Food and Drug Administration

Pediatric Device Consortia Grantee Meeting
Summary

Emory Conference Center
Atlanta, Georgia
February 17–18, 2016
Introduction

In response to requests from the Pediatric Device Consortia (PDC) grantees for an opportunity to meet together in person to discuss issues related to pediatric device development, the Office of Orphan Products Development (OOPD) of the Food and Drug Administration (FDA) and the Atlantic Pediatric Device Consortium, in co-sponsorship with Emory University, organized a meeting at the Emory Conference Center on February 17–18, 2016.

The conference brought together the PDC leaders, PDC-related children’s hospitals, FDA, and various medical device companies, large and small. The intent of the meeting was to encourage dialogue about ways to improve pediatric medical device development and address commercialization issues at a national level. These goals are well aligned with the mission of the PDC Program of furthering the development of multiple pediatric medical devices.

The meeting organizers encouraged participants to talk about issues related to pediatric medical device development. This document provides a summary of the meeting discussions, and its appendices consist of the agenda, a participant list, and the slides that were presented.

Speakers’ expressed opinions and slide sets do not constitute an official document, guidance, or policy of the U.S. Government, the Department of Health and Human Services, or the FDA; nor should any official endorsement of opinions expressed at this meeting or in this summary be inferred. Suggestions for PDC collaboration that are beyond the scope of the program’s current legal mandate are marked by an asterisk (*) in this meeting summary. They are included to relay suggestions raised in the meeting discussions.

Day 1: Wednesday, February 17, 2016

Welcome and Meeting Overview

Wilbur A. Lam, M.D., Ph.D., Co-Director of the Atlantic PDC, welcomed participants to this meeting. Dr. Lam stated that the meeting goal was for leaders of the PDCs to meet face to face to share ideas with one another and interact with representatives of the medical device industry and Federal agencies. The meeting organizers plan to produce a white paper and a peer-reviewed publication summarizing the meeting proceedings. Dr. Lam thanked the meeting sponsors and organizers: the FDA, Emory University, and the Atlantic PDC.

The PDC Program’s Progress to Date

Linda Ulrich, M.D., Director, Pediatric Device Consortia Grant Program, OOPD, FDA, explained that this meeting was a response to requests for an in-person meeting from PDC leaders and fell within the scope of OOPD’s 2016 Rare Disease Day (February 29, 2016) commemorative activities.

PDC Program accomplishments include assisting with the development of at least six devices now used in children, offering advice on more than 400 pediatric device projects (since 2103;
more than 650 since 2009), securing more than $85 million for pediatric medical devices research (which compares favorably to the $21 million that the FDA has invested in the program since 2009), and producing more than 115 publications and 125 presentations as well as fellowships and new medical education curricula affiliated with the consortia. Dr. Ulrich briefly discussed the currently ongoing PDC mid-cycle review, comprised of metrics and comments sheets from the PDCs and a survey of innovators assisted by the consortium. She also shared a few preliminary, overall highlights from the innovator survey. The feedback from the mid-cycle review will be available to the consortia in May.

PDC Overview Presentations

Kevin O. Maher, M.D., Co-Director, Atlantic PDC, asked the leaders of each PDC to briefly describe their PDCs and to identify their greatest nonfinancial challenges. Principal investigators (PIs) and their responses are listed here:

David Ku, M.D., Ph.D., Georgia Tech and Atlantic PDC, identified the following challenges to the PDC and to pediatric device development:
- Providing individual assistance to inventors who are developing several products as opposed to group-based assistance, which could be more efficient
- Distinguishing between education and support
- Addressing marketing during product development

R. Scott Olson, M.B.A., Michigan PDC, identified the following challenge to the PDC and to pediatric device development:
- Distractions for innovators, who often have a full-time job that leaves little time for product development

Peter Kim, M.D., Ph.D., Children’s National and National Capital Consortium for Pediatric Device Innovation, identified the following challenges to the PDC and to pediatric device development:
- The culture changes required for academic institutions to encourage device development by faculty members and for companies to conduct clinical trials in academic medical centers
- The difficulty of encouraging clinicians to recognize unmet needs for devices

Richard M. Greenwald, Ph.D., New England PDC, identified the following challenges to the PDC and to pediatric device development:
- Developing devices that benefit patients and clinicians while improving workflow and ensuring reimbursement

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1 Value reported for total number of devices assisted during this meeting (775) was incorrect due to calculation error. Actual number was at least 650.
2 Total funds raised through advising services was reported as more than $100 million since 2009. Correct value is more than $85 million since 2009 and more than $70 million since 2013.
• Providing innovators with the tools needed to commercialize pediatric devices, including support in overcoming regulatory hurdles
• Providing innovators who lack the time to develop their device concepts with appropriate business partners

Yaniv Bar-Cohen, M.D., University of Southern California, Children’s Hospital Los Angeles, and Southern California Consortium for Technology and Innovation in Pediatrics, identified the following challenges to the PDC and to pediatric device development:
• Attracting talent and investors for pediatric devices that are perceived by industry and investors to have high risks and low returns
• Addressing assumptions about what payors (insurance companies, the Centers for Medicare & Medicaid Services [CMS], pediatric hospitals, and patients) are willing to pay for the technology
• Validating a device’s value and pricing assumptions with relevant payor groups, which would de-risk the opportunity for investors
• Collecting supporting economic endpoint data for reimbursement in addition to endpoints for safety and efficacy or for probable benefit for regulatory approval adds to an already complex, lengthy, and costly process (and lowers return on investment)

Matthew Maltese, Ph.D., The Children’s Hospital of Philadelphia and Philadelphia PDC, identified the following challenges to the PDC and to pediatric device development:
• The small amount of resources and funding from all sources available for the development of pediatric devices compared to the development of adult devices
• Need for a collective effort to enhance the value propositions for pediatric devices

Pedro J. del Nido, M.D., Harvard Medical School and Boston PDC, identified the following challenges to the PDC and to pediatric device development:
• Identifying manufacturing partners willing to develop pediatric devices for a small-to-medium-sized market
• Need for formal training for inventors or entrepreneurs of pediatric devices to learn market research techniques for identifying the clinical need addressed by a pediatric device

Shuvo Roy, Ph.D., University of California, San Francisco (UCSF) and UCSF PDC, identified the following challenge to the PDC and to pediatric device development:
• Obtaining follow-on risk-capital funding for the “valley of death”

After presentations by the PDC leaders, the remaining meeting participants introduced themselves.

The Pathway to Medical Device Commercialization

Susan Alpert, M.D., Ph.D., SFA Consulting, LLC, commented that a significant accomplishment of the last few years has been clinicians’ increased understanding of the need to talk to innovators, engineers, and entrepreneurs about the problems that might be solved by new
pediatric medical devices. Developing solutions to these problems is challenging because pediatric populations with a given disease are often spread out all over the world, and no one clinician sees enough of these patients to formulate an answer.

Dr. Alpert offered suggestions to help innovators move their pediatric medical devices along the pathway to commercialization. One suggestion is to bring pediatric devices to the attention of programs that support novel technology development at universities (often based in engineering schools). Furthermore, in choosing products to develop, innovators must determine whether these products can be designed, developed, and manufactured in efficient ways; what their impact will be; and what skills are needed to develop them.

Dr. Alpert offered several thoughts about complying with regulatory requirements. For example, understanding the reasons for the regulatory process—to protect patients, public health, and device developers—is important. Dr. Alpert also highlighted the value of using data to establish the product’s reliability, manufacturability, safety, and efficacy and of contacting the Division of Industry and Consumer Education [http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/ContactUs--DivisionofIndustryandConsumerEducation/ucm20041265.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/ContactUs--DivisionofIndustryandConsumerEducation/ucm20041265.htm) early on to begin working with the FDA throughout the development process. Other useful strategies are to learn about FDA programs that can help move products more quickly into the market and to remember that premarket approvals (PMAs) and approvals for Class III devices need not take a long time if the developers can make a good case for the product’s use and cost.

A significant challenge is to ensure that a product is appropriately developed for its patient population. Device developers should consider assembling groups of investigators who will thoroughly evaluate a product to determine whether it can and should be developed. They should also seek support for the middle stage of development from programs at large medical device companies that offer pro bono assistance from staff members and from family foundations. Other ideas were to collect a small amount of initial data to persuade investors to make commitments in the early stages that could help developers reach subsequent stages and to recognize that developing a device will take much longer than expected, and take this into consideration in development plans.

In addition to participants in this PDC meeting, potential pediatric medical device collaborators include companies that manufacture devices for large companies as well as graduate students and postdoctoral fellows. Some business schools evaluate technology for free through their medical device courses.

Medical devices must be easily and repeatedly manufactured, which requires the fewest possible components to minimize risk of failure through collaborations with people who understand manufacturing issues. Medical device approval requires animal studies in good laboratory practice facilities, possibly in collaboration with veterinary schools. Clinical studies also require partners, such as networks of children’s hospitals. Electronic medical records (EMRs) can be valuable for studies of rare diseases, and EMR vendors are potential pediatric medical device development partners. For a venture capital or large medical device company to invest in a
product, the pathway (e.g., PMA) to develop that product must be identified in advance. Insurance companies are potential investors and sources of reimbursement.

Large companies succeed because they can complete all aspects of design and manufacturing in house. Tips for PDCs are to create an environment similar to that of large companies by partnering with different industries; communicate what PDCs are doing with one another and with the public because the more people who know of this work, the easier it will be to find potential collaborators; use online professional networking sites to find people with the needed skills, such as retired health-care executives and local business roundtables; and articulate a complete vision for commercializing a project at the earliest stages because partial ideas cannot be sold to investors.

**Discussion**

In response to questions from the audience, Dr. Alpert offered the following additional thoughts:

- Learn what CMS and other payors consider in their technology assessments
- Show hospitals how a device will save time or money while helping patients
- Conduct preclinical studies on devices that use biodegradable materials to determine how the material biodegrades and disposition of the final end products

Dr. Alpert also pointed out that although the FDA might not regulate both components of a combination product, the agency will need data on both components in order to evaluate the product. In addition, the FDA has tried to make it easier to conduct early studies in the United States as opposed to overseas. The European standard for devices seeking market approval is safety and performance (the device does what the sponsor says it will do), not efficacy (whether it benefits the patient). In the past, it was easier to obtain European approval for medical devices than FDA approval. An advantage of starting development in the United States, however, is that the process moves forward more quickly.

**Day 2: Thursday, February 18, 2016**

**Creating PDCs/Industry/Investor Partnerships**

Gerald Moore, M.B.A., President and CEO, Nido Surgical, described the challenges of raising capital for small startup medical device companies. The potential revenues of pediatric devices do not seem sufficient to generate the returns that venture capital companies expect. Options for small companies are therefore to seek other types of funding sources, reduce up-front investment costs, or find ways to generate higher revenues in the future. Many individual and family investors have a personal or philanthropic interest, and they are therefore open to smaller investment returns. The platform technology Mr. Moore’s company developed solves a problem in pediatrics and could also be used in the larger, adult market.

In the course of raising money to fund the development of their products, inventors relinquish ownership (typically 20–30%) of their company shares each time (funding round) they raise capital. As a result, by the time a device is fully developed and sold for use in patients, inventors...
might own only 10% of their companies. However, their share in the company means nothing until the company is sold or starts paying dividends. To be able to focus their energy on the technologic or scientific aspects of their product, innovators should consider saving enough funds to pay a full-time director to raise money and manage personnel.

Discussion

Participants offered the following suggestions:

- Receiving Small Business Technology Transfer (STTR) awards gives small companies credibility with investors
- Help companies seeking PDC assistance define their market, beyond size considerations, to assess how a device will reach the market at an affordable cost
- Seek FDA advice early, before investing in studies that the FDA would not consider relevant to supporting device clearance or approval
- Plan to bring multiple products into the market to generate economies of scale and capture the attention of large companies
- Use data generated in pediatric settings to help make the case for expanding a device’s use in the adults
- Seek small grants from technology-development funds of pediatric hospitals

Another suggestion was for the PDCs to coordinate with one another and identify patients to participate in clinical trials.*

Participants also identified the several needs for PDCs, including a convincing commercialization plan for STTR and Small Business Innovation Research (SBIR) funders for pediatric devices that do not have a potential adult market, National Institutes of Health (NIH) funding mechanisms to help fill the funding gaps, and ways to persuade hospitals to adopt an approved device quickly.

An FDA representative clarified that the agency provides limited business and research grants. However, several FDA programs can help pediatric devices that address unmet needs reach the market earlier. [Although it was not mentioned in the discussion, the FDA waives application fees for 510(k) and PMA applications intended solely for a pediatric population.] Furthermore, although devices approved for adults via the humanitarian device exemption (HDE) pathway are not permitted to make a profit, those developed for pediatric patients can make a profit. The approval threshold for HDEs is safety and probable benefit, not safety and effectiveness applied to PMAs, making approval for HDE clinical trials somewhat easier to achieve.

Hospital Administration and Supply Chain Perspectives for Introducing New Pediatric Device Technology into the Hospital Setting

Joni Rittler, Vice President, Supply Chain, The Children’s Hospital of Philadelphia, and John McMillen, Senior Director, Supply Chain, Children’s Healthcare of Atlanta, explained that supply chain departments in pediatric hospitals choose devices and suppliers based on products’ costs and ability to increase quality of care. The Children’s Hospital Association offers group
purchasing for participating hospitals through Vizient, one of the major group purchasing organizations (the others are HealthTrust and Premier). Vendors can demonstrate new technologies at Vizient’s annual innovation conferences.

Most requests for new products at pediatric hospitals are generated by clinicians who learn about a new product at a conference or through research. Hospitals rely heavily on clinician input in making purchasing decisions about new products. The length of time required for a hospital to approve a new product depends, in part, on how risk averse the hospital is and the product’s potential to have negative effects. A value analysis process takes time to ensure that a product is safe and that a supplier can meet the hospital’s needs. Components of a value analysis program include an assessment of a device’s impact on efficiency, how to clean and store the device, how quickly it expires, and how to educate nurses and physicians about its utilization. Hospitals will replace existing products if the new product is less expensive and of higher quality. Hospitals consider overall value, not just cost.

**Discussion**

Suggestions from the session moderators and participants were to:

- Develop an innovations conference focused on pediatrics
- Use trade shows to introduce hospital personnel to new products
- Bring PDCs together to conduct some of the initial quality analyses for hospitals*
- Help PDCs understand the supply-chain processes in pediatric hospitals
- Present products to hospitals for purchase only after a manufacturer has been identified
- Consult with supply-chain representatives early on to understand their needs and inform them of what products are on the horizon

**Surviving the Valley of Death after the Prototype**

Tiffany Wilson, M.B.A., Executive Director, Global Center for Medical Innovation, moderated this session. Michael Fitzgerald, Managing Partner, CareAline Products, explained that his wife, Kezia Fitzgerald, the company’s CEO and Chief Innovation Officer, developed the CareAline Sleeve and CareAline Wrap. The sleeve and wrap were designed to prevent their infant daughter from pulling out her peripherally inserted central catheter and central line during chemotherapy for neuroblastoma and to avoid irritation from the medical tape. Because Ms. Fitzgerald was also battling cancer, the Fitzgeralnds’ products received a substantial amount of attention from the media, resulting in interest from a representative of a financial services firm and his wife. After their daughter died, the couple provided the Fitzgeralds with seed funding and guidance on developing and marketing their devices. Obtaining funding for the next stage has been challenging because of the product’s small potential market.

Ms. Wilson asked participants to comment on their fundraising experiences. She added that the center she leads addresses the gap between innovation and commercialization for medical technology development in the southeast region. She warned against spending PDC or SBIR funds in ways that are not commercially relevant. For example, instead of using funds to make
their products incrementally better, PDCs should focus on achieving the more significant milestones that private investors require to fund potential high impact devices.

**Discussion**

Participants noted that the shift from developing a product to forming a company is challenging. Many clinicians focus more on research than on commercialization, and confuse investors with customers. Although customers are interested in products that solve a problem, investors are interested in companies (including personnel, nature of the competition, market size, and commercialization plans).

Participants also noted that foundations are a potential source of funding to surmount the “valley of death” if a device focuses on a specific disease or condition. However, foundations do not typically provide advice on how to form a company or develop a product. Venture-capital firms have generally stopped providing startup funds after the 2008 financial downturn. Angel investors have recently become more systematic and thoughtful in their approach to product analysis as well.

Another comment was that developing a commercially viable product requires the right team, which might include clinicians, engineers, and business experts. The team determines how to sell the product in ways that would interest investors. Participants also pointed out that although global markets have advantages, they can make it challenging to protect intellectual property and can be difficult to enter. Furthermore, in business, the metric of success is commercialization, and many pediatric products cannot meet this metric.

Suggestions were as follows:

- Form a consortium of PDCs* to (1) share expertise with one another, (2) make matches between products and angel investors or family groups in each community, and (3) work with philanthropists to determine how to proceed when the likely return on investment is low
- Do not guess about regulatory requirements—consult with regulatory experts
- Identify partners that do not necessarily provide funding but that can offer expertise in various aspects of development, such as distribution or manufacturing
- Change the plan based on lessons learned from the initial experiences

**Exploring Collective Strategies/Synergies to Accelerate the Development, Assessment, and Commercialization of Pediatric Devices Among the PDCs**

William Bentley, M.Eng., Ph.D., Co-Director, National Capital Consortium for Pediatric Innovation, described the University of Maryland Center of Excellence in Regulatory Science and Innovation (CERSI). The FDA funds four CERSIs to advance regulatory science through innovative research, education, and scientific exchanges. The University of Maryland CERSI provides master’s degrees and certificates in regulatory science. Its activities include the America’s Got Regulatory Science Talent Competition, monthly lectures for FDA employees, and scientific exchange workshops throughout the Washington, DC, region. The CERSI is
establishing industrial consortia to facilitate communication with industry and enhance public transparency for regulatory processes and procedures.

The talent competition connects students with clinicians who identify a problem that the students try to solve. It has been noted that the vast majority of these products do not move forward because students who graduate need jobs and do not have time to develop their products. In response to this need, a new program at the University of Maryland provides two years of funding support for the student with the best product idea to develop that product while earning a master’s degree.

Dr. Bentley recommended that PDCs engage with the NIH Clinical and Translational Science Awards and connect to more training and education programs.

Discussion

Participants noted that standalone pediatric hospitals face economic pressure to fold into larger adult institutions because large payors want to bundle their payments. A related concern is that the focus on children will be lost in merged institutions. Another pressure on pediatric hospitals comes from changes in reimbursement policies. Currently, hospitals in academic medical centers support the institution’s research activities. If clinical revenue shrinks, research will suffer. Finally, students and clinician trainees are an enthusiastic and underutilized resource to support pediatric product development.

Participants made the following suggestions:

- The Prescription Drug User Fee Act and the SBIR/STTR programs could be expanded to provide funding for small companies to market products, including pediatric devices.
- NIH could create P50 research centers focused on pediatric device development in a given area, such as cardiovascular disease. P50 centers have resulted in products that have reached the clinic, and some centers have spun off small companies.
- PDCs should consider seeking SBIR awards for the development of pediatric devices from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD).

The group also discussed ways to sustain devices developed in student capstone projects. Dr. Bentley said that in a few academic programs, students develop devices as a group project. When those students graduate, the next class continues to work on the device. Most universities do not use this approach, however, because students want to come up with their own concepts. A few capstone projects do move forward, and some have become PDC projects.
Federal Programs to Encourage Pediatric Device Development

Device Development Ecosystem and SBIR/STTR Update

Steven Hirschfeld, M.D., Ph.D., Associate Director for Clinical Research, NICHD, explained that in the NIH framework, device development integrates clinical, fiscal, engineering, regulatory, and other activities that are interactive and mutually supportive. A second layer of the ecosystem focuses on care delivery and use. In this layer, the patient is at the center and can be affected by surgical procedures, medical follow-up, customer support from the device manufacturer, caregivers who interact with the device, and regulatory oversight. Device developers must anticipate all potential touch points.

The SBIR and STTR programs are congressionally mandated set-aside programs for U.S. small businesses to conduct research and development that has strong potential for commercialization. Currently, the NIH budget for SBIR and STTR programs totals almost $1 billion. Other agencies that offer small-business funding include the Departments of Defense, Energy, and Homeland Security as well as the National Science Foundation and the National Aeronautics and Space Administration. The NIH I-Corps™ (http://sbir.cancer.gov/programseducation/icorps) is an 8-week training program that offers SBIR and STTR grantees real-world, hands-on entrepreneurship training facilitated by domain experts from the biotechnology sector.

OOPD Programs for Pediatric Device Development

Karen Russell, M.P.H., M.H.S., Pediatric Device Consortium Grant Project Officer, OOPD, FDA, explained that OOPD’s mission is to promote the development of products, including drugs, devices, biologics, and medical foods, for the treatment, diagnosis, and prevention of rare diseases and conditions. More than 7,000 rare diseases have been identified, and most affect pediatric patients.

The Orphan Products Grants Program (http://www.fda.gov/forIndustry/DevelopingProductsforRareDiseasesConditions/WhomtoContac taboutOrphanProductDevelopment/default.htm) supports the development of products for rare diseases through R01 grants for clinical trials. To qualify for the program, devices must target a U.S. population of fewer than 200,000 people per year.

The FDA’s Humanitarian Use Device (HUD) Designation Program (http://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/premarktsubmissions/humanitariandeviceexemption/default.htm) can apply to devices for diseases and conditions with an incidence of fewer than 4,000 individuals in the United States per year. Designation as a HUD makes a device eligible to be approved via the HDE pathway, based on its safety and probable benefit. Between 2007 and 2013, FDA approved 18 HDEs. Of these, 13 had data from clinical trials demonstrating their safety and probable benefit (the remainder were approved based on clinical experience or retrospective analysis) and 72% of the approved HDEs could be used in pediatric patients.
Finally, OOPD is currently conducting a needs assessment to identify unmet device needs for rare diseases, including pediatric rare diseases, through a web-based survey.

**Medical Device Development for Pediatric Rare Diseases**

John Laschinger, M.D., Medical Officer, Center for Devices and Radiological Health (CDRH), FDA, explained that most devices are not made for children and are used off label in pediatric patients based on expert opinion and inferences from adult medicine. CDRH rarely receives proposals for randomized controlled trials of devices in children because samples are often small, studies must accommodate children’s growth, and parents and children must accept randomization. However, CDRH is open to studies that use other designs, especially when an unmet need exists.

CDRH believes that on-label use of medical devices is important because it ensures that a device’s safety, effectiveness or probable benefit, quality, and long-term performance have been tested. CDRH is trying to make the device approval process less cumbersome. For example, the Early Feasibility Study Program facilitates the clinical evaluation of medical devices in the United States under Investigational Device Exemptions regulations.

Early engagement with CDRH can help product developers understand CDRH’s expectations, identify FDA programs that can facilitate their product’s development, and help them optimize their clinical trial designs. CDRH also encourages developers to seek HDE designation and meet with the appropriate CDRH Review Division early on to help determine clinical evidence needs and identify the least burdensome pathway to market.

**CDRH Strategic Priorities: Creating an Ecosystem for Innovation in Public Health**

Vasum Peiris, M.D, M.P.H., Chief Medical Officer, Pediatrics and Special Populations, CDRH, FDA, discussed how the mission and vision of CDRH/FDA are supported by strategic priorities. The presentation was structured around the accomplishments of the 2014–15 strategic priorities and the evolution toward the 2016–2017 strategic priorities, which are as follows (without prioritization):

1. Establish a national evaluation system for medical devices
2. Partner with patients
3. Promote a culture of quality and organizational excellence

Within the context of strategic priorities, Dr. Peiris described specific initiatives supporting the needs of pediatric patients and pediatric device development. He highlighted the planned evolution toward development of an ecosystem that supports device innovation with dynamic regulatory paradigms informed by risk/benefit considerations and more efficient recognition, evaluation, and feedback regarding safety signals.

Activities under the first priority include shifting some premarket data requirements to the post-market surveillance period for specific PMA devices. The FDA also launched the Expedited Access Pathway Program.
(http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/ucm441467.htm) to help reduce the time and cost from development to marketing decision for PMA and de novo devices. In partnership with the Brookings Institution, the FDA is creating a national surveillance system for medical devices (http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHHReports/UCM435112.pdf).

Within the context of the second priority, CDRH has issued guidance on factors to consider when making benefit-risk determinations in medical device pre-approvals and de novo classifications and has issued draft guidance on patient preferences.

Efforts to address the 2014–15 priority of strengthening the clinical trial enterprise and the third 2016–17 priority include support for clinical trial simplification and adaptive designs as well as engagement of Bayesian methodology for extrapolation of existing data in one population to benefit another population, such as to inform evaluations for pediatric subpopulations. Through a partnership that includes the FDA, the Virtual Family Project is developing anatomically correct, whole-body computer models, including two children, for computer simulation studies, making it possible to decrease the sample sizes required for studies in humans. CDRH is committed to strengthening the FDA’s culture of quality within CDRH and strengthening product and manufacturing quality within the medical device ecosystem.

**Discussion**

Dr. Laschinger clarified that the HDE pathway is for small-market devices with fewer than 4,000 uses per year and typically involves small pivotal trials. To be approved, HUDs must demonstrate safety and probable benefit, which is a lower threshold for approval than the safety and effectiveness requirement for devices approved as PMAs. Because the FDA can now review post-market data, devices approved under the HDE pathway can potentially shift to the PMA pathway. One of the challenges faced by devices approved via the HDE pathway is the requirement for institutional review board approval of the device’s use at least once, and possibly for each use of the device.

The FDA does not review data on costs or cost-effectiveness. However, developers may collect the cost and market information that their investors need during their clinical trials. The ability to obtain reimbursement is important for a product’s viability, and parallel reviews may be possible.

A participant pointed out that parent preferences should play a role in pediatric device development. Dr. Peiris agreed, explaining that pediatric patients’ preferences can be communicated to study design teams once their patients reach the age of assent or consent. For younger children, parent perspectives must play a major role.
Meeting Conclusion

Logistical arrangements for Dr. Hirschfeld to present his slides remotely were made after the preparation of the final meeting agenda. The addition of his talk to the final session increased the length of that session and led the organizers to shorten the remaining presentations in that session.

Dr. Maher summarized the meeting by highlighting the benefits of having the various PDCs work together to advance pediatric medical device development.

Dr. Lam thanked participants for attending the meeting. He also thanked the contractors who provided logistical support for the meeting. The meeting’s recurring theme was the need for the PDCs to collaborate with one another, which will be the subject of ongoing discussions.

*Suggestions made by meeting participants that fall outside the current legal mandates of the PDC Grant Program.*
Appendix A: Agenda
AGENDA

DAY 1 — WEDNESDAY, FEBRUARY 17

2:30 P.M.  REGISTRATION

3:00 P.M.  Welcome and Meeting Overview
Wilbur A. Lam, M.D., Ph.D. — Co-Director, Atlantic Pediatric Device Consortium

3:05 P.M.  The PDC .... Progress So Far ....
Linda Ulrich, M.D. — Director, Pediatric Device Consortia Grant Program, Office of Orphan Product Development (OOPD), U.S. Food and Drug Administration (FDA)

3:15 P.M.  PDC Overview Presentations
Kevin O. Maher, M.D. — Co-Director, Atlantic Pediatric Device Consortium
Wilbur A. Lam, M.D., Ph.D. — Co-Director, Atlantic Pediatric Device Consortium

3:55 P.M.  Industry and Other Participant Introductions
Kevin O. Maher, M.D. — Co-Director, Atlantic Pediatric Device Consortium
Wilbur A. Lam, M.D., Ph.D. — Co-Director, Atlantic Pediatric Device Consortium

4:35 P.M.  The Pathway to Medical Device Commercialization
Susan Alpert, M.D., Ph.D. — SFA Consulting, LLC

5:15 P.M.  Dinner and Bowling Reception, Wisteria Lanes at Emory Conference Center
Sponsored by the Department of Pediatrics, Emory University School of Medicine

DAY 2 — THURSDAY, FEBRUARY 18

7:00 A.M.  CONTINENTAL BREAKFAST
Sponsored by the Department of Pediatrics, Emory University School of Medicine

8:05 A.M.  Creating PDCs/Industry/Investor Partnerships
Wilbur A. Lam, M.D., Ph.D. — Co-Director, Atlantic Pediatric Device Consortium
Gerald Moore, M.B.A. — Nido Surgical

8:50 A.M.  Hospital Administration and Supply Chain Perspectives for Introducing New Pediatric Device Technology into the Hospital Setting
Joni Rittler — The Children's Hospital of Philadelphia
9:35 A.M.  **BREAK**

9:50 A.M.  **Surviving the Valley of Death after the Prototype**  
*Tiffany Wilson, M.B.A. — Global Center for Medical Innovation*

10:35 A.M.  **Exploring Collective Strategies/Synergies to Accelerate the Development, Assessment, and Commercialization of Pediatric Devices among the PDCs**  
*William Bentley, M.Eng., Ph.D. — Co-Director, National Capital Consortium for Pediatric Innovation*

11:20 A.M.  **LUNCH AND NETWORKING (ECC DINING HALL)**  
*Sponsored by the Department of Pediatrics, Emory University School of Medicine*

12:30 P.M.  **Federal Programs to Encourage Pediatric Device Development**  
*Karen Russell M.P.H., M.H.S., PA-C — Commander, U.S. Public Health Service, OOPD, FDA  
Vasum Peiris, M.D., Ph.D. — FDA  
John C. Laschinger, M.D. — FDA*

1:15 P.M.  **Meeting Debrief, Summary, and Defining our Next Steps**  
*Kevin O. Maher, M.D. — Co-Director, Atlantic Pediatric Device Consortium*

2:00 P.M.  **ADJOURN**
Appendix B: Participants
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<tr>
<th>Last &amp; First Names, Credentials</th>
<th>Address</th>
<th>Email &amp; Phone Number</th>
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Appendix C: Presentations
Pediatric Devices 2.0: Identifying Approaches to Foster Development

Wilbur Lam, MD, PhD
Co-Chair
Aflac Cancer and Blood Disorders Center
Children’s Healthcare of Atlanta
Department of Pediatrics
Wallace H. Coulter Department of Biomedical Engineering
Georgia Institute of Technology and Emory University

Kevin Maher, MD
Co-Chair
Director, Cardiac Intensive Care Unit
Sibley Heart Center
Children’s Healthcare of Atlanta
Department of Pediatrics
Emory University

Stacy Heilman, PhD
Program Director & Grants Advocate
Children’s Healthcare of Atlanta
Department of Pediatrics
Emory University

Martha Willis
Program Manager
Atlantic Pediatric Device Consortium
Atlanta Clinical & Translational Science Institute
Georgia Institute of Technology
What Do These Two Have in Common with Us Here Today?

DID YOU KNOW?

Two-thirds of people with rare diseases are children
Pediatric Device Consortia Grants—
Progress so far.....

Pediatric Device Consortia Grantee Meeting

Emory Conference Center Hotel
February 17-18, 2016

Linda C. Ulrich, M.D., F.A.A.P.
Accomplishments So Far*....

• 658
  (Total Number of Projects Assisted since 2009)

• 406
  (Total Number of Projects Assisted since 2013)

• 148
  (Currently Active Projects)

• 11
  (Collaborations, Multi-Consortia Projects)

*Numbers updated to reflect correct values at time of report finalization
Devices Now Used in Kids.....
Thanks to Some Help from the PDC

Buzzy—cold and vibration for relief of pain with needlesticks (Class 1)

Rhinoguard—Assists in nasotracheal intubation (510K)

Hypothermic Control Device—head wrap for infants recovering from hypothermia induced in cardiopulmonary bypass surgery (Class 1)

TIVA (Velano Vascular)—needle-free, blood collection device—allows blood draw through a peripheral IV (approved 20 and 22 guage)....developing 24 guage (510 k)

External Compressor Brace for Pectus Cariniitum (Class 1 exempt)

Geiger Pyloric Clamp for Pyloric Surgery (Class 1)
Other Early Successes....

- Biodegradable tracheobronchial airway splint for tracheomalacia, reported in May 2013 NEJM

- Ureteroscopy-assisted nephrostomy for percutaneous nephrolithotomy (percutaneous removal of kidney stones)

- Bone tumor removal with incisionless surgery—
  - (MR-HIFU device) Tumor ablation with externally focused ultrasound under MRI guidance
  - Used in two patients to treat osteoid osteoma (benign bone tumor, most common between ages 4 and 25 years old)
Oh, by the way*....

Helped secure additional funding for PDC medical devices research

> $ 85 Million since 2009

> $ 70 Million since 2013

*Numbers updated to reflect correct values at time of report finalization
FDA (Taxpayer) Investment in the Program....

- **$ 3.535 Million** awarded in FY 15 to support **8** consortia

$ 10.435 Million awarded since 2013 RFA

$ 21.435 Million awarded since 2009
You have also.....

Created opportunities for outreach, publications, and education

• > 115 Publications
• > 125 Presentations

• Established Fellowships

• Medical Education Curriculum Development
PDC Mid-Cycle Review
Mid-Cycle Review

• Components
  – Your Metrics Sheet
  – Your Comments Sheet
  – Survey of Innovators

• How we’ll be using this information

• Expect Feedback by May
  – Will be considered towards future funding

• Preliminary Results
PDC Top 5 (n=139):

Types of assistance received

1) Assisting with the Regulatory Process, 37%
2) Financial Support from the Consortium, 36%
3) Advice on Funding Sources, 32%
4) Planning or Conducting a Market Analysis, 17%
5) Advice /Assist with Technology Marketing, 17%
PDC Top 5 (n=125):
PDC interactions, most positive aspect

1) Staff professionalism and encouragement, 25%

2) Staff advice, support, and dedication, 21%

3) Access to Experts, 16%

4) Staff accessibility and responsiveness, 14%

5) Overall Support, 12%
Overall Satisfaction Measures

(n = 138)
Pediatric Component of OOPD’s Devices for Rare Diseases Needs Assessment

- 63 Number of PDC Clinicians Surveyed

- January 28th through February 29th

- Draft report expected later this year
This workshop is intended to encourage discussion of issues related to pediatric medical device development.

We have invited speakers from a variety of professional backgrounds and experiences.

Speakers’ expressed opinions and slide sets are not an official document, guidance, or policy of the US Government, the Department of Health and Human Services, or the Food and Drug Administration, nor should any official endorsement be inferred.
Leadership in four institutions: Physicians and Engineers

1. Idea to Product: Human Factors, Scalable mfg = Right Design
2. Lean Startup: Market analysis, Customer input = Right Product
3. Design Control: Efficiency = Faster, Cheaper Product
4. Practical regulatory path
5. GMP, Clinical trials, Statistics to Patient Use

Metrics
- 60 devices assisted (2013)
- 11 Active Projects
- 37 External Projects
- 18 Direct mentorship and plan
- Products licensed, FDA cleared, in clinical use

Biggest non-Financial Challenges: Indiv vs group: Education vs Support, Prod Dev
National Capital Consortium for Pediatric Device Innovation (NCC-PDI)
(www.innovate4kids.org)

Since 2013
# Projects assisted: 51
# Projects receiving discretionary funding: 10
# Regulatory clearances (CE, 510(K)): 6
$$ Raised by projects we assist: > $19 million

NCC-PDI Team
Peter Kim, MD, PhD – co-PI
William Bentley, PhD – co-PI
Kolaleh Eskandanian, PhD, MBA - Executive Director
Lex Schulteis, MD – Regulatory Consultant
Kevin Cleary, PhD – Engineering Consultant
Axel Krieger, PhD - Engineering Consultant
Emmanuel Wilson, MS – Rapid Prototyping Engineer
Bala Balachandran, PhD – Liaison Capstone Projects
Martha Connolly, PhD – IP Consultant
Craig Dye, PhD – Business Plan Consultant
Tim Moran, MBA – EIR
Mark Chandler, MBA – EIR

A partnership between:
New England Pediatric Device Consortium

NEPDC is a multidisciplinary consortium that provides infrastructure, consultation, and core resources to incentivize and accelerate commercialization of devices for pediatric care.

Opportunities to Participate:
- Pre-Seed and Seed Grant Program
- In-Kind Commercialization Services
- Target Challenge Partnerships
- Ad-hoc Reviewer
- Resident Entrepreneur Fellowship
- PICNIC Program

To learn more about NEPDC resources, services, and programs, visit us at: http://www.nepdc.org/

Challenge to Pediatric Device Development:
Like all medical technologies, commercializing pediatric devices requires a full complement of technical, business, regulatory, and clinical evaluation expertise. With small market size, there is an even greater need to implement a carefully assessed and effective commercialization strategy.
Challenge:
Attracting talent and investors for a pediatric device when there are perceptions of greater risk and lower returns.

- Developing a credible commercial model requires assumptions on pricing. We need to be able to validate these assumptions early and directly with insurance companies, CMS and pediatric hospitals.

- In addition, once the health economic endpoints are established, gathering supporting data in addition to proving safety and efficacy adds to an already complex, lengthy and costly process (and lowers ROI).
PhillyPDC Inception 2013

Mission:
Bring new pediatric medical devices to market.

Outcomes
- 40+ devices assisted (mostly Class I and II)
- Private investment 10x public funding
- 9 devices with significant FDA interaction
- Growing Philly Med Device Ecosystem

Creating the Value Proposition

1. Early vetting of IP, trials, reg path, reimbursement (NAMSA)
2. Clinical reviews by specialty experts (CSAC)
3. Med device business luminaries (OC)

Goals for this Meeting
- Reverse adult vs. child priority in Industry, Private Equity, Academia and Government
- PDC-wide cooperative effort on specific Class III device(s)?
  - What can WE do to ENHANCE the Value Propositions for peds devices?
    - PDC-led pediatric device clinical trials network?
• **Significant Challenge 1:** Identifying small or medium size manufacturing partners willing to develop pediatric devices given the usual small to medium size market. The best solutions identified so far are small to medium size manufacturers that are willing to develop the technology to first-in-man with a plan to then sell the technology to a larger distributor.

• **Significant Challenge 2:** Most inventors understand the technology they are developing but have not done the market research to identify the clinical need. There is a need for formal training for inventors or entrepreneurs of pediatric devices to learn market research techniques.
# UCSF Pediatric Device Consortium

**Innovation formula:** Engineering skills & knowledge + Real clinical needs = Innovative devices & new treatment approaches

## PROGRAM STRUCTURE

| Leadership: | Michael Harrison, MD (Ped Surgery)  
| Shuvo Roy, PhD (Bioengineering) |
| Twice weekly “open innovation” meetings |
| Interactive web portal |
| Trainee involvement (Innovation Pathway) |
| Resources for innovators: |
| - Clinical, scientific & business advising |
| - Consultant network |
| - In-house engineering services |
| - Prototyping and testing facilities & equip. |
| - Linked to UCSF-Stanford CERSI |

## KEY ACCOMPLISHMENTS

| >50 devices assisted; 16 active projects |
| $21M in follow-on funding attracted |
| 6 startups launched |
| 5 devices in clinical trials |
| 1 marketing approval (Dynamic Compressor) |
| 1 UCSF PDC replica (Philippines) |

**Biggest challenge:** Follow-on funding to get thru preclinical & FIM studies
THE PATHWAY TO COMMERCIALIZATION

DR SUSAN ALPERT; RETIRED SVP MEDTRONIC
DIRECTOR ODE, CDRH 1993-1999; PEDS ID
OVERVIEW

• The landscape
• The regulatory environment
• The challenge
• The opportunity
• Defining success
LANDSCAPE

- Current availability of devices for children
- Programs to enhance device development
- Pediatric specific programs
- What to look for in products
- How/who can help
REGULATORY ENVIRONMENT

- FDA responsibilities and challenges
- Medical Device pathways
- Regulatory opportunities
- Working with FDA
THE CHALLENGE

• The product
• Development time
• Partners in the work
• Evidence – non-clinical and clinical
• Time
THE OPPORTUNITY

• Collaboration

• Broad outreach

• Shared resources

• Volunteer/student help

• Communication
SUCCESS

- Product prototype
- Manufacturing pilot access
- Research partners- pre-clinical and clinical
- Identified pathway to market
- Payers engagement
CONCLUSION

• Collaborate
• Communicate
• Consult
• Complete
• Commercialize
Gerry Moore

Entrepreneur

President, CEO & Co-founder
Nido Surgical

Angel Investor

Partner, Converge Venture Partners
Member, Launchpad Venture Group

Background

Managing Director, Putnam Investments
20+ years Small-cap Healthcare Portfolio Manager & Analyst
BSEE, University of Wisconsin
MBA, Dartmouth College

gmoore@nidosurgical.com
800.819.NIDO x700
Minimally Invasive Instruments for Cardiac Surgery

Goals
1. Reduce cross-clamp time or eliminate need for cardiopulmonary bypass
2. Enable smaller incisions

Technology
- Developed by Dr. Pedro del Nido and the Cardiovascular Research Lab
- Exclusive license to 7 patents
- 4th generation prototype, successfully tested in multiple large animal studies

Status
Incorporated, formed team, applied for STTR grants, raising seed capital.
CERSI Academic Programs

- Certificate / MEng in Regulatory Science and Engineering (College Park)
- MS in Regulatory Science (Baltimore)

Events - America’s Got Regulatory Science Talent Competition

Monthly Lectures

- Lectures held at FDA - 2193 FDA employees participated from 2012 to January, 2016, 149 CE credits earned.

Scientific Exchange Workshops

- Workshops held in region - ~8-10 per year; ~100 attendees per workshop; 3987 Attendees
M-CERSI Industry Consortia
(organically grown Public Private Partnership - thus far!)

Grass roots CEO’s club

CSA Medical

Juxtapedia

RoosterBio

Sisu Global Health

PathSensors

WellDoc

Clear Guide Medical

Harpoon Medical

VasoOptic Medical Inc.

Advancing Healthcare through Innovative Diagnostics

Key Tech
Startup fever on campus

Makerbot Innovation Center
Robert E. Fischell Institute Pipeline!

Minimally Invasive Neurosurgical Intracranial Robot (MINIR)

Mapping ocular elasticity
How do we leverage PDCs and other resources?

- Engage CERSIs and ORSI Office
- Engage CTSA(I)s
- Form a formal PDC “network” (i.e., CERSI Network)?
- Provide team approaches across Centers?
- Socialize concepts (Feb 29 - rare disease day)?
- Provide prototype manufacturing nodes?
- Hackathons for Peds?
- Education/Training Programs?
Creating an Ecosystem for Innovation in Public Health

Vasum Peiris, MD MPH
Chief Medical Officer
Pediatrics and Special Populations

Food and Drug Administration
Center for Devices and Radiological Health
CDRH Strategic Priorities
2016-2017

• Establish a National Evaluation System for Medical Devices
  ▪ GOAL: INCREASE ACCESS TO REAL-WORLD EVIDENCE TO SUPPORT REGULATORY DECISION MAKING
  ▪ GOAL: INCREASE THE USE OF REAL-WORLD EVIDENCE TO SUPPORT REGULATORY DECISION MAKING

• Partner with Patients
  ▪ GOAL: PROMOTE A CULTURE OF MEANINGFUL PATIENT ENGAGEMENT BY FACILITATING CDRH INTERACTION WITH PATIENTS
  ▪ GOAL: INCREASE USE AND TRANSPARENCY OF PATIENT INPUT AS EVIDENCE IN OUR DECISION MAKING

• Promote a Culture of Quality and Organization Excellence
  ▪ GOAL: STRENGTHEN FDA’S CULTURE OF QUALITY WITHIN THE CENTER FOR DEVICES AND RADIOLOGICAL HEALTH
  ▪ GOAL: STRENGTHEN PRODUCT AND MANUFACTURING QUALITY WITHIN THE MEDICAL DEVICE ECOSYSTEM
Patients are at the Heart of What We Do

CDRH Mission: To Protect and Promote the Public Health and Facilitate Medical Device Innovation
We face a critical public health challenge

The U.S. regulatory standard for market approval protects patients by setting a high public health bar but imposes costs that make the U.S. marketplace less attractive for innovators thereby delaying patient access to important technologies.

The solution is to reduce the time and cost of the total product life cycle...

device development, assessment, review, manufacturing, monitoring, and reimbursement – without compromising the reasonable assurance of safety and effectiveness standard.
OUTLINE

• CDRH Strategic Priorities
• Accomplishments
  ▪ Pediatric Highlights
• Learning Medical Device Ecosystem
CDRH Strategic Priorities
2014-2015

▪ Strengthen the Clinical Trial Enterprise
  ❖ **GOALS:** Reduce the time and number of cycles needed to reach appropriate IDE full approval for medical devices;
    Increase the number of early feasibility/first-in-human IDE studies submitted to FDA and conducted in the U.S.

▪ Provide Excellent Customer Service
  ❖ **Goal:** Achieve at least 90% customer satisfaction

▪ Strike the Right Balance Between Premarket and Postmarket Data Collection
  ❖ **GOAL:** Assure the appropriate balance between premarket and postmarket data requirements

2016 - 2017 Strategic Priority Areas of Focus will build on our Current Accomplishments
**2014 - 2015 CDRH Strategic Priorities**

**Strengthen the Clinical Trial Enterprise**

**CDRH FY 2015 Target:** By June 30, 2015, reduce the number of IDEs requiring more than two cycles* to an appropriate full approval decision by 50 percent compared to FY 2013 performance.

*Each cycle is defined as 30 days decision time by FDA*
2014 - 2015 CDRH Strategic Priorities

Strengthen the Clinical Trial Enterprise

CDRH FY 2015 Target: By June 30, 2015, reduce the overall median time to full appropriate IDE approval to 30 days (1 cycle).

[Graph showing median days to IDE study full approval from FY 2011 to FY 2015]
Strengthen the Clinical Trial Enterprise

CDRH FY 2015 Target: By June 30, 2015, increase the number of early feasibility/first-in-human IDE studies submitted to each premarket Division compared to FY 2013 performance.

☑ Over 100% increase in EFS approvals for CDRH

Many EFS currently under pre-submission discussion

**Early Feasibility Studies (EFS) IDEs**

- FY2013 (thru 7/30/13): 9 EFS approved, 22 EFS received
- FY2014 (thru 7/30/14): 11 EFS approved, 18 EFS received
- FY2015 (thru 7/30/15): 22 EFS approved, 33 EFS received
2014 - 2015 CDRH Strategic Priorities
Strengthen the ClinicalTrial Enterprise

Next Areas of Focus include:
• Promote a Culture of Quality and Organizational Excellence
  • Improve IDE submission quality
  • Quality by Design for medical device clinical studies
  • Continued growth of EFS Program
  • Leveraging evidence from clinical experience
  • Clinical trial simplification and adaptive design
  • Use of modeling to reduce clinical trial size*

✓ Guidance for the Use of Bayesian Statistics in Medical Device Clinical Trials
✓ Draft guidance on Adaptive Design for Medical Device Clinical Studies

*Advancing medical device regulatory science generally, such as through the Medical Device Innovation Consortium, is critical
Strengthen the Clinical Trial Enterprise
Adaptive Designs

What is adaptive design?

• A study that includes prospectively planned opportunity(ies) to change the study design based on accumulating data during the course of the study
  ▪ Potentially includes modifications after a trial is underway but before unmasking/unblinding
  ▪ Does NOT include retrospective or \textit{ad hoc} changes introduced after outcomes are known, nor attempts to salvage failed trials

Why a Bayesian approach?

• When good prior information on clinical use of a device exists, the Bayesian approach may enable this information to be incorporated into the statistical analysis of a trial.
• In some circumstances, the prior information for a device may be a justification for a smaller-sized or shorter-duration pivotal trial
Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices (Draft Pediatric Extrapolation Guidance)

• Despite a recognized need, relatively few medical devices have pediatric-specific indications and labeling.
• The draft guidance proposes a framework to consider leveraging data from adult and other populations to augment what is known about a device’s performance in pediatric patients.
• The approach described in this draft guidance could stimulate growth in the number of devices specifically indicated and labeled for pediatric patients.
Strengthen the Clinical Trial Enterprise

• Premarket Assessment of Pediatric Medical Devices (March 2014)
  - To help define the pediatric population and pediatric use for medical devices
  - To help identify the types of information needed to provide reasonable assurance of the safety and effectiveness of medical devices intended for use in the pediatric population
  - To help define the guiding principles and protections sponsors should consider for pediatric subjects in device clinical trials
The Virtual Family Project is a collaboration between FDA, the Foundation for Research on Information Technologies in Society (IT’IS), and other partners to develop four anatomically correct whole-body computer models for electromagnetic (EM), thermal, computational fluid dynamic, and other computer simulations.

Virtual Family models
DUKE: 34-year-old male
ELLA: 26-year-old female
BILLIE: 11-year-old female
THELONIOUS: 6-year-old male
Strengthen the Clinical Trial Enterprise

Computational Modeling

Medical Device Regulatory Evaluation

Sources of Scientific Evidence

Credit: MDIC Modeling and Simulation Project
2014 - 2015 CDRH Strategic Priorities
Provide Excellent Customer Service

CDRH FY 2015 Target: By December 30, 2015, achieve at least 90 percent customer satisfaction.

OVERALL CUSTOMER SATISFACTION RATING
As of June 30, 2015

EXTERNAL CUSTOMER RATING
91%

INTERNAL (FDA) CUSTOMER RATING
84%

88%
Next Areas of Focus include:

- Expanding our engagement with customers, particularly patients (Partner With Patients)
  - Guidance - Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approvals and de Novo Classifications, 2012

- For device developers, resources permitting, earlier and greater interaction, as well as ability to track premarket submissions
“Risk tolerance will vary among patients, and this will affect individual patient decisions as to whether the risks are acceptable in exchange for a probable benefit. ... FDA realizes that some patients are willing to take on a very high risk to achieve a small benefit, whereas others are more risk averse. Therefore, FDA would consider evidence relating to patients’ perspective of what constitutes a meaningful benefit when if the device is effective, as some set of patients may value a benefit more than others.”
Patient Preference Initiative

Launched September 2013 – Public Workshop

GOAL: Develop a systematic way of eliciting, measuring, and incorporating patient preference information (PPI) where appropriate throughout the total product life cycle (TPLC) and to drive more patient-centric device development, evaluation and delivery

To do this, we must:

- Understand the barriers patients have faced in trying to participate in the regulatory process
- Incorporate patient perspectives to inform benefit-risk decisions
- Advance the state of the science of measuring patient preferences
CDRH Strategic Priorities

Provide Excellent Customer Service
Partner with Patients

Where can patient perspectives inform the medical device TPLC?

- Patient-Informed Needs
- Patient-Informed Clinical Trial Design, Patient Reported Outcomes
- Patient Preference Benefit-Risk Information
- Communicating Benefit-Risk Information to Patients
- Patient-Centered Outcomes

Flowchart:
- Discovery + Ideation
- Invention + Prototyping
- Pre-Clinical
- Clinical
- Regulatory Decision
- Product Launch
- Post-Market Monitoring
Providing Information about Pediatric Uses of Medical Devices
(Pediatric Tracking Guidance, May 2014)

• Helps promote communication with sponsors about unmet need

• Potential pediatric use information must be provided with
  ▪ any request for a humanitarian device exemption (HDE), premarket approval application (PMA), or product development protocol (PDP)
2014 - 2015 CDRH Strategic Priorities

Strike the Right Balance Between Premarket and Postmarket Data Collection

CDRH FY 2015 Target: By June 30, 2015, review 75 percent of device types subject to a PMA that have been on the market to determine whether or not to shift some premarket data requirements to the postmarket setting or to pursue down classification, and communicate those decisions to the public.

85% CDRH reviewed 85 percent of device types subject to a PMA that have been on the market.

In addition CDRH:

✓ Issued final guidance document* on achieving the right balance between premarket and postmarket data collection
✓ Launched the Expedited Access Pathway Program

*Pre-post market balance final guidance issued April 13, 2015:
2014 - 2015 CDRH Strategic Priorities
Strike the Right Balance Between Premarket and Postmarket Data Collection

Expedited Access Pathway* Launched the Expedited Access Pathway Program in April 2015 for breakthrough devices

- Eligible devices are those subject to a PMA or de novo intended to treat or diagnose a life-threatening or irreversibly debilitating disease and address an unmet need
- Early, ongoing, and extensive interaction with review team, engagement by senior management, assignment of a case manager, and collaborative creation of a Data Development Plan
- Where appropriate, some premarket data collection shifted to the postmarket setting for PMA devices

*EAPMA final guidance issued April 13, 2015: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm393879.htm
Next Areas of Focus include:

• Developing a framework for using evidence from clinical experience

• Establishing the National Evaluation System
  • Multi-stakeholder **Planning Board** developing 5-year implementation plan
  • Pilot studies being launched
  • Medical Device **Registry Task Force** Report
A National Device Evaluation System
Taking the Next Steps

STRENGTHENING OUR NATIONAL SYSTEM FOR MEDICAL DEVICE POSTMARKET SURVEILLANCE
Center for Devices and Radiological Health
U.S. Food and Drug Administration
September 2012

STRENGTHENING OUR NATIONAL SYSTEM FOR MEDICAL DEVICE POSTMARKET SURVEILLANCE
Update and Next Steps
Center for Devices and Radiological Health
U.S. Food and Drug Administration
April 2013
National “Surveillance” System
Planning Board Report

In February 2015, the multi-stakeholder Planning Board, convened by the Brookings Institution, issued a report with recommendations for how to establish the national system

- Provides a pathway to realizing a national system that harnesses novel data sources, modern analytical techniques and the participation of all stakeholders to optimize patient care
- Set out an organizational structure and directions for pilots
- Proposed next steps
  - 5-year Implementation Plan
  - Pilots

• Develops and *communicates* an evolving understanding of device *benefits and risks* throughout their marketed life using high-quality and linked *electronic health information*

• Identifies potential *safety signals in near real-time* from a variety of privacy-protected data sources serving as a safety net

• *Reduces* burdens and *costs* of medical device postmarket surveillance

• *Facilitates* clearance and approval of new devices or *new uses of existing devices*
National “Evaluation” System
Current Step: Medical Device Registry Task Force Report

• Builds on the core strategy of the White Papers and the Planning Board Report
• Discusses the role of registries in the evolving National Medical Device Evaluation System
• Provides a direction for the development of “coordinated registry networks”

National Evaluation System

Core Strategy

• Build on existing information systems
• Link registries to longitudinal data (claims data, Sentinel, PCORnet, EHRs)
• Establish “Coordinated Registry Networks”
• Remain flexible to accommodate evolution of parts (IT, medical device development, science, health care delivery system)
Learning Medical Device Ecosystem

INFORMATION FLOW

- Expedited Access Pathway
- Premarket Review
  - Benefit Risk

TIME TO MARKET

- Premarket Decision
  - Evidence from Clinical Experience
  - “Safety Net”

Center for Devices and Radiological Health
What Will It Take to Succeed

- It starts with trust among the medical device ecosystem members: “It Takes an Ecosystem”
- Shared commitment
- Shared responsibility
- Shared governance (with leadership)
- Sharing financial support
- Sharing data and expertise … and knowledge
- (And we can have different needs as long as we all get value out of the system)

If we build it together, we have arrived
Thank You!
Device Development as Ecosystems with SBIR/STTR Update

Steven Hirschfeld, MD PhD

_Eunice Kennedy Shriver_ National Institute of Child Health and Human Development
National Institutes of Health
Bethesda, MD
Layered or integrated ecosystems

- Product Development Ecosystem

- Clinical
- Engineering
- Acceptability testing
- Manufacturing
- Fiscal
- Scale up
- Regulatory
Care Delivery & Utilization Ecosystem

- Surgical
- Customer Support
- Family Caregivers
- Education & Recreational
- Medical
- Patient
- Regulatory
Congressional Mandate

• The SBIR and STTR programs are congressionally-mandated set-aside programs for U.S. small businesses to engage in R&D that has a strong potential for commercialization
• The approximate budgets for Fiscal Year 2016 NIH awards are:
  – $800 M SBIR = 3.0 %
  – $125 M STTR = 0.45 % or ~ $925 M in total for program
• The set-aside increases each year through 2017 as a result of the SBIR/STTR Reauthorization Act of 2011 to 3.2% for SBIR and 0.45 % for STTR
• To date, over $16 billion has been awarded by the SBIR program to various small businesses
Major Programs

SBIR
• The NIH Small Business Innovation Research (SBIR) program funds early stage small businesses that are seeking to commercialize innovative biomedical technologies. This competitive program helps small businesses participate in federal research and development, develop life-saving technologies, and generate jobs.

STTR
• The NIH Small Business Technology Transfer (STTR) program is similar to the NIH SBIR program, but requires that the small business formally collaborate with a research institution in Phase I and Phase II.
SBIR/STTR Differences

• **Program Director (PD)/Principal Investigator (PI)**
  – Under SBIR, the PD/PI must be primarily employed (>50% time) with the small business concern at the time of award and for the duration of the project period, unless a waiver is granted by the NIH.
  – Under the STTR Program, primary employment is not stipulated so the PD/PI may be primarily employed by either the small business concern or the collaborating non-profit research institution at the time of award and for the duration of the project period.
SBIR/STTR Differences

• The SBIR program permits and encourages research partnerships. Under SBIR, the research institution can complete up to 33 percent of the total effort for a Phase I and up to 50 percent of the total effort for Phase II.

• STTR requires that the small business concern formally collaborate with a non-profit research institution. Under STTR, the small business must perform at least 40 percent of the work and the research institution must perform at least 30 percent. The remaining 30 percent may be with the small business concern, the collaborating non-profit research institution, or an additional third party.
SBIR/STTR Phases

- **Phase I: Feasibility and Proof of Concept** The objective of Phase I is to establish the technical merit, feasibility, and commercial potential of the proposed R/R&D efforts and to determine the quality of performance of the small business awardee organization prior to providing further federal support in Phase II. Phase I awards normally do not exceed $150,000 total costs for 6 months (SBIR) or 1 year (STTR).

- **Phase II: Research/Research and Development** The objective of Phase II is to continue the R/R&D efforts initiated in Phase I. Funding is based on the results achieved in Phase I and the scientific and technical merit and commercial potential of the project proposed in Phase II. Only Phase I awardees are eligible for a Phase II award. SBIR/STTR Phase II awards normally do not exceed $1,000,000 total costs for 2 years.

- **Phase III: Commercialization** The objective of Phase III, where appropriate, is for the small business to pursue commercialization objectives resulting from the Phase I/II R/R&D activities. The NIH SBIR/STTR programs do not fund Phase III, and NIH does not provide any Phase III funding to small businesses.
Major non-NIH Small Business Funding Programs with budgets > $1B

• Department of Defense (DOD)
  – a. Air Force
  – b. Army
  – c. Defense Advanced Research Projects Agency (DARPA)
  – d. Missile Defense Agency (formerly BMDO)
  – e. Navy
• Department of Energy (DOE)
• Department of Homeland Security (DOHS)
• National Aeronautics & Space Administration (NASA)
• National Science Foundation (NSF)
I-Corps™ at NIH

• Is an 8-week training program.
• Introduces the concept of a “Business Model Canvas,” which provides the framework for pursing a hypothesis-driven validation approach to customer discovery.
• Is taught by experienced, business-savvy instructors who work closely with project teams to help them explore potential markets for their Federally funded innovations.
• Instructors teaching this pilot program are selected based on their specific domain expertise in the major product areas that comprise the biomedical industry.
I-Corps Participation Requirements

• To participate in the I-Corps™ at NIH pilot program, eligible SBIR/STTR grantees are required to assemble three-member teams that will work collaboratively to complete the activities and assignments required by the I-Corps™ training curriculum. These team members include:
  – C-Level Corporate Officer: A high-level company executive with decision-making authority;
  – Industry Expert: An individual with a prior business development background in the target industry; and
  – Program Director/Principal Investigator (PD/PI): The assigned PD/PI on the SBIR/STTR Phase I award.
For further information

http://sbir.nih.gov/

hirschfs@mail.nih.gov
Office of Orphan Products Development Overview and Programs for Pediatric Device Development

Karen Russell, MPH, MHS, PA-C
Commander, U.S. Public Health Service
Pediatric Device Consortium Grant Project Officer
Office of Orphan Products Development (OOPD)
Food and Drug Administration
February 18, 2016
Objectives

• Describe the Office of Orphan Products Development (OOPD) Mission and Pediatric Device Related Programs and Activities

• Highlight the Orphan Products Grants and the Humanitarian Use Device (HUD) Designation Programs
OOPD Mission

To promote the development of products, including drugs, devices, biologics, and medical foods, for the treatment, diagnosis, and prevention of rare diseases and conditions.

<table>
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<tr>
<th>DESIGNATION PROGRAMS</th>
<th>GRANT PROGRAMS</th>
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<tr>
<td>Orphan Drug Designation</td>
<td>~$15M Orphan Products Grants Program</td>
</tr>
<tr>
<td>Rare Pediatric Disease Designation</td>
<td>$3M Pediatric Device Consortia Grants Program</td>
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<tr>
<td>Humanitarian Use Device Designation (HUD)</td>
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What are the Needs? .... and What is Being Done?

• ~7000 rare diseases, the majority of which affect pediatric patients

• HUD/HDE Pathway – Alternative pathway to market
  – More than 230 HUDs designated
  – 69 HDEs approved by FDA

• Grant funding for pediatric consortia and clinical studies
OOPD Programs

- Orphan Drug Designation Program
- Rare Pediatric Disease Designation Program
- Pediatric Device Consortia Grants Program
- Orphan Products Grants Program
- Humanitarian Use Device Designation Program

www.fda.gov/orphan
Medical Devices for Pediatrics and Rare Diseases

- **Dexcom G4 PLATINUM** (Pediatric) Continuous Glucose Monitoring System
- **DLP Pediatric One-Piece Arterial Cannulae**
- **Berlin Heart Pediatric Ventricular Assist Device**
- **Lixelle® β2-microglobulin Apheresis Column**
- **Argus® II Retinal Prosthesis System**
Orphan Products Grants Program
Orphan Products Grants Program

• Supports the development of products for rare diseases by funding **clinical trials**
  – 55 products to marketing approval
  – ~$15 million/year
  – 7% device projects – we encourage more device participation

• Recently funded devices:
  – Cytopheretic device for the treatment of pediatric patients with acute kidney injury
  – String test in diagnosing eosinophilic esophagitis
  – Hemi-bridge system for treatment of idiopathic scoliosis
Orphan Products Grants Program

- R01 funding mechanism for **clinical trials** only
  - Approved Investigational Device Exemption (IDE), or
  - Non-significant Risk devices – letter from CDRH

- Devices eligible – **200,000 prevalence** (instead of **4,000 incidence** maximum for HUD designation)

- Amounts awarded:
  - $250,000 per year for up to 3 years for Phase 1
  - $500,000 per year for up to 4 years for Phase 2 or 3

http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/WhomtoContactaboutOrphanProductDevelopment/default.htm
Humanitarian Use Device Designation Program
Humanitarian Use Device Designations Program

• First step in HDE approval process

• Incidence of fewer than 4,000 individuals in the US per year
  - Therapeutic-- # newly diagnosed cases
  - Diagnostic-- # subjected to diagnosis

• HUD Designation makes the device eligible for an HDE application based on safety and probable benefit instead of safety and effectiveness

*HUD Designations Guidance available at:*
HUDs and HDEs

To date
Recent Analyses on the Basis of HDE Approvals.....
# Level of Evidence

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th># of HDE Approvals</th>
</tr>
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<tbody>
<tr>
<td>Clinical Experience</td>
<td>2</td>
</tr>
<tr>
<td>Retrospective Analysis</td>
<td>3</td>
</tr>
<tr>
<td>One Prospective Trial</td>
<td>10</td>
</tr>
<tr>
<td>Two or More Prospective Trials</td>
<td>3</td>
</tr>
</tbody>
</table>

Valid Scientific Evidence: “evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device” (21 CFR 860.7(c)(2))

HDEs with Clinical Trials: N=13
HDEs without Clinical Trials: N=5
Target Population of HDEs

- **HDE approvals:** 2007 to 2013
- **Pediatric Indications:** Majority of rare diseases affect children
- 11% of HDE approvals are labeled for pediatric patients only
- 22% are labeled for pediatric and adult patients
- 72% could be used in pediatric patients

![Bar chart showing number of HDE Approvals by age group](chart.png)
Strategic Plan for New Therapies for Pediatric Rare Diseases

- Enhance foundational and translational science
- Increase regulatory science
- Improve FDA review process

Available at:
Device Needs Assessment

• Goal: To identify unmet device needs for rare diseases, including pediatric rare diseases, to understand the extent of these needs

• Plan:
  – Web-based clinician survey has begun
  – Report and publication will capture and demonstrate the compelling nature of rare disease medical device needs
Contact Information

• For more information on OOPD’s programs:
  www.fda.gov/orphan
  Email/call us at orphan@fda.hhs.gov 301-796-8660

• For more information on CDRH’s programs:
  www.fda.gov/MedicalDevices
  Email/call CDRH at DICE@fda.hhs.gov 301-796-7100
Thank You
Medical Device Development for Pediatric Rare Diseases

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DISCLOSURES

• I am a full time employee of the FDA
• I have no conflicts of interest to report
• The views expressed in this presentation are those of the presenter and do not represent the official policies of the FDA
Pediatric Rare Diseases (PRDs)
Reality of Medical Device Therapy

- Few are supported by randomized clinical trials
- "Off-label" use supported by:
  - Expert opinion
  - Single institution observational studies
  - Extrapolations from adult cardiovascular medicine
  - Evolutionary – historical literature based comparisons
- Desire for innovative less-invasive treatments
  - Hybrid approaches
  - Targeted therapies - disease/lesion specific devices
Evaluation of Pediatric Devices

Trial Design Challenges

- Relatively small number of children affected
- Large range of device sizes often required
- Accommodation for Growth
- Longevity
- Acceptance of randomization - parents and children
- Available Off-label use of adult devices

Evaluation of Pediatric Devices

RCT Challenges?

- Rarity and Heterogeneity – Enrollment, Expertise, and Generalizability problems
- Appropriate populations and clinical endpoints - hard to identify
- New therapies → dropout
- Equipoise
- Ethical Considerations
- Infrastructure
Clinical Trials for Pediatrics
Device Company Perspective

- High Costs often Prohibitive
  - R & D – growth, long term durability
  - Trial
  - FDA - PMA
  - Marketing

- Small end market limits return
- Available Off-Label use
Consequences for PRDs
Patients and Physicians

• Few “on-label” devices for PRDs
• Human costs – unmet clinical need
  – Persistence of unproven or even unsafe treatment alternatives
  – No or limited access to new technology
  – Palpable time lag
    • OUS Device Development
    • Device development for OUS Markets
Why is On-label Use Important

Device Evaluation:
- Safety
- Effectiveness or Probable Benefit
- Quality
- Performance

For the intended use and conditions of use in a specific target population

• **Pre-clinical evaluation** - appropriate for the intended use
• **Clinical Testing** - performed in accordance with the instructions for use (e.g., preconditioning, sizing)
• **Clinical information** - provided in the label, reflects the intended use and conditions of use in a specific target population
• **Warnings and Precautions** Identify:
  - potential performance problems under studied circumstances or conditions, or
  - potential limitations of the evaluation (e.g., populations not included in studies)
Early engagement - FDA & product developers

• Efficient Execution of Product Development
  – Data development plan - tools, standards and approaches for assessing safety, efficacy, quality, and performance
  – Optimization of Clinical trial design and performance
    • Instrument and endpoint development
    • Pre-Post-market balance
  – Facilitating navigation of the regulatory processes

• Identification of Appropriate Facilitative Programs and Initiatives
  – Early Feasibility Study - Expedited Access Program
  – Extrapolation - Pre-Post-Market Balance
FDA Initiatives to Facilitate Pediatric Device Development

• Early Feasibility Program (Guidance)

• Extrapolation (Draft Guidance)
  – existing clinical data in another studied population (such as adults, or a different pediatric subpopulation) may be leveraged (“extrapolated”) to support marketing approval and labeling of medical devices for use in pediatric patients

• Expedited Access Program – Unmet clinical need (Guidance)

• Pre-Post Market Balance (Guidance)
  – Conversion of HDE to PMA (Melody)
  – Potential PMA/HDE Approval - existing clinical data from SOC device therapy
FDA Strategies to Enhance Review Process for PRD Products

• **Better perspective** - patients’ and caregivers’ preferences

• **Benefit–risk framework** - all phases of device development, evidence acquisition and regulatory review

• **Better communication** of reasoning behind regulatory decisions

• **Consideration of Unmet medical need** - decisions taking into account the severity of the treated condition and the adequacy of available therapies

• **Innovation in data analysis** - small population clinical trials
Early Feasibility Study (EFS) Program

• Intended to facilitate the clinical evaluation of medical devices in the US under the Investigational Device Exemptions (IDE) regulations
  – Uses risk mitigation strategies that appropriately protect study subjects

• Elements that define an early feasibility study:
  • Small number of subjects
  • Device early in development, typically before the device design has been finalized
  • Does not necessarily involve the first clinical use

Early Feasibility Program: Goals

- Providing the earliest and broadest patient access to beneficial medical devices
- Regaining and maintaining innovation in the US
- Encourage device development for unmet clinical needs
Key Principles of the Program

Further exhaustive nonclinical testing unable to provide the information needed to further device development

- Approval of an early feasibility study IDE may be based on less nonclinical data

Early clinical use of the device in a limited number of subjects is needed:

- To provide initial insights into clinical safety and device function and performance
- To inform subsequent clinical and non-clinical testing requirements
- To improve device performance through iteration before finalizing the design
After Study Initiation:

Iterative Device Development Process

• The EFS Guidance includes new approaches to facilitate timely device and clinical protocol modifications during an early feasibility study

• When appropriate - allows additional time for completion of non-clinical testing (JIT)

• Needed Clinical experience/feedback on device use – design modification

• Early identification of Pivotal Trial needs or Regulatory Pathway Choice
Opportunities Associated with US Early Feasibility Studies (EFS)

- **Early Contact** between inventors, developers, investigators, and regulators
  - Geographically closer
  - More collaborative
  - Enhanced understanding of the pathway for regulatory approval or clearance
- **Patient Centered Outcomes** - Developed and tested based on disease and technology
- **Patient/Physician Access** to promising novel technology
  - Earlier
  - Continuous
  - Expanded
Decision Framework

Application of benefit/risk principles throughout the total product life-cycle:

Keeping the clinical context at the forefront
Device Development for PRDs

Recommendations

• **Early HUD Designation** if appropriate

• **Meet with FDA Review Division**
  – Pre-Submission meetings – Early and Often
    • Free
    • Take advantage of the Early Feasibility Program
    • Enhances Collaboration
      – Determine appropriate clinical evidence needs
        » Extrapolation
        » Clinical trial designs and endpoints
        » Pre- post-market balance
      – Identify least burdensome pathway to market
        » PMA or HDE
        » DeNovo 510k
        » Expedited Access Pathway
Bench to Bedside

Steps:
• Early Entry: FIH and EFS
• Rapid Transitions
  • Tailored Data Requirements
  • 30 day data
• “Staged” Trial Design

Rapid Transitions:
• Device design is near-final or final,
• Early feasibility study results support the initial safety of the device and proof of principle, and
• Adequate non-clinical data are available