



Patient Access to High-Risk Devices for Unmet Medical Needs Jan. 30, 2014

A Summary of a Meeting on Exploring Access to Innovative Devices for Patients Without Alternatives

Conference overview

The U.S. Food and Drug Administration, or FDA, promotes public health by ensuring that marketed medical devices are safe and effective, and by facilitating the delivery of cutting-edge products into patient care without unnecessary delay. Currently, FDA reviews all high-risk devices (with the exception of Humanitarian Device Exemptions*) according to the same standard of safety and effectiveness.

Recently, FDA's Center for Devices and Radiological Health, or CDRH, decided to explore whether some data currently collected before device approval could be collected postmarket, to speed patient access to devices that fill an unmet medical need. The center's 2014 strategic priorities document proposed the data shift to "strike the right balance between premarket and postmarket data collection."¹ In an article in *The Gray Sheet*, CDRH director Jeff Shuren explained that the proposed change would incorporate aspects of the center's prior innovation pathway pilots.²

On Jan. 30, 2014, The Pew Charitable Trusts held a meeting titled "Patient Access to High-Risk Devices for Unmet Medical Needs." Stakeholders discussed FDA's current regulatory authority and whether new approaches were needed to facilitate patient access to high-risk medical devices for serious, unmet medical needs.³ The conference drew more than 100 participants representing manufacturers, providers, payors, patients, and other health stakeholders.

Shuren delivered the keynote address, followed by two panel discussions moderated by Allan Coukell, Pew's senior director of drug and medical device initiatives, and two panels moderated by Josh Rising, Pew's director of medical devices. To examine the potential shift of some premarket evidence collection to the postmarket setting, the panels focused on the following questions:

- What steps can FDA take under current authority? What do stakeholders want the agency to do that would require new authority?
- What effectiveness data should be collected prior to approval, and what could potentially be assessed in the postmarket setting?
- If some evidence is shifted to the postmarket setting, what postmarket controls would ensure the ultimate collection of this data?
- How should these products be covered and paid for, and how can reimbursement complement the regulatory process?

* Humanitarian Device Exemption applications are intended to treat or diagnose a disease or condition that affects a patient population of fewer than 4,000 individuals per year in the United States.

Stakeholders at the meeting arrived at the following key findings:

- The benefits and risks of a device are never known with 100 percent certainty at the time of approval. Patients with unmet needs might be willing to tolerate a higher level of uncertainty for devices when they have no other treatment options. However, patient preferences vary significantly, and more work must be done to understand these and to include patients in the decision-making process.
- FDA intends to publish a guidance document clarifying its authority to shift some premarket evidence to the postmarket setting for devices that fill an unmet need;* this guidance will serve as a springboard for further discussion.
- Ensuring the collection of postmarket data is essential in any effort that shifts premarket data to the postmarket setting. Other challenges include removing a device from the market that is ultimately found to be ineffective. Congress may have to approve new authorities for FDA to address these issues.
- Early engagement between manufacturers and payors—including the development phase of a new device—will foster greater understanding of the perspectives of each, and of the requirements for payor coverage.

* Subsequent to the meeting, on April 23, 2014, FDA published two draft guidances on (1) balancing premarket and postmarket data collection for high-risk devices, and (2) expediting access to certain devices intended for an unmet medical need.

Conference Summary

Opening remarks

Shuren described the uncertainty around specific benefits and risks of a medical device at the time FDA approves it, citing two reasons. First, a clinical trial would have to enroll an extremely large number of patients and follow them for an extended period of time in order to eliminate any uncertainty, which would significantly slow device innovation. Second, clinical trials are often not representative of clinical practice. These two factors prevent 100 percent certainty about a device's safety or effectiveness at the time of approval.

He gave examples of how the agency handles this uncertainty. If a rare adverse event is seen in a particular device prior to its approval, FDA might address the issue by requiring the manufacturer to conduct additional postmarketing surveillance. Resolving the issue definitively before approval could unnecessarily delay approval. In the example of a knee implant, FDA does not require a manufacturer to conduct 15 to 20 years of research before approving the device, even if the knee is expected to last for decades. Instead, the agency reviews enough premarket data and uses its experience to determine whether the benefits outweigh the risks.

To explore the audience's tolerance for uncertainty, Shuren polled the attendees on whether there were times when they, as patients, might be willing to accept less certainty around a device's effectiveness. He used a type of advanced brain cancer, glioblastoma multiforme, or GBM, as an example of a disease for which few treatments are available, and from which most patients die within two years. He then described a scenario where he had a device that would cure 70 percent of GBM patients with a 5 percent risk of death and a 5 percent risk of a serious adverse event, and he asked the audience what level of confidence they would need in the device's effectiveness before using it for themselves or a loved one. Most raised their hands to indicate their comfort with a confidence level of 70 percent for the device's effectiveness. Many kept their hands raised as Shuren proposed lower levels of certainty.

Understanding patient preferences—and how well patients tolerate uncertainty—is essential in any discussion on improving access to devices that fill an unmet need, Shuren emphasized. FDA's 2012 guidance on benefit-risk determination describes how the agency intends to incorporate patient preferences in its decision-making process. It also discusses the use of postmarket controls to ensure that manufacturers collect the necessary data.

Shuren highlighted one of CDRH's strategic priorities: providing patients in the United States with access to high-quality, safe, and effective medical devices of public health importance.⁴ He said the agency has made great strides in reducing unnecessary delays for low- and medium-risk products, but a large and expanding gap exists between European Union and U.S. approval for high-risk devices. For example, approval in the United States lagged three to five years behind that in the European Union for devices such as transcatheter aortic valve replacements and newer-generation drug-eluting stents.

In an effort to address this gap, CDRH is working on guidance to shift some of the premarket evidence to the postmarket setting for devices that address unmet medical needs. Shuren noted that the Federal Food, Drug, and Cosmetic Act mandates consideration of this approach, citing the statute: "the Secretary shall consider whether the extent of data that otherwise would be required for approval of the application with respect to effectiveness can be reduced through reliance on postmarket controls."⁵

Although such a shift could initially raise the uncertainty surrounding a device's effectiveness, the benefits could still outweigh the risks for patients who have no other options. Data collected in the postmarket setting would

either confirm the device’s effectiveness or, if it showed the device was ineffective, would prompt FDA to remove it from the market. Shuren finished by discussing the need to further explore the willingness of patients—as demonstrated in his informal audience poll—to accept more uncertainty about the benefits and/or risks of innovative treatments and diagnostics that address an unmet public health need for life-threatening diseases.

The value in shifting premarket evidence to the postmarket setting

Following Shuren’s remarks, the panels discussed the potential to improve patient care by shifting some premarket data to postmarket.

From a manufacturer’s perspective, Michael Mussallem, chairman and CEO of Edwards Lifesciences, said an ideal system would have enough flexibility “to judge each device based on the patient population, and severity of the illness. Then FDA and the manufacturer can agree on how narrow the group of patients and providers should be in both the premarket and postmarket settings.”

Bray Patrick-Lake, director of stakeholder engagement at the Clinical Trials Transformation Initiative, felt patients could suffer harm if the bar for premarket data collection were set so high that the cost of clinical trials became a barrier to approving innovative devices. Given that collecting data in perpetuity is financially unsustainable, high-quality premarket trials must focus on key elements of device safety and effectiveness that patients and clinicians need to know to make informed decisions.

Diana Zuckerman, president of the National Research Center for Women & Families*, was skeptical of approaching device approval by moving premarket data (which she described as “already very limited”) to the postmarket setting. She described the difficulties of quantifying the uncertainty of a device’s benefit-risk profile, and she said companies have little incentive to conduct postmarket studies quickly or to ensure that patients stay in long-term studies. She also felt that data from postmarket studies were not generally available to the public. “What becomes the least burdensome for the device companies may end up being most burdensome for the patients and the physicians who are trying to make judgments based on limited information,” she said.

David Nexon, senior executive vice president of the Advanced Medical Technology Association, endorsed the effort to help devices reach patients with no other treatment options more quickly, and he indicated that shifting the balance between premarket and postmarket data collection could be useful. However, he cautioned that companies might fear that without careful implementation, this approach could result in an increase in postmarket burdens without streamlining the premarket data requirements. Ultimately, this would make investment in novel treatments less attractive.

Nexon said that FDA’s Center for Drug Evaluation and Research, or CDER, has four different pathways—breakthrough, fast track, accelerated, and priority review—to speed review of products that address important clinical gaps. He felt that, although CDRH does not have the same legislative pathways as CDER, it has the needed legislative authorities to establish approaches like these, and it has occasionally done so on an ad-hoc basis. He said Shuren’s suggestion of publishing draft guidance to formalize additional device pathways is promising for industry, and he expressed interest in working with FDA on future ideas to shorten the development and review time for innovative products. He went on to discuss the need to improve existing pathways—such as priority review, which lets the agency move an innovative product to the front of the review line—before creating new pathways, and he said the agency should explore whether it is using its existing authority to its full capacity.

* Since the meeting, the National Research Center for Women & Families changed its name to the National Center for Health Research.

Although FDA has numerous pathways to accelerate the approval of drugs that fill unmet needs, Shuren emphasized that the agency does not have the same tools for medical devices and that there may be value in formalizing accelerated pathways for devices. Shuren said detailing the standards for how the agency approaches uncertainty in benefits and risks would allow for “greater investment in important technologies for patients.” He added that he hoped CDRH’s guidance will provide an impetus to further the discussion.

Involving patients in decisions with increased uncertainty around the benefits and risks

Many participants emphasized that any proposal that could increase the uncertainty around the benefits and risks would require regulators and physicians to understand patient preferences and incorporate patients more actively into the decision-making process.

Tom Fogarty, a cardiovascular surgeon and inventor, noted that patients must be more involved if FDA shifts premarket data to the postmarket setting. “Patients have their own criteria of what is a risk and what is a benefit,” he said, adding that physicians need to understand these preferences. Creating a single standard for the level of certainty around benefits and risks that makes sense for all patients is difficult, as each patient has different needs.

The level of uncertainty in the data may change the conversation with patients. Murray Sheldon, associate director for technology at CDRH, said that clinicians must understand patients’ preferences in terms of benefits they want and the risks they are willing to take. In turn, clinicians would need to present the safety and effectiveness factors of devices to patients and ensure that they make informed decisions. Sheldon cautioned that obtaining patient preferences in practice is extremely difficult.

Panelists highlighted the shortcomings of the current process of informed consent. Many patients with debilitating conditions must read lengthy informed consent documents. Communicating the risks of a procedure in such documents is difficult, given the many purposes the document serves. Nancy Stade, deputy director for policy at CDRH, said informed consent documents should be made less cumbersome for patients and integrated more fully into patient care. Susan Campbell, director of public policy at WomenHeart: The National Coalition for Women with Heart Disease, said the coalition tries to help women with heart disease become more informed, and a great deal of work remains in the world of patient consent. She said there are “issues of communication styles, health literacy, language, and culture that really define whether this message is going to get across, and in fact, the patient can make the decision.”

Challenges also exist in keeping patients engaged for long-term studies after a device is approved. Patrick-Lake described newly developed systems to obtain patients’ consent and make sure they are comfortable with providing data, but said, “I really feel like we are failing patients in the way of what information we give them back.” Kate Ryan, senior program coordinator at National Women’s Health Network, agreed about the problem of keeping patients involved in the postmarket arena. She said that successful models of patient engagement involve educating patients about how their data are used, enabling them to see how their contributions help patients like themselves and improve public health.

Patrick-Lake discussed the need to change the culture of research in two ways. First, it should be the standard, rather than an anomaly, for patients to contribute to research by participating in randomized, controlled clinical trials. Second, health care should shift to a learning system which involves patients in a rapid, cyclical feedback loop. Such a system would allow patients to analyze and respond to data in real time, as opposed to the current system in which the publication of data and subsequent reaction of the public takes years.

An accelerated pathway: Hypothetical and real models provide a frame of reference

Before the second panel, Rising presented three case studies of devices with varying levels of evidence about their safety and effectiveness. He posed questions regarding the appropriate approval measures under the following circumstances:

- Retinal prosthesis.
 - FDA has approved this device via the Humanitarian Device Exemption, or HDE. It is intended for patients with retinitis pigmentosa, a rare condition that can lead to blindness.
 - All 30 patients in the trial benefited in visual tests. Some patients suffered serious adverse events.
 - If this device were available to treat blindness more broadly, would this level of evidence be appropriate for initial approval?
- Transcatheter aortic valve replacement, or TAVR.
 - FDA has approved this device via premarket approval, or PMA.* It is delivered via transcatheter, rather than open heart surgery, for patients with severe aortic stenosis who are not surgical candidates.
 - Early observational studies showed better 30-day survival rates (92 percent and 94 percent) when compared with historical controls (80 percent).
 - Had the manufacturer brought only this level of evidence to FDA, would this have been appropriate for initial approval? (Rising noted that in this example, which is not hypothetical, the manufacturer actually brought far more evidence to FDA before it was approved.)
- Hypothetical prosthetic heart muscle.
 - This hypothetical device is not FDA-approved. It would replace damaged heart tissue for patients who have had extensive heart damage and are ineligible for a transplant.
 - A 50-patient observational study showed a similar proportion of patient survival when compared with historical controls (60 percent versus 50 percent at six months, respectively) and a similar rate of strokes in the survivors.
 - If this device were available for patients with severe heart damage who cannot undergo open heart surgery, is this level of evidence appropriate for device approval?

Rising noted that in each example, no alternative medical treatment for its intended patient population exists (see Appendix D for additional details).

Defining a clear and appropriate standard for the balance of premarket and postmarket data

Coukell began by asking the panelists to react to the case studies and to articulate their thoughts on balancing premarket and postmarket data collection.

The case study of the prosthetic heart muscle, which had the least evidence of the benefits and risks, was not widely discussed. In the opinion of Michael Mack, director of cardiovascular surgery at Baylor Health Care

* Premarket approval is an FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices prior to marketing the device. Class III devices, also known as high-risk devices, support or sustain human life, are of a substantial importance in preventing impairment of human health, or present a potential, unreasonable risk of illness or injury.

System, the situation was not appropriate for an accelerated pathway.

The hypothetical retinal prosthesis example included evidence of probable benefit but also presented some safety concerns (13 percent of patients had serious adverse events). Michael Morton, vice president of Global Regulatory Affairs at Medtronic, said the approval pathway for this device was HDE and the device demonstrated safety and probable benefit, as required for HDE approval. He brought up the issue of how effectiveness could be shown in the postmarket setting to expand indications or achieve a PMA approval. Jeff Allen, executive director of Friends of Cancer Research, felt that in such a case, where the safety data might raise questions, the type of pathway for approval was not as important as having the right risk-communication strategies in place.

Mack pointed out that the assessment of the benefits and risks of a device is less clear when the device affects quality of life (blindness in the retinal prosthesis example), as opposed to mortality (in the TAVR therapy). Drawing from the real-life example of the TAVR therapy, he said, “Taking four years [longer than] Europe and being the 43rd country in the world to have access to TAVR, at a cost of greater than \$100 million, is probably not where we want to be.”

Although FDA defines an unmet need in its priority review guidance (Appendix C), Mack emphasized that assessing unmet need is very difficult in practice. For example, he said clinicians would give different opinions on whether severe aortic stenosis in patients who are not surgical candidates was an unmet need. A surgeon would not know there was an unmet need because only patients who were surgical candidates would be referred, whereas a general cardiologist would see a number of aortic valve stenosis patients who were ineligible for surgery, demonstrating “that there were patients that were dying because of a clinical unmet need.”

Several panelists agreed that more clarity about the goals and approaches of any new FDA pathway is needed before premarket and postmarket requirements can be addressed. Allen emphasized the need for clear standards. He noted that regulation and legislation were necessary to develop the accelerated approval pathway of drugs, which allows FDA to evaluate surrogate endpoints to determine reasonable likelihood of benefit for new drugs. Morton said that bringing devices to market through an expedited pathway would create positive momentum, as well as the ability to learn from problems that arise. Allen thought FDA and manufacturers should clearly delineate information required for premarket data collection and which low-risk elements are acceptable to postpone for postmarket data collection.

Ryan and Patrick-Lake warned the audience that even if a device is approved for a specific, narrow unmet need, “indication creep” can occur. Ryan emphasized that it is important to be cautious about off-label use—especially when there is little or no evidence of safety and effectiveness in particular populations. She said FDA and the manufacturers should clearly communicate any evidence about populations for which the device is or is not effective to providers.

Mack speculated that one issue in moving some evidence collection to the postmarket setting is enrolling patients into a randomized trial for a device that is already on the market. Matthew Hillebrenner, deputy director of the Division of Cardiovascular Devices at CDRH, echoed this problem, saying that maintaining patient randomization after a device is approved is very difficult, since patients who have not received a therapy will desire it.

Monitoring devices postmarket

Panelists emphasized the need for strong postmarketing surveillance for new devices and discussed whether additional authorities might be appropriate if FDA shifted the collection of some data to the postmarket setting.

Ryan and Joseph Drozda, director of outcomes research at Mercy Center for Innovative Care, praised the new unique device identifier as a powerful tool that has the potential to greatly enhance postmarket data collection. Drozda discussed FDA's initiatives for strengthening postmarket surveillance and the need to use registries and new methodologies to evaluate implanted medical device performance.

Mussallem said an effective postapproval process would need enough patient data to evaluate and fully understand how a device interacts with a population. He mentioned the Transcatheter Valve Therapy, or TVT, registry, saying it provides a large database for analysts to do a "deep dive" when there is concern about a product. Sheldon added that registries are useful in the postmarket setting because the effect seen in a randomized trial rarely corresponds directly to the effects of the device in a broader population.

Zuckerman discussed the difference between simply completing required postmarketing studies and completing them well. She said FDA should be more aggressive in ensuring that manufacturers fulfill their postmarketing obligations. Additionally, she raised the concern that larger studies are necessary for subgroup analyses of women, minorities, and older patients who are underrepresented in postmarket and premarket studies.

Panelists also discussed additional approaches that may be needed to ensure that evidence shifted to the postmarket setting is ultimately collected. Both Shuren and Stade stated that one important factor in any FDA decision to shift premarket evidence collection to the postmarket setting was the agency's confidence that the data would be obtained.

Ryan suggested addressing this challenge by automatically sunseting approvals if the needed information is not collected by a prescribed deadline. Manufacturers would thus have a strong incentive to collect the data. FDA would need new legislative authorities for such an approach.

Mack said the agency could face challenges in removing a device from the market if evidence showed that it did not work. Shuren responded that FDA has the ability to remove the device from the market, but that other groups can also take action. In particular, clinicians could stop using the device, and payors could stop reimbursing its use.

Finally, Bill Murray of the Medical Device Innovation Consortium said that some of the need to conduct postmarketing studies on devices stems from the lack of data on outcomes from standard clinical care.

Levels of evidence to determine payor coverage

The concluding panel of the meeting discussed coverage and reimbursement decisions regarding devices which fill an unmet medical need but may come to market with less evidence.

Naomi Aronson, executive director of Clinical Evaluation, Innovation, and Policy at Blue Cross Blue Shield Association, or BCBSA, described three dimensions of evidence used by the association to evaluate a new device: the relevance of the evidence to the population of interest, the quality of evidence, and the magnitude of the benefit or the clinical significance of the evidence. BCBSA sends this information to their 38 individual plans (with 100 million beneficiaries), which vet policies with societies and academic experts. Aronson said, "In general, when there is a divergence between the expert opinion and the evidence, the evidence tends to win in the development of our policy. But there are provisions for circumstances in which there's a greater flexibility there, and that includes unmet medical need."

Aronson added that if a new device offers clinically significant benefits with robust evidence, it will be covered. By contrast, "if you don't actually know that something works, you don't really know that you need it," said Louis Jacques, director of the Coverage and Analysis Group at the Centers for Medicare & Medicaid Services, or

CMS.* Aronson said she had seen instances where there is “a lot of marginal intervention with a lot of marginal evidence.”

Aronson expressed concern about one potential, unintended consequence of payor coverage for a device that fills an unmet need but comes to market with less evidence: another manufacturer might decide not to pursue an alternative treatment for the unmet need. The end result, if the original device were not effective, would be a lack of treatment options for patients.

Jacques reported that since 2009 CMS has moved away from non-coverage decisions for new devices. Instead, the agency has relied on coverage with evidence development, or CED. Under CED, CMS agrees to cover the use of the device as long as additional patient data are captured as part of a protocol designed to answer outstanding questions. This has helped the agency address the need for promising technologies that do not yet have an adequate evidence base to merit broader coverage.

Mark Leahey, president and CEO of the Medical Device Manufacturers Association, stated that getting CED determination aligned with FDA review should be taken into consideration. This is particularly important for smaller companies that do not have a broad product portfolio, and therefore are not otherwise generating revenue to subsidize the delay in obtaining payor coverage. He noted that a combined FDA/CMS approach might be good for novel devices, but that other approaches were sufficient for the majority of technologies.

Early engagement between manufacturers and payors

Many panelists highlighted the importance of early discussions among all stakeholders, including manufacturers, regulators, payors, and clinicians.

Pankaj Pasricha, physician and director of the Johns Hopkins Center for Neurogastroenterology, described the American Gastroenterological Association’s Center for GI Innovation and Technology as an example of a professional society effort that incorporates multiple stakeholders in discussions to advance innovative technologies.

Pasricha said payment is the most important roadblock to getting devices to patients because “if nobody ever pays for your device, it’s as good as never making it.” He said CMS and FDA need a more proactive process, not only in the review phase, but earlier, when medical device companies begin planning a trial. Leahey agreed that there should be a concurrent process with FDA, CMS, and payors to ensure that U.S. patients have access to innovative technologies first in the world—a CDRH goal discussed earlier by Shuren. Additionally, he brought up the dearth of incentives to pull innovative technologies through to market when unmet clinical needs exist. An effective system to create those incentives would improve patient care and bend the country’s cost curve in the right direction.

The panelists agreed that early engagement is critical. Jacques said that a recent aim of CMS is to have conversations with manufacturers before they are so deep into their pivotal trial that they cannot make changes to their protocol. Such conversations are voluntary, but he said if manufacturers engage early enough, they can determine which patients to include in a trial to provide sufficient evidence for Medicare review. Pasricha agreed, adding that medical societies provide an opportunity for stakeholders—FDA and sponsors included—to come together in a nonthreatening environment and to “actually initiate the kinds of dialogues that are critical to the development of the technology.”

* Louis Jacques is no longer affiliated with CMS.

Next steps

The FDA guidance document published in April 2013 provides stakeholders an opportunity to further discuss which devices would qualify for a new pathway, what evidence could be shifted to the postmarket setting, how FDA can ensure the collection of postmarket data, and whether creation of new authorities is merited. Additional discussions will be needed to determine how payors would cover and reimburse these devices. Ultimately, this work has the potential to improve patient outcomes and to better incorporate patient preferences into the decision-making process.

Appendix A: Agenda

Patient Access to High-Risk Devices for Unmet Medical Needs January 30, 2014

The Pew Charitable Trusts, Carolinas Room, 10th Floor, 901 E Street, NW, Washington, D.C.

Meeting Goals:

- Describe the Food and Drug Administration's (FDA's) current authorities and programs to facilitate patient access to high-risk devices for serious, unmet medical needs.
- Discuss options for adjusting the balance of premarket and postmarket effectiveness data collection for products meeting unmet medical needs.
- Discuss whether and how the collection of some data on device effectiveness in the postmarket setting would impact patient safety.
- Identify mechanisms to ensure the collection of postmarket data and discuss other needed postmarket controls.
- Discuss coverage and reimbursement approaches for innovative devices.

8:30-9:00 **Coffee and Light Breakfast**

9:00-9:15 **Welcome**

Allan Coukell, Senior Director, Drugs & Medical Devices, The Pew Charitable Trusts

9:15-9:45 **Keynote: FDA's Authorities and Programs to Accelerate Access to Novel Devices**

Jeff Shuren, Director, Center for Devices and Radiological Health (CDRH), FDA

- What tools does FDA have to speed access to new devices for patients with few or no options?
- What new policies is FDA considering to accelerate patient access to innovative high-risk devices while ensuring safety?
- Under FDA's current authorities, can the agency rebalance premarket and postmarket data collection for innovative products that address a serious unmet need?
- Does FDA require any new authorities to facilitate patient access to novel technologies for serious unmet medical needs?
- Are FDA's authorities sufficient to ensure the collection of postmarket data if the balance of premarket and postmarket data collection on device effectiveness is adjusted?

9:45-10:45 **Panel Response: Assessing the Effectiveness of Existing Efforts**

- Tom Fogarty, Chairman, Director and Founder, The Fogarty Institute for Innovation
- David Nexon, Senior Executive Vice President, Advanced Medical Technology Association
- Diana Zuckerman, President, National Research Center for Women & Families

- How effective are FDA's tools in getting innovative devices to patients with serious unmet needs more quickly while maintaining safety standards?
- Under FDA's current approach, do the benefits outweigh the risks of accelerating devices for these patients?
- Should FDA be doing more to speed access to high-risk devices for specific patients?
- If yes, how can this be done while still ensuring product safety and effectiveness?
- Are current authorities appropriate to ensure prompt patient access to devices for serious unmet medical needs that are safe and effective or is legislation needed?

10:45-11:00 **Break**

11:00-11:15 **Presentation: Case Studies**

These case studies will provide hypothetical examples of devices to facilitate the discussion.

Josh Rising, Director, Medical Devices, The Pew Charitable Trusts

11:15-12:30 **Panel: Considering Devices and Data for Accelerated Approval**

- Jeff Allen, Executive Director, Friends of Cancer Research
- Michael Mack, Director, Cardiovascular Surgery, Baylor Health Care System
- Michael Morton, Vice President Global Regulatory Affairs, Medtronic, Inc.
- Murray Sheldon, Associate Director for Technology, CDRH, FDA
 - Are there unmet medical needs where it is appropriate to adjust the balance of premarket and postmarket effectiveness data collection to get devices to patients more quickly?
 - If so, what effectiveness data could be shifted to the postmarket setting?
 - How could such a pathway be implemented?
 - What role does patient risk-tolerance play, and how can that best be considered?

• **12:30-1:15** **Lunch (Provided)**

1:15-2:15 **Panel: Post-market Monitoring for Devices Accelerated to Patients**

- Joseph Drozda, Director, Outcomes Research, Mercy Center for Innovative Care
- Michael Mussallem, Chairman and CEO, Edwards Lifesciences
- Bray Patrick-Lake, Director of Stakeholder Engagement, Clinical Trials Transformation Initiative
- Kate Ryan, Senior Program Coordinator, National Women's Health Network
- Nancy Stade, Deputy Director for Policy, CDRH, FDA
 - How can FDA ensure prompt and sufficient collection of postmarket data for devices that are accelerated to patients?
 - Will patients and providers participate in randomized, controlled trials for approved products? Is non-randomized or uncontrolled data sufficient?

- What are appropriate restrictions on the use of these devices—such as limiting their use to centers of excellence or requiring provider certifications?
- What remedies are available if the postmarketing experience shows a device does not meet either the safety or effectiveness standards?
- What is the appropriate way to convey to patients and clinicians the evidence that supports the device?

2:15-3:30

Panel: Payor Coverage of Devices Accelerated to Patients

- Naomi Aronson, Executive Director, Clinical Evaluation, Innovation, and Policy, Office of Clinical Affairs, Blue Cross Blue Shield Association
- Louis Jacques, Director, Coverage and Analysis Group, Centers for Medicare & Medicaid Services
- Mark Leahey, President and CEO, Medical Device Manufacturers Association
- Pankaj Pasricha, Director, Johns Hopkins Center for Neurogastroenterology
 - How do payors currently make coverage and reimbursement decisions regarding innovative devices entering the market?
 - How would adjusting the premarket-postmarket balance of data collection on device effectiveness affect coverage and reimbursement decisions for devices that fill unmet medical needs?
 - Are payors more willing to cover a device if it fills an unmet medical need? Should they be?
 - What is the appropriate way to involve payors in FDA efforts to accelerate patient access to innovative medical devices?

3:30-3:50

Final Questions and Answers

3:50-4:00

Wrap-up

4:00

Adjourn

Appendix B: Speaker biographies

Jeff Allen, Ph.D. serves as the Executive Director of Friends of Cancer Research (*Friends*), a think tank and advocacy organization in Washington, D.C. *Friends* is one of our country's leading voices in advocating for policies and developing solutions that will get treatments to patients in the safest and quickest way possible.

As a thought leader on many issues related to the U.S. Food and Drug Administration, regulatory strategy, and healthcare policy, he is regularly published in prestigious medical journals and policy publications. In addition to participating in major scientific and policy symposiums around the country each year, Jeff has had the honor to be called to testify before Congress, and to contribute his expertise to the legislative process on multiple occasions. Recent initiatives at *Friends* include the establishment of the new Breakthrough Therapies designation and the development of the Lung Cancer Master Protocol, a unique partnership that will accelerate and optimize clinical trial conduct for new drugs.

As Executive Director of *Friends*, Jeff has the privilege to also serve on a variety of influential committees, boards, and advisory councils. Allen received his Ph.D. in cell and molecular biology from Georgetown University, and holds a Bachelor of Science degree in Biology from Bowling Green State University.

Naomi Aronson, Ph.D. is the Executive Director of Clinical Evaluation, Innovation, and Policy at the Blue Cross and Blue Shield Association (BCBSA).

Aronson has overseen the development of the Blue Cross Blue Shield Association Technology Evaluation Center (TEC) as a nationally recognized technology assessment program and an Evidence-based Practice Center (EPC) of the Agency for Healthcare Research and Quality (AHRQ). She has directed over 300 technology assessments and 20 evidence reports for AHRQ. Aronson is a member of the Methodology Committee of the Patient-Centered Outcomes Research Institute (PCORI).

Aronson is a member of the Health Technology Assessment International Health Policy Forum, the Institute of Medicine Genomics Roundtable, and the National Business Group on Health Committee on Evidence-Based Benefit Design. Previously, she has represented the private sector on the U.S. Agency for International Development Team providing technical assistance to the Hungarian government on building evidence-based medicine capacity and also served on the Ontario Health Technology Assessment Evaluation Review Team. She was a member of the Institute of Medicine Forum on Drug Discovery Translation and Development, and a review committee co-chair for the International society for Pharmacoeconomics and Outcomes Research Annual Meeting.

Prior to joining BCBSA, Aronson was a member of the Northwestern University faculty, specializing in the sociology of science and medicine. She also was a post-doctoral fellow in the Science, Technology and Society Program at the Massachusetts Institute of Technology and received research awards from the National Science Foundation and the American Council of Learned Societies. Aronson's academic research focused on how the organization of scientific specialties in biomedical and clinical research affects the process of scientific discovery.

Allan Coukell, B.Sc.Pharm. is the senior director of drugs and medical devices at The Pew Charitable Trusts—including the prescription project, the drug safety project, the antibiotics and innovation project, and the medical device initiative, as well as other activities related to medical products and services.

Coukell practiced as a clinical pharmacist in oncology at the Victoria Hospital and London Regional Cancer Center in London, Ontario and was subsequently a senior medical writer and editor with Adis International, publisher of the peer-reviewed journals *Drugs*, *Drugs & Aging*, and *PharmacoEconomics*, among others.

He also spent a decade in journalism, ultimately as health and science reporter for WBUR, Boston's NPR news station. He was the founding producer and host of the weekly *Eureka!* science program on Radio New Zealand, and has written for *The Economist*, the *New York Times*, *New Scientist* and *Discover*, among other publications. He is the recipient of an Edward R. Murrow award for hard news reporting.

Allan Coukell serves as the consumer representative on the FDA Cardiovascular and Renal Drugs Advisory Committee.

Joseph Drozda, Jr., M.D., F.A.C.C. is the chair of the research and development team for the Healthcare Transformation Group, as well as a cardiologist and Director of Outcomes Research at Mercy Health—a four-state regional health system.

He is a member of the American College of Cardiology Board of Trustees, chairs the ACC's Clinical Quality Committee, is a member of the National Cardiovascular Data Registry Management Board, and represents ACC at NQF. He chairs the Measures Advisory Committee and sits on the Executive Committee of the AMA's Physician Consortium for Performance Improvement.

He was VP, Medical Management for SSM Health Care—the first healthcare organization to receive the Malcolm Baldrige award—and was a managed care executive for 25 years. He has also been involved in clinical quality improvement efforts and research for over 25 years.

He is leading the development of health services research at Mercy emphasizing medical device research. He leads a research team from five major U.S. health systems developing a unique device identifier system for doing post-market safety surveillance and research. He has been active in developing practice guidelines, disease management programs, and performance measures co-chairing the PCPI multi-society workgroups that developed measures in congestive heart failure, coronary heart disease, hypertension, and stroke and stroke rehabilitation.

Tom Fogarty, M.D. is an internationally recognized cardiovascular surgeon, inventor, entrepreneur, and vintner. He has been involved with a wide spectrum of innovations in business and technology. Fogarty has served as founder/co-founder, and Chairman/Board Member of over 33 various business and research companies, based on medical devices designed and developed by Fogarty Engineering, Inc. During the past 40 years, he has acquired 135 surgical patents, including the "industry standard" Fogarty balloon catheter and the widely used Aneurx Stent Graft that replaces open surgery aortic aneurysm. Fogarty is the recipient of countless awards and honors; most significantly, he is the recipient of the Jacobson Innovation Award of the American College of Surgeons, the 2000 Lemelson-MIT prize for Invention and Innovation and was inducted into the Inventors Hall of Fame and the National Academy of Engineering.

Recently, Fogarty and his colleagues founded the Fogarty Institute for Innovation at El Camino Hospital. The purpose of the Institute is to create an environment where innovation in medicine is encouraged, supported, and nurtured.

Fogarty was born in Cincinnati, Ohio and received his undergraduate education at Xavier University and his medical degree from the University of Cincinnati. He completed his residency at the University of Oregon and later served as Medical Staff President at Stanford Medical Center from 1973-1975. After thirteen years directing the Cardiovascular Surgery Program at Sequoia Hospital, Redwood City, California, he returned to academic life at Stanford University School of Medicine in July 1993, as Professor of Surgery. Fogarty now spends his time creating new medical devices with Fogarty Engineering and the Institute for Innovation.

Louis B. Jacques, M.D. joined the Centers for Medicare & Medicaid Services (CMS) in 2003 and has been director of the Coverage and Analysis Group since October 2009. The group reviews evidence and develops Medicare national coverage policy.

Prior to his arrival at CMS, Jacques was the Associate Dean for Curriculum at Georgetown University School of Medicine, where he retains a faculty appointment. He served on a number of university committees including the Executive Faculty, Committee on Admissions and the Institutional Review Board. He previously worked in the Palliative Care program at Georgetown Lombardi Comprehensive Cancer Center, where he covered the gynecologic oncology service.

Mark Leahey, J.D. is the President & CEO for the Medical Device Manufacturers Association (MDMA), a national trade association in Washington, D.C. that represents hundreds of research-driven medical technology companies. Mr. Leahey's responsibilities include advocating on behalf of the entrepreneurial sector of the medical device industry to Congress, the U.S. Food and Drug Administration (FDA), the Centers for Medicare & Medicaid Services (CMS), and other federal and state agencies.

He has lobbied for a more reasonable user fee for smaller companies, worked to open access to the hospital marketplace by challenging the exclusionary and anti-competitive nature of certain large group purchasing organizations (GPOs), as well as ensured that medical device technologies are reimbursed adequately. Mr. Leahey has been named one of the medical device industry's top lobbyists and sits on the Editorial Advisory Board of Medical Product Outsourcing.

He is a member of the Massachusetts Bar and a graduate of Georgetown University, the Georgetown Law Center, and Georgetown's McDonough School of Business.

Michael Mack, M.D. has been a practicing cardiothoracic surgeon for 24 years. He is a Cardiac Surgeon, COR Specialty Associates of North Texas (CSANT). He is Director of Cardiovascular Research and Cardiovascular Medicine of the Heart Hospital Baylor Plano. He is Director of Cardiovascular Surgery for the Baylor Healthcare System.

Mack serves as Chairman of the Board for the Cardiopulmonary Research Science & Technology Institute, as well as Medical Director of Cardiovascular Services and Director of Transplantation for Medical City Dallas Hospital. He has been actively involved in research and development of minimally invasive surgical techniques for the heart

and spine since 1992. Mack serves as a Member of Scientific Advisory Board of CardiAQ Valve Technologies, Inc. He serves as a Member of Medical Advisory Board at ValveXchange, Inc. He served as a Scientific Advisor of Cardica Inc. He co-founded the Cardiopulmonary Research Science and Technology Institute (CRSTI) in 1996. He has held office on numerous committees of the AATS and STS including chair of the STS Committee on New Technology Assessment. He is Board Certified in Internal Medicine, General Surgery, and Thoracic Surgery.

He began practice in cardiothoracic surgery in 1982 in Dallas, Texas, being a founding member of Cardiothoracic Surgery Associates of North Texas (CSANT). Mack has over 250 peer-reviewed medical publications. He is a member of the Editorial Board of the Annals of Thoracic Surgery and is a reviewer for over 10 medical journals. His current areas of interest include minimally invasive surgery and percutaneous heart valve therapy. He has been a Visiting Professor at the Cleveland Clinic Foundation, Northwestern University, Emory University, and the University of Virginia. He has performed surgery in over 10 foreign countries including China, Egypt, Taiwan, Sweden, Germany, and Brazil. Mack holds a number of positions in national organizations. He is the President of the Thoracic Surgery Foundation for Research and Education (TSFRE) and is the President of the Southern Thoracic Surgical Association (STSA). He was Second Vice President (President-elect 2011) of the Society of Thoracic Surgeons (STS) and is Secretary of the Board of Directors of the Joint Committee for Thoracic Surgical Education (JCTSE). He is also the Co-Chairman of the Industry Alliance Committee of the STS/AATS.

Mack is a founding organizer of the Dallas-Leipzig International Valve Conference and is considered today to be the most noted authority on the emerging field of transcatheter valves. Mack obtained his undergraduate degree in Philosophy from Boston College in 1969 and his medical degree from St. Louis University in 1973. He completed a residency in Internal Medicine at the University of Minnesota in 1976, and completed his training in General Surgery and Thoracic Surgery at the University of Texas Southwestern Medical School in Dallas, Texas in 1982.

Michael C. Morton is Vice President for Global Regulatory Affairs at Medtronic, Inc. He is responsible for public health policy advocacy and for internal regulatory policy within corporate regulatory affairs.

Morton has over 25 years of experience in the medical device industry, including quality, clinical, and regulatory affairs. Before joining Medtronic, Inc., he worked with CarboMedics, Inc., W.L. Gore and Associates, Alcon Labs, and Sorin Group.

Morton has been recognized as a Fellow of the Regulatory Affairs Professional Association (RAPS). He is active in industry groups, including the Advanced Medical Technology Association (AdvaMed). He chairs the AdvaMed PMA Working Group, co-chairs the Pediatric Devices Working Group, and is a member of the Heart Valve Task Force. He represented industry within Study Group 1 (Premarket) of the Global Harmonization Task Force. He served as the industry representative to the FDA Circulatory System Devices Advisory Panel from 2001 to 2005.

Michael Mussallem has been chairman and chief executive officer of Edwards Lifesciences since 2000 when the company spun-off from Baxter International.

Prior to his current position, Mussallem held a variety of positions with increasing responsibility in engineering, product development, and senior management at Baxter, including group vice president of its cardiovascular business from 1994 to 2000, and group vice president of the biopharmaceutical business from 1998 to 2000. From 1996 until 1998, he was the chairman of Baxter's Asia board overseeing Baxter's operations throughout Asia.

Mussallem is the former chairman of the board of directors of the Advanced Medical Technology Association (AdvaMed). He is currently on the boards and executive committees of AdvaMed, California Healthcare Institute and OCTANe, and is a trustee of the University of California, Irvine Foundation. Mussallem received a bachelor's degree in chemical engineering and an honorary doctorate degree from the Rose-Hulman Institute of Technology in Terre Haute, Indiana.

David Nexon, Ph.D. is Senior Executive Vice President of the Advanced Medical Technology Association ("AdvaMed"), where he is responsible for reimbursement policy, regulatory policy, and government affairs.

Prior to joining AdvaMed in February 2005, Nexon served for more than 20 years as the Democratic Health Policy Staff Director for the Senate Health, Education, Labor and Pensions (HELP) Committee and as the Senior Health Policy Advisor to Senator Edward M. Kennedy (D-MA). In these capacities, he has been involved with most of the major health policy issues of the last two decades. Prior to joining Sen. Kennedy's staff, Nexon served as Senior Budget Examiner in the Health Branch of the Office of Management and Budget (OMB), where he was responsible for the Health Care Financing Administration (now known as the Centers for Medicare & Medicaid Services).

Nexon held several academic appointments prior to entering government service. He received his bachelor's degree from Harvard College and his Ph.D. from the University of Chicago.

Pankaj Pasricha, M.D. received his medical degree from the All-India Institute of Medical Sciences, New Delhi in 1982. Subsequently he trained in internal medicine and pulmonology at Georgetown University-D.C. General Hospital and Tufts-New England Medical Center, respectively. Thereafter he trained in Gastroenterology at Johns Hopkins Hospital and then stayed on faculty at Johns Hopkins University, as Director of Therapeutic Endoscopy at Johns Hopkins Hospital and Associate Director of the Marvin Schuster Center for Gastrointestinal Motility.

In 1997, Pasricha assumed leadership of the GI Division at the University of Texas Medical Branch, where he was the Bassel and Frances Blanton Distinguished Professorship in Internal Medicine until August 2007 prior to assuming the position of Chief of Gastroenterology and Hepatology at Stanford, Professor of Medicine, Professor of Surgery, and Stanford Biodesign faculty. In 2012, Pasricha moved back to Johns Hopkins, where he is Professor of Medicine, Director of Digestive Disorders (Bayview) and Director of the Johns Hopkins Center for Neurogastroenterology.

These diverse appointments reflect his research interests, which span endoscopic, clinical and bench research. He has been a recipient of federal funding for his research since 1995 and currently is principal investigator on several National Institutes of Health (NIH) grants, in addition to numerous other grants and awards. His laboratory is interested in molecular mechanisms of visceral pain and restoration of enteric neural function with novel strategies including neural stem cell transplants. His clinical interests include GI motility disorders and abdominal pain as well as the development of novel endoscopic procedures and devices.

Pasricha has authored more than 200 manuscripts and book chapters including contributions to Cecil Textbook of Medicine, Yamada Textbook of Gastroenterology, and Goodman and Gilman's Pharmacological Basis of Therapeutics. His work has been presented at several national and international forums. He has consistently been on Castle Connelly list America's "Top Docs" as well as "Best Doctors" in Gastroenterology. Pasricha serves on numerous national gastroenterological committees including the AGA, ACG and ASGE; he was Chair

of the Research Committee of the American Society of Gastrointestinal Endoscopy until 1998, served as chair of the NIH Special Emphasis Panel on Endoscopic Clinical Research in Pancreatic and Biliary Diseases. He is currently the chair of the NIH-funded multi-center gastroparesis consortium. In addition, he served on the National Commission on Digestive Diseases, appointed by the Congress to provide a “roadmap” for progress in gastrointestinal disorders.

Pasricha’s career represents an exciting blend of clinical expertise, creativity, and medical entrepreneurship that has resulted in several innovative solutions to common gastrointestinal healthcare problems. He has over 30 issued patents related to gastrointestinal diagnostics and therapeutics and has co-founded several companies in this space including Apollo Endosurgery and several other emerging businesses in this space. In addition, he is a consultant to several companies both in medtech and biotech.

He currently Chairs the American Gastroenterological Association Center for Gastrointestinal Innovation and Technology whose mission is to facilitate the translation of effective and safe devices to the market to address unmet needs of patients with GI disorders.

Bray Patrick-Lake serves as a patient representative in a number of capacities and works to actively engage patient advocacy organizations in efforts to improve clinical trials through her work at Clinical Trials Transformation Initiative.

In 2010, Patrick-Lake founded the PFO Research Foundation in response to the lack of definitive scientific information regarding the condition of patent foramen ovale (PFO) after being a patient in an aborted implantable cardiac device trial. She has served as a patient representative at FDA on a variety of advisory committees and panels, in workgroups for the European Medicines Agency (EMA) and the NIH National Institute of Neurological Disorders and Stroke, as a guest lecturer and an external reviewer for the Institute of Medicine (IOM), and as a patient stakeholder or co-investigator for Agency for Healthcare Research & Quality (AHRQ) and PCORI grants.

She is a member of the PCORnet Coordinating Center’s Executive Leadership Committee, ACC Foundation’s Patient-centered Care (PC3) Shared Decision Making Workgroup, DIA’s Patient Fellowship Selection Committee, TVT Registry Stakeholder Advisory Committee, and is a board member for the Alliance for Headache Disorders Advocacy. She holds a bachelor of science degree in zoology from University of Georgia and a master of forensic sciences degree from National University in La Jolla, CA.

Josh Rising, M.D., M.P.H. directs Pew’s work on medical devices, which seeks to enhance patient safety and foster innovation.

Before joining Pew, Rising helped establish the Office of Policy in the U.S. Food and Drug Administration’s Center for Tobacco Products. He also served as health policy analyst for the Connecticut legislature, focusing on issues of healthcare access, Medicaid policy, health IT and healthcare quality. He also served as legislative affairs director for the American Medical Student Association.

Rising received his M.D. and his M.P.H. at Boston University, completed his pediatric residency at the University of California, San Francisco, and trained for a year as a Robert Wood Johnson Clinical Scholar at Yale University. He has published peer-reviewed literature on, among other topics, children with special healthcare needs and the expansion of a county-run health insurance program.

Kate Ryan, M.P.A. is the Senior Program Coordinator at the National Women's Health Network. In this role, she is responsible for developing and implementing a program of legislative and regulatory advocacy that focuses on reducing women's exposure to unnecessary drug and medical treatment risks.

Kate leads advocacy efforts to ensure women have complete and accurate information about the health products and services that are marketed to them, challenge dangerous medical products, and strengthen the public protections against such threats. Through work with Members of Congress, the U.S. Food and Drug Administration, and the National Institute of Child Health and Human Development, Kate brings women's voices to the health policy debates in Washington, D.C.

Prior to joining the NWHN, Kate worked in the Capitol Hill office of U.S. Representative Joe Sestak (D-PA), where she worked on health care reform, the women's issues portfolio, and managed a variety of constituent services programs. Before moving to Washington, D.C., Kate volunteered in Ghana with the Alliance for Reproductive Health Rights to monitor and assess availability of, and access to, women's sexual and reproductive health services under the Ghanaian National Health Insurance Scheme. As part of this work, Kate also monitored Ghana's progress on Millennium Development Goals 4 & 5—to reduce child mortality and improve maternal health.

Kate received her M.P.A. in International Public & Non-Profit Management and Policy Analysis with a focus in women's rights from the NYU Wagner Graduate School of Public Service.

Murray Sheldon, M.D. received his medical degree from the University of Michigan Medical School in 1975. He completed his general surgical residency with Kaiser Permanente Medical Center in Oakland and his cardiovascular fellowships at the University of California, Davis and the Montefiore Hospital and Medical Center in New York.

In 1983, he entered private practice as a staff surgeon in several medical centers in Northern California performing cardiac, thoracic, and vascular surgery. In 2003, he chose to become engaged in a highly productive career in the medical device industry leading device development projects and providing expert consultative services to numerous device development firms. From 2003-2009, Murray was the Medical Director for Arbor Surgical Technologies, which developed a unique two-piece, sutureless aortic valve for clinical aortic valve replacement. Most recently, prior to joining FDA, he was the Medical Director for the minimally invasive surgical program at BioVentrix, Inc. and developed a catheter-based procedure for surgical ventricular reconstruction for heart failure patients. This device has recently obtained a CE mark in Europe. He also was the Medical Director for Solinas Medical, Inc. and was instrumental in developing a unique device for dialysis access. That device has recently received two 510 (k) clearances.

Sheldon has recently joined FDA as the Associate Director for Technology and Innovation. He oversees the Center's initiative to proactively facilitate medical device innovation to address unmet public health needs and to align what is traditionally done at FDA with what is required to support the U.S. medical device ecosystem. His primary focus is working with staff, the medical device industry, the clinical community and others on ways to facilitate bringing innovative medical devices to the patients in the U.S. first in the world. Sheldon currently leads the Medical Device Reimbursement Task Force, identifying methods to streamline the path from FDA approval to reimbursement.

Jeff Shuren, M.D., J.D. is the Director of the Center for Devices and Radiological Health (CDRH) at the U.S. Food and Drug Administration. He previously served as Acting Center Director. Shuren has held various policy and planning positions within FDA from 1998 to 2009, including Acting Deputy Commissioner for Policy, Planning, and Budget; Associate Commissioner for Policy and Planning; and Special Counsel to the Principal Deputy Commissioner.

Shuren is board certified in neurology and served as an assistant professor of neurology at the University of Cincinnati. In 1998, Shuren joined FDA as a Medical Officer in the Office of Policy. In 2000, he served as a detailee on the Senate HELP Committee. In 2001, he became the Director of the Division of Items and Devices in the Coverage and Analysis Group at the Centers for Medicare & Medicaid Services. Shuren returned to FDA as the Assistant Commissioner for Policy in 2003, and assumed his current position in September 2009.

He received both his B.S. and M.D. degrees from Northwestern University under its Honors Program in Medical Education and his J.D. from the University of Michigan Law School.

Nancy Stade, J.D. has served as the Deputy Director for Policy, Center for Devices and Radiological Health (CDRH), U.S. Food and Drug Administration since August 2010, after serving as the Acting Associate Director for Regulation and Policy, CDRH from September 2009. In her current position, Stade plays a leading role in the development of regulatory and legislative policy on devices. Recently, she had the lead advisory role in the development of the device-related provisions of FDA Safety and Innovation Act of 2012 and has led a number of initiatives in support of the Center's processes for developing policy.

Stade worked in the Office of Chief Counsel of FDA before joining CDRH and left FDA to work as a junior partner in the Food and Drug law group of Hale and Dorr LLP for two years before returning to public service in 2004. She received her Bachelor's degree from Columbia College and her J.D. from Columbia University School of Law.

Diana Zuckerman, Ph.D. is the President of the National Research Center for Women & Families, a nonprofit research and education organization that works to improve policies and programs that affect the health of adults and children. In 2007, she founded the Center's Cancer Prevention and Treatment Fund. She has testified about the safety and effectiveness of medical devices and drugs several dozen times before Congress and FDA, as well as several state legislative committees and the health committee of the Canadian Parliament.

After starting her career as a faculty member at Vassar and Yale and a research director at Harvard, Zuckerman worked for a dozen years as a Congressional staffer on health policy issues in the House Government Operations Committee (now Oversight and Government Reform) and the Senate Committee on Veterans Affairs. She then served as a senior policy advisor in the White House. She has been president of the National Research Center for Women & Families since 1999, and at the same time was a fellow at the University of Pennsylvania Center for Bioethics for seven years. In 2010, she was inducted as the first non-physician into the Women in Medicine International Hall of Fame. She serves on the Board of Directors of the Congressionally mandated Reagan-Udall Foundation, and the Alliance for a Stronger FDA.

She is the author of five books, several book chapters, and dozens of articles in medical and academic journals and national newspapers. She has been interviewed on all the major TV and radio news programs and morning shows, numerous talk shows, and has been quoted in all the major newspapers and news magazines in the U.S.

Appendix C: Devices appropriate for priority review

The following is the specific eligibility criteria from Section III of the “Guidance for Industry and Food and Drug Administration Staff—Priority Review of Premarket Submissions for Devices.”⁶

Using the criteria in section 515(d)(5) of the Federal Food, Drug, and Cosmetic Act, FDA considers a device, or a combination product containing a device, appropriate for priority review if the device or combination product:

1. is intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition, and
2. meets at least one of the following:
 - **The device represents a breakthrough technology that provides a clinically meaningful advantage over existing technology.** Breakthrough technologies should be demonstrated to lead to a clinical improvement in the treatment or diagnosis of the life-threatening or irreversibly debilitating condition.
 - **No approved alternative treatment or means of diagnosis exists.**
 - **The device offers significant, clinically meaningful advantages over existing approved alternatives.** The device should provide for a clinically important earlier or more accurate diagnosis or offer important therapeutic advantages in safety and/or effectiveness over existing alternatives. Such advantages may include demonstrated superiority over current treatments for effects on serious outcomes (e.g., morbidity), ability to provide clinical benefit for those patients unable to tolerate current treatments, or ability to provide a clinical benefit without the serious side effects associated with current treatments.
 - **The availability of the device is in the best interest of patients.** That is, the device provides a specific public health benefit, or meets the need of a well-defined patient population. This may also apply to a device that was designed or modified to address an unanticipated serious failure occurring in a critical component of an approved device for which there are no alternatives, or for which alternative treatment would entail substantial risk of morbidity for the patient.

Appendix D: Case studies

Pew selected three high-level case studies as concrete examples of devices which address an unmet need. The purpose of the studies is to demonstrate different unmet medical needs and different levels of safety and effectiveness evidence. The studies were presented to facilitate discussion about the appropriate amount of evidence for approval; however, the discussion was not meant to review FDA's decision on approved devices.

The devices presented were retinal prosthesis system, approved through Humanitarian Device Exemption; transcatheter aortic valve, approved through a premarket approval; and a hypothetical prosthetic heart muscle device.

Device 1: Retinal prosthesis system (HDE)

Description and indication/unmet need

This device is the first implanted retinal prosthesis. Images from a camera are converted into electrical impulses that stimulate the retina. The device is intended for adults with severely limited or no light perception due to advanced retinitis pigmentosa, a rare condition that can lead to blindness. There are no FDA-approved alternatives.

Safety and effectiveness data

The approval was based on trial data of 30 patients. The results were:

- All patients benefited in visual tests, although the extent varied.
- 63 percent (19) did not experience any adverse events at two years.
- 13 percent (four) suffered serious adverse events.

Device 2: Transcatheter aortic valve (PMA):

Description and indication/unmet need

The transcatheter aortic valve is a replacement heart valve to treat aortic stenosis delivered via a transcatheter approach (rather than open heart surgery). The device is intended for patients with severe aortic valve stenosis who are not surgical candidates and lack other options.

Safety and effectiveness data

Two observational studies were compared to historical controls. The results of the studies are below.

- First observational study (300 patients).
 - 94 percent survival at 30 days.
- Second observational study (50 patients).
 - 92 percent survival at 30 days.
 - 90 percent survival at 180 days.
- Historical control.
 - 80 percent survival at 30 days.
 - 60 percent survival at 180 days.

Device 3: Prosthetic heart muscle device (hypothetical):*Description and indication/unmet need*

This device is a nonbiologic muscle prosthesis to replace damaged heart tissue. It is intended for patients who have had extensive damage after a heart attack and are ineligible for a transplant or other therapeutic options.

Safety and effectiveness data

An observational study was compared to historical controls. The results of the studies are below.

- Observational study (50 patients).
 - 60 percent of patients are alive at six months.
 - 50 percent of these (30 percent of total) have had a stroke.
 - Three patients (6 percent) died within 24 hours of surgery.
- Historical control.
 - 50 percent of historical controls are alive at six months.
 - 50 percent of these (25 percent of the total) have had a stroke.

Endnotes

- 1 U.S. Food and Drug Administration, "CDRH 2014 Strategic Priorities," accessed March 6, 2014, <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/ucm384132.htm#introduction>.
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- 3 N. Bompey, "Device Center to Expand, Codify Measures to Speed up Breakthrough Dx," Inside Health Policy, Sept. 9, 2013, <http://insidehealthpolicy.com/201309092446162/Health-Daily-News/Daily-News/device-center-to-expand-codify-measures-to-speed-up-breakthrough-dx/menu-id-212.html?s=mu>.
- 4 U.S. Food and Drug Administration, Center for Devices and Radiological Health, "2013 Strategic Priorities," accessed March 4, 2014, <http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM330379.pdf>.
- 5 Federal Food, Drug, and Cosmetic Act, 21 U.S. Code 360c (2010).
- 6 U.S. Food and Drug Administration, "Guidance for Industry and Food and Drug Administration Staff—Priority Review of Premarket Submissions for Devices (2013)," accessed March 4, 2014, <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089643.htm#s3>.

For further information, please visit:

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