulatory requirements for review of source data must be anticipated. A plan for device-specific safety data reporting to regulatory agencies, both at the individual report level and at the aggregate level should be in place. Manufacturers also have specific responsibilities for the reporting of device-related issues and may require relevant information. Even issues related to patent protection must be considered in the plan for management and control of data and its potential release to outside parties.

Coincident with data linkage, appropriate policies, processes, and information technologies are required to assure appropriate degrees of privacy (and security) of the data within the larger framework of device evaluation. As applicable law and regulation varies from jurisdiction to jurisdiction, the approach to data linkage and the degree of de-identification of protected health information should obviously consider the legal environment of the local jurisdiction. There are several legal issues concerning registry operation, data protection, and data re-use. At the international level, aggregation of analyses – where the data are completely de-identified – may ultimately prove to be the common denominator approach that permits the findings of a “system of systems” to inform medical device evaluation and decision making. Finally, the publication of findings in the medical literature, particularly where patient consent for same may not have been obtained *a priori*, must be handled using an approach where there is minimal risk to patient privacy.

7.4 Envisioning Linkage of Registry and Patient Reported Information

While currently in its infancy, patient reported information is poised to greatly contribute to our understanding of device performance and outcomes. Multiple sources, including implanted devices, external monitoring, social media, mobile apps, periodic surveys, directly reported information, and other approaches have the potential for providing signals (both beneficial and detrimental) about device performance. The movement from traditional healthcare models of transactional care to a nearly continuous flow of information will undoubtedly require advancements in analytics to filter relevant, high value signals from the torrent of data potentially provided by patients and patient monitoring systems. While admittedly a forward-looking perspective, the IMDRF Registry Workgroup recommends that registries begin the process of incorporating or otherwise linking to patient reported information.