



# Advancing Regulatory Science: Research Success in a Public-Private Partnership

**By Ross Jaffe, MD, Kathryn O’Callaghan, Anindita Saha, Stephanie Christopher and William Murray**

In May 2015, the Medical Device Innovation Consortium (MDIC) published a first-of-its-kind report, “A Framework for Incorporating Information on Patient Preferences Regarding Benefit and Risk into Regulatory Assessments of New Medical Technology.” This “Framework” is not only a break-through publication in the field of patient preference assessment for regulatory submissions, but also a model for how public-private collaborations can advance medical device regulatory science.

## **History of the Medical Device Innovation Consortium**

MDIC is the first public-private partnership created with the sole objective of advancing regulatory science regarding the development, assessment and review of medical devices. Members of MDIC share a vision of providing US citizens with access to high-quality, safe and effective medical devices without unnecessary delay.(2)

MDIC was formed in 2012, building on discussions between the Food and Drug Administration (FDA) and LifeScience Alley, a Minnesota-based health technology trade association, about how medical device stakeholders, including FDA Center for Devices and Radiological Health (CDRH) and industry, could work together to tackle regulatory science challenges specific to medical devices to accelerate US patient access to beneficial medical devices of public health importance. Regulatory science in medical devices focuses on the development of tools, standards and approaches to assess the safety, efficacy, quality and performance of regulated products.(3) Regulatory challenges specific to the medical device industry include clinical trial design and costs, developing valid and credible models and assuring medical device manufacturing quality.

Participation in MDIC activities is open to representatives of organizations substantially involved in medical or medical device research, development, treatment or education;

public health promotion or expertise or interest in regulatory science. MDIC members include public entities, such as FDA, Centers for Medicare and Medicaid Services (CMS), National Institutes of Health (NIH) and Patient-Centered Outcomes Research Institute (PCORI); large and small medical device and diagnostics companies; patient advocacy groups and other interested nonprofits; and experts in the scientific fields of statistics, engineering, health economics, risk evaluation and communication.

MDIC has been designed to pursue the following strategies supporting its mission:(4)

- Create a forum for collaboration and dialogue, working within a flexible governance structure to encourage broad participation from medical device stakeholders, including nonprofits, industry and government
- Make strategic investments in regulatory science, utilizing working groups to identify and prioritize key issues, and to request, evaluate and implement project proposals supporting MDIC's mission
- Provide tools from these projects driving cost-effective innovation and emphase education and the development of new methods and approaches with well-documented data and details to enable implementation

Member organizations help set MDIC priorities and provide experts to work on its projects. To date, much of MDIC's work has centered on five high-priority projects: Patient Centered Benefit-Risk Assessment, Clinical Trial Innovation and Reform, Computational Modeling and Simulation, Clinical Diagnostics and Case for Quality. Through these projects, MDIC seeks to help develop methods, tools and resources used in device development and assessment throughout the total product lifecycle of a medical device, thereby improving patient access to beneficial cutting-edge medical technology.

### **MDIC's Patient Centered Benefit-Risk Project**

MDIC's Patient Centered Benefit-Risk (PCBR) Project developed from CDRH's increasing emphasis on benefit-risk assessment as a central component of regulatory decision-making for Premarket Approvals (PMAs) and *de novo* classifications.(5) Given there are no widely accepted approaches for assessing patient preference used in the regulatory process to date, MDIC saw an opportunity to help industry and FDA think about when and how patient preference information might be incorporated into benefit-risk assessments by developing a patient preference framework and catalog of methods. The importance of benefit-risk assessment and a structured framework for such regulatory decisions is discussed in the 2012 CDRH guidance document, "*Guidance for Industry and Food and Drug Administration Staff: Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications.*"(6) The Guidance emphasizes potential value of the patient perspective in regulatory decisions and the importance of a patient-centric approach to benefit-risk determinations. The guidance states "it may be appropriate to approve a device where only a minority of the intended patient population would accept the risks as weighed against the benefits if the information necessary for patients and healthcare practitioners to make well-informed decisions is available and can be presented in a manner understood by the practitioners and patients."

As an initial step in the MDIC PCBR project, MDIC set up a PCBR Steering Committee to oversee the project. Members of the PCBR Steering Committee were recruited from MDIC's member organizations. The committee leadership attempted to ensure wide representation from CDRH, large, mid-sized and small device companies, government agencies and patient groups. Because the goal of the project was to create a framework useful to both sponsors and regulators, the committee sought a wide variety of regulatory perspectives. Representatives from CDRH included statisticians, reviewers and medical officers. CDRH representatives and regulatory representatives from industry were asked to comment on draft sections of the report and comment on whether topics and questions addressed in the report would be helpful and how it could be made more useful. In addition, the committee brought in experts in decision science and preference assessment methods from academic and other organizations.

MDIC also engaged members who were not on the project committee by providing regular updates on the project and opportunities to review and discuss draft versions of the report before completion and public release of the final Framework and its major appendix,

“Catalog of Methods for Assessing Patient Preferences for Benefits and Harms of Medical Technologies” (the “Catalog.”)

The MDIC project received funding from a FDA Broad Agency Agreement contract (HHSF223201400011C) used primarily to fund external academic experts.

### **CDRH's Patient Preference Draft Guidance**

While the 2012 CDRH Benefit-Risk Guidance outlined a decision framework including patient preferences in the premarket review process, it did not specify which methods, tools and approaches could be used to collect this information or provide guidance on how to establish and evaluate the validity of evidence for regulatory consideration. Therefore, in 2013, CDRH launched the Patient Preference Initiative providing information, guidance and framework necessary to incorporate patient preferences on benefit-risk tradeoffs of medical devices into the full spectrum of CDRH regulatory processes. In the process, the initiative aims to advance the science of measuring medical device preferences of patients, caregivers and providers.

Earlier this year, CDRH published a study with RTI International illustrating how patient preferences can inform medical device approval decisions, by capturing patient sentiment and translating it into a decision aid tool for incorporating patient preferences into clinical trial design for obesity treatments.<sup>(7)</sup> Using the data from the study, they were able to estimate the tradeoffs in risks obese patients are willing to accept in exchange for a certain amount of weight loss, and the minimum number of pounds they would have to lose to tolerate a certain amount of risk associated with a weight loss device.

In May 2015, CDRH issued draft guidance, “*Patient Preference Information – Submission, Review in PMAs, HDE Applications, and De Novo Requests, and Inclusion in Device Labeling.*”<sup>(8)</sup> This guidance outlines how CDRH will take Patient Preference Information (PPI) into account in benefit-risk determinations, and the qualities of the patient preference data FDA will consider in determining whether patient preference studies would be considered “valid scientific evidence” (21 CFR 860.7(e)(1)). The draft guidance encourages voluntary submission of PPI to FDA and clarifies that PPI could be useful for those product types and diseases or conditions where patient decisions to use a technology are “preference-sensitive,” such as devices where there are multiple treatment options, devices meeting an unmet need, and devices directly affecting quality of life. The draft guidance further describes how patient preference information should be communicated to patients and providers using terminology and numerical data easily understood and recognized.

### **Benefits of Multi-Stakeholder Collaboration Under a Public-Private Partnership Model**

Participation in MDIC's PCBR Working Group provided the opportunity for members to gain insight into and understanding of what the other expert members of the PCBR group saw as the state of the science of studying and applying patient preference information. There was robust scientific dialogue regarding how to study and apply patient preferences across the total product lifecycle, and discussion of the strengths and limitations of various methodologies. While CDRH's internal policy discussions were independent and not shared with non-agency members, CDRH staff members in the PCBR group were able to discuss scientific methods and broad, already public FDA perspectives on structured benefit-risk decision-making for regulatory contexts. Additionally, CDRH reviewers who were not part of the MDIC PCBR work group, along with other MDIC members, provided feedback on the Framework and Catalog and helped ensure clarity of the report. Overall, CDRH's regulatory science collaboration with MDIC on the PCBR project was useful to the agency as well as other MDIC members in continuing to develop the science of patient preference assessment to ensure the patient voice is incorporated where appropriate in medical devices development, assessment and product use.

## Lessons Learned

Working in the context of our public-private partnership facilitated collaboration with regulatory, device industry and patient stakeholders to help assure the patient preference Framework Report would be useful to all medical device stakeholders. Working together, our public-private partnership was collectively able to accelerate the pace of progress in the emerging field of patient preference assessment by combining the resources and expertise of all stakeholders together toward a common goal: advancing regulatory science and accelerating patient access to innovative and beneficial medical technologies. The MDIC public-private partnership and the patient preference Framework Report it developed demonstrate what is possible when different groups work together to advance science. It serves as a model for future collaborative research endeavors.

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**William Murray** joined MDIC in August 2013 as its first President and CEO. He has more than 25 years of senior leadership experience spanning the range of privately financed start-up to billion dollar plus global businesses. Murray's small company experience spans five years as CEO and executive consultant, including three years as CEO of ReShape Medical. His large company experience includes leadership as the Molecular Biology Division president at Applied Biosystems, and at Medtronic where he spent nearly 20 years in various senior leadership positions, including president of the pacemaker business. He can be contacted at [bmurray@mdic.org](mailto:bmurray@mdic.org).

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