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September 14, 2018

Division of Dockets Management Staff (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

***Re: Docket No: FDA-2018-N-0404: Pediatric Medical Device Development Public Meeting;  
Request for Public Comments***

Dear Sir/Madam:

On behalf of the Advanced Medical Technology Association (AdvaMed), we are pleased to submit these comments in response to the Food and Drug Administration's (FDA's) request for comments on the Pediatric Medical Device Development Public meeting.

AdvaMed represents manufacturers of medical devices, diagnostic products, and health information systems that are transforming health care through earlier disease detection, less invasive procedures, and more effective treatments. These members range from the smallest to the largest medical technology innovators and companies. AdvaMed's nearly 400 members manufacture the vast majority of all medical technology products sold in the U.S. AdvaMed advocates for a legal, regulatory and economic environment that advances global health care by assuring worldwide patient access to the benefits of medical technology. The Association promotes policies that foster the highest ethical standards, rapid product approvals, appropriate reimbursement and access to international markets.

We'd like to take this opportunity to congratulate FDA on a very successful public meeting on Pediatric Medical Device Development on August 13-14, 2018. The meeting included a diverse range of speakers, many of whom presented original and creative recommendations for improving pediatric medical device development. AdvaMed's Pediatric Working Group has developed a number of recommendations that are intended to improve pediatric medical device development which are detailed below.

## **Barriers to Pediatric Device Development**

In order to develop appropriate solutions to pediatric device development, it is important to understand existing barriers. Many of these have been catalogued in previous public meetings focused on pediatric device development so the following is intended to briefly recap the most important challenges.



- As reported at the public meeting, the primary challenge to pediatric device development is that pediatric populations associated with various pediatric diseases and conditions may not represent a commercially viable market opportunity for device companies. This is particularly true when one considers the multiple pediatric sub-populations which range from neonates to age 21. Although there is little information on overall pediatric device needs, it is likely that for many diseases, the numbers of pediatric patients may essentially qualify as rare diseases. Early stage investors are reluctant to invest in pediatric devices given the high research and development costs, the perceived small market size and the perception there will be low financial returns on investment. To overcome this immutable challenge, pediatric medical device development must be de-risked – that is, the costs and barriers to device development must be reduced to the greatest extent possible while simultaneously offering device development incentives.
- The small numbers of geographically dispersed pediatric patients with a given medical condition can make it difficult to accrue enough patients over reasonable timeframes and within a manageable number of investigational sites to assure an adequately powered clinical trial that meets FDA requirements. Each investigative site adds significantly to the costs of the studies required for regulatory review or approval. Some pediatric devices may also have to factor in issues associated with pediatric growth and development, a need for multiple sizes to accommodate different age groups, and/or hormonal and metabolic changes.
- In January 2017, the American Academy of Pediatrics (AAP) issued a policy statement on off-label use of devices in children. It said, “the majority of medical devices and surgical devices used in children do not have approval or clearance from the Food and Drug Administration for use in pediatric populations.”<sup>1</sup> Some devices approved for use in adults may be used off-label in pediatric patients as practice of medicine. In some cases, the products have been on the market for many years and have become the standard of care. The AAP statement is supported by other clinicians who have reported at past public workshops that they feel compelled to jerry-rig or modify existing devices to treat pediatric patients. As a result, data that could be used to improve device research and development, obtain on-label indications, or improve patient outcomes is never collected. A concerted effort must be made to find ways to break this cycle and enable companies and clinicians to begin to obtain and to collect the data that will allow devices for pediatric diseases and conditions to be on-label.
- There is a lack of reliable information on pediatric device needs and on associated clinical or surrogate endpoints. In some cases, there are still many unanswered basic pediatric research questions.

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<sup>1</sup> Policy Statement: Off-Label Use of Medical Devices in Children; Section on Cardiology and Cardiac Surgery and Section on Orthopaedics. Pediatrics Volume 139, Number 1, January 2017

- Unlike adults over age 65, there is no overarching mechanism or government entity which makes determinations about the coverage and reimbursement of pediatric medical devices. Instead, device sponsors must navigate each state's Medicaid program – each of which has unique rules and requirements related to the reimbursement, or lack thereof, for non-approved investigational devices.

## Recommended Solutions

AdvaMed's Pediatric Working Group has developed a series of recommended solutions that are intended to de-risk pediatric device development by: reducing the costs and burden associated with FDA review or approval while maintaining FDA's bar for strong safety and effectiveness; providing an initial income stream by providing coverage and reimbursement policies in early device development phases; and creating tax-related and other financial incentives to develop pediatric devices. These are discussed in detail below.

### ***FDA-Related Solutions to Reduce Costs and Burdens of Pediatric Device Development***

**Designation of Pediatric Devices as Breakthrough** – In order to facilitate development and review of pediatric devices, all pediatric devices should be designated as breakthrough devices. Section 3051 of the 21<sup>st</sup> Century Cures Act of 2016 created the Breakthrough Devices program to “provide the Secretary with sufficient authority, to apply efficient and flexible approaches to expedite the development of and prioritize the FDA's review of devices that represent breakthrough devices.” The statute provides priority review for any device that; “(1) provides for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions; and (2) that represent breakthrough technologies; for which no approved or cleared alternatives exist; that offer significant advantages over existing approved or cleared alternatives, including the potential, compared to existing approved alternatives, to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patients' ability to manage their own care (such as through self-directed personal assistance), or establish long-term clinical efficiencies; or *the availability of which is in the best interest of patients* [emphasis added].” Many pediatric device submissions meet many of the Section 3051 criteria but in almost every instance, the availability of a pediatric-labeled device over no device at all or use of a device off-label, will certainly be “in the best interests of patients.” This designation would also benefit pediatric patients' parents and health care personnel. Some may argue that there are insufficient resources to designate every pediatric device submission as breakthrough, however we note there are very few pediatric device submissions in any year.

**Development of Pediatric-Specific Review Team** – As reported by numerous industry speakers at the public meeting who detailed their challenges with the FDA review or approval process, FDA still struggles with consistent and least burdensome approaches to pediatric device reviews and approvals. Thus, in conjunction with treating all pediatric device submissions as breakthrough, we also recommend the development of a specific pediatric review team comprised of individuals with pediatric medical and pediatric population expertise. This team

would provide a high level of attention and consistency of review to pediatric device submissions and would provide added expertise to the branch review teams. Given their knowledge and expertise, this review team would be expected to bring insights and understanding to the assessment of the benefits and risks of pediatric devices that branch reviewers may not have. As a note, FDA has already established the Pediatric Extrapolation for Devices (PEDs) Team which creates precedence for this concept. FDA could do more to publicize the existence of the PEDs team.

**Use of MDUFA IV FTEs** – Some may argue there are insufficient resources to create a pediatric specific review team. However, under the Medical Device User Fee Amendments 2017 (MDUFA IV), the device industry is providing FDA over \$1 billion in user fees. As part of this agreement, industry is funding over 200 review Full Time Equivalents (FTEs). This is additive to the 230 FTEs industry funded under MDUFA III for a total of more than 400 FTEs. FDA has yet to fill the many open review positions they committed to fill under MDUFA IV. We believe FDA can use these existing industry-funded FTE openings to prioritize hiring of pediatric experts for a dedicated pediatric device review team. Given the small number of pediatric submissions, these experts could spend much of their time reviewing non-pediatric device submissions.

**Use of Collaborative Communities** – We also recommend that the pediatric-specific review team develop a series of collaborative communities on which they may call for help to provide additional insights and perspectives on difficult issues or challenges. For example, the pediatric team could consult with pediatric experts in the field, patient groups or patient representatives and/or experts at the National Institutes Health (NIH) regarding potential clinical trial endpoints or surrogates, benefit-risk determinations, use of real world evidence (RWE), information on incidence and prevalence, and natural history of the disease, etc.

**Interim Supervisory Review** – Until such time as an expert pediatric specific review team is created, FDA should require supervisory review of all pediatric device development and clinical data requirements to ensure that a least burdensome approach is being considered and employed for device submissions, allowing the earliest possible access to safe and effective pediatric specific devices.

**Establishment of Global and Domestic Clinical Trial Networks** – Although FDA cannot mandate the creation of clinical trial networks, they can help facilitate the creation of such networks to reduce costs associated with clinical trial investigative sites and to facilitate recruitment of scarce pediatric patients. FDA is a key leader and driver of policy development in the International Medical Device Regulators Forum (IMDRF) and FDA can help facilitate development of a global network of trial sites for pediatric devices. Data collected via this international network of global trial sites should help alleviate current FDA reviewer concerns about use of OUS (outside the United States) data in pediatric submissions.

FDA can similarly facilitate public private partnerships to facilitate a domestic network of trial sites at Pediatric Device Consortia grantees, children's hospitals and Academic Medical Centers. To reduce costs associated with multiple Institutional Review Board (IRB) reviews, and per the

revised Common Rule which supports use of a single IRB for drug and device trials (as opposed to the current requirement of obtaining IRB by each individual institution), FDA could also support use of a single IRB for pediatric device trials conducted within the domestic network of trial sites.

### **Reduction of Burden While Maintaining the Safety and Effectiveness Bar**

Over the last few years, FDA has developed new guidance for industry and staff in an effort to provide least burdensome approaches to device reviews and approvals that maintain the current safety and effectiveness bar. These include: extrapolation of data collected in adult clinical studies for devices with the same indication in the pediatric population, use of real world evidence in regulatory submissions and evaluating the pre- and postmarket balance for clinical data collection. Reviewers should be encouraged to take advantage of these new approaches for pediatric devices. Importantly, a dedicated pediatric review team could help socialize and facilitate uptake and use of these new regulatory approaches for pediatric devices.

Other steps FDA should take to reduce the costs and burden associated with pediatric device review or approval include developing adaptive clinical trial designs and regulatory models to respond to small population sizes. An example of a new regulatory model that FDA has employed is allowing use of small confirmatory pediatric trials with supportive data from registries or other RWE<sup>2</sup>. Small confirmatory trials can be combined with adult data extrapolation and/or Bayesian statistical approaches. Where possible, FDA can also post on its webpage examples of adaptive clinical trial designs that have been successfully used to obtain on-label pediatric indications.<sup>3</sup>

Additionally, any data available from any use of medical devices in the pediatric population (compassionate use, emergency use, off-label use) should be reviewed and considered to support the approval of pediatric-specific medical devices. For example, what may have evolved as the pediatric standard of care may be off-label (e.g., a minimally invasive procedure supersedes a surgical procedure and becomes the standard of care). Doctors will be reluctant to randomize pediatric patients to a surgical control arm if the minimally invasive procedure is the standard of care. Parents will also be reluctant to have their child participate in such trials. In this instance, an FDA requirement to randomize pediatric patients to the surgical procedure creates a barrier

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<sup>2</sup> See Yoganathan AJ, Fogel M, Gamble S, Morton M, Schmidt P, Secunda J, Vidmar S, del Nido P. October 2013. A new paradigm for obtaining marketing approval for pediatric-sized prosthetic heart valves. *The Journal of Thoracic and Cardiovascular Surgery*. Volume 146, Number 4: 879-886.

Also see FDA commentary endorsing this approach: Aguel F, Kurtzman S, Patel-Raman S, Hillebrenner M, Zuckerman B. Food and Drug Administration Commentary on “A new paradigm for obtaining marketing approval for pediatric-sized prosthetic heart valves”. *The Journal of Thoracic and Cardiovascular Surgery*. Volume 146, Number 4: 887.

<sup>3</sup> FDA must take care not to reveal proprietary or trade secret or confidential commercial or financial information when sharing trial designs.

that prevents the off-label use of the device from ever becoming on-label. Where numerous articles document the effectiveness of a particular off-label use of a device and it has become the standard of care, FDA should be encouraged to develop mechanisms that make use of this data. FDA should also work to ensure acceptance of such data at the reviewer level.

A related issue is the understandable desire to be able to answer all the questions related to a particular pediatric device submission. Unfortunately, that may be extremely challenging given the small populations involved and the unanswered questions that may exist on basic research questions related to the pediatric disease or condition. In this context, the comment made by Ms. Christy Foreman, former Director of the Office of Device Evaluation (ODE), at the January 8, 2014 public workshop on pediatric patients affected by rare diseases, suggesting that all parties may have to be willing to accept a level of uncertainty with respect to these devices, is critically important. It will be challenging to obtain the certainty in data for pediatric devices that is currently achievable in adult devices. In effect, there must be a willingness by all parties to start data collection somewhere with the understanding that over time, more data and information can be obtained to guide clinical evidence requirements for pediatric devices (e.g., appropriate endpoints, etc.).

FDA could also develop guidance that provides for greater acceptance of pre-clinical modeling in lieu of large burdensome and costly animal studies and which provides recommendations on the types of pre-clinical testing that is acceptable for pediatric devices. In many cases there is often not an appropriate animal model for the pediatric population. Additionally, computer modeling and advanced bench testing techniques have become so advanced that the initial functional studies can now be better calculated than they can be measured in an inappropriate animal model. Finally, where appropriate, a great deal of population-relevant information can be obtained at a lower burden through the small confirmatory early feasibility pathway that has been established by FDA – a pathway that maintains high safety requirements.

**Enhance Use of Existing FDA Regulatory Tools and Valid Scientific Evidence Other Than Well-Controlled Trials** – Section 513(a)(3)(A) of the Federal Food Drug and Cosmetic Act and 21 CFR 860.7 give FDA authority to utilize valid scientific evidence other than well-controlled trials. Importantly, the standard of reasonable assurance of safety and effectiveness is the same no matter what type of scientific evidence is required. While FDA relies on many types of valid scientific evidence (other than well-controlled trials) in other areas, it is our sense that FDA has been reluctant to take advantage of this statutory authority in the case of pediatric devices. FDA should be encouraged to make better use of all forms of valid scientific evidence, which could help address the problems associated with the extremely small numbers of pediatric patients that are afflicted with any one condition or disease state.

While maintaining the existing standard of safety and effectiveness, where appropriate FDA should:

- Use objective performance criteria (OPCs), historical controls or well-documented case histories as endpoints to show probable benefit or effectiveness. Reliance on well-documented case histories and historical controls would take advantage of the existing

literature, respond to the extremely small numbers of orphan or pediatric patients with any one condition (which makes it difficult to run statistically valid clinical trials in a timely fashion – as one person put it “20 years of literature vs. years to put together a control group”) and help minimize the use of surgical interventions as the control where devices have been established as the standard of care.

- Allow the extrapolation of clinical data between different sizes of the same device based on engineering testing and other non-clinical data. Currently, FDA requires clinical evidence on the full range of device sizes for a particular device and it can be difficult to assemble enough patients at either end of the size ranges to be valid. It is often extremely challenging to get significant data on the smallest and largest sizes. This proposal would allow the use of non-clinical and bench data as well as the potential to do post-market clinical work to approve the full range of sizes.
- Allow use of non-clinical data for modifications of devices specifically approved for pediatric patient populations when such modifications are unrelated to changes in intended use and do not affect safety. Modifications made to an already cleared or approved device to improve its performance or safety require that the device be cleared or approved again. For devices, much of the data about a product’s function can be established non-clinically (e.g., relying on animal, bench and/or reliability testing). Every time a minor modification is made (e.g., material changes or minor design changes), FDA often requires that the device be cleared or approved again. The requirements for clinical data in the modification process create a challenge and limit improvements for pediatric devices. Due to the barriers associated with gathering clinical data for pediatrics (small populations, widely dispersed populations, parental unwillingness to have children participate, timeliness, etc.), the intent of this provision – for devices specifically approved for pediatric use – is to enable use of engineering and bench testing, rather than clinical testing for minor device changes when the changes are not related to changing the intended use of the device and do not affect safety. FDA has the flexibility to do this – and allows it for adult devices – but should be specifically encouraged to do so in the case of pediatric products.
- For devices with the same intended use, allow the cleared adult 510(k) device to serve as a valid predicate for a pediatric use population. Similar to the language in the Food and Drug Administration Amendments Act of 2007 (FDAAA) pediatric device law, which allows FDA to use adult data to support effectiveness in pediatric populations and to extrapolate data between pediatric populations, FDA has authority, where the course of the disease or effect of the device is the same in adults and in pediatrics, to use the adult 510(k) device as a predicate for the pediatric device. Doing so would be responsive to the extremely small numbers of pediatric patients – particularly of a given age range – with any one condition (which makes it difficult to run valid clinical trials in a timely fashion) and would help limit the number of children exposed to surgical controls. FDA could still require a clinical trial for a 510(k) device but the trial would be smaller and pediatric access to the device would be faster.

- Allow the acceptance – as an appropriate control for investigational pediatric devices – of devices intended for use in adult populations when such devices provide the only device-related means for treating, diagnosing or preventing diseases or conditions in pediatric patients and have become the standard of care for such patients. Similar to the language in the pediatric device law, which allows FDA to use adult data to support effectiveness in pediatric populations and to extrapolate data between pediatric populations, FDA has authority to utilize as the control for studies under the Investigational Device Exemption (IDE) process, devices that are not approved for pediatric use but that are already being used in pediatric populations. This would enable the adult data on already approved devices or these devices themselves to serve as the “control” for the pediatric trial, responding to the limited number of pediatric patients available for pediatric trials and reducing the number of children exposed to a surgical control.
- Allow use of general device claims where appropriate rather than requiring specific device claims for each pediatric age bracket to respond to the broad definition of pediatric (from neonate to age 21). FDA requirements for limited and very specific claims and their associated data can be an important barrier to device development for small and dispersed pediatric populations. For example, FDA may require 100 patients in each pediatric age group to demonstrate device safety and effectiveness. FDA should allow for more general claims to enable device approval. Subsequent condition of approval requirements, such as requirements for a registry, could then be used to ascertain whether there are particular issues associated with specific age ranges.

**Establish a Small Population Pediatric/Orphan Regulatory Pathway** – As mentioned above, clinicians report they feel compelled to “jerry-rig” or modify existing devices to treat pediatric patients. Rather than having pediatric clinicians across the country individually jerry-rig devices during surgery, AdvaMed proposes a well-regulated mechanism to provide device access for super-small pediatric populations that are not likely to be served by the Humanitarian Device Exemption (HDE) program. Such a program would allow manufacturers to distribute a manageable number of unapproved devices annually – based on the medical condition – to pediatric patients who are afflicted with diseases or conditions that affect too few patients to justify the expense necessary to achieve an approved device under the HDE program. Appropriate controls would be specified by the FDA and appropriate pediatric clinicians with expertise in the specific small population.

## ***Incentives for Pediatric Device Development***

### **Tax-Related Incentives**

As noted above, the primary challenge to pediatric device development is that pediatric populations associated with pediatric diseases and conditions may not be commercially viable for device companies for multiple pediatric sub-populations which range from neonates to age 21 – especially when combined with high research and development costs. In addition to the recommendations above, which are intended to reduce pediatric device development costs

through least burdensome device review and approval approaches, AdvaMed proposes a number of tax-related incentives to encourage venture capital and other device company interest in pediatric devices.

- To offset the costs of pediatric device research and development and to address small market size and commercialization risks, a strong pediatric device research and development tax credit program should be established similar to the tax credit program that currently exists for orphan drugs.
- A tax incentive that promotes early stage investors to provide early valuation to attract longer-term investment or exit opportunities could address a concern expressed by smaller pediatric device developers that investors and larger medical device companies are unwilling to invest in device development for the limited pediatric device market. Similar state tax credits could potentially provide a model for a federal tax credit along these lines. Investors could be provided a tax incentive for early stage investment or when the pediatric device company is acquired. Similarly, a tax incentive could be provided for device companies with an adult device that invests in a pediatric device for the same indication, especially where there is pediatric need and no on-label devices exist.
- Explore tax incentives for commercial insurers to incentivize options for pediatric reimbursement.

#### **FDA-Related Incentives**

Proposals that could encourage larger device companies to consider development of a pediatric device include:

- Allowing for expedited FDA review for a follow-up adult indication if the company first develops a pediatric device and has obtained clearance or approval for the pediatric indication.
- Allowing for data extrapolation of data collected in clinical trials for approved pediatric devices to support the approval of an adult submission for similar indications.

#### **Reimbursement-Related Incentives**

As mentioned above, unlike adults over age 65 who rely on the Medicare program, there is no single government entity (i.e., Centers for Medicare and Medicaid [CMS]) which makes determinations about the coverage and reimbursement of the pediatric population. Instead, device sponsors must navigate each state's Medicaid program – each of which has unique rules and requirements, or they must work individually with private insurers to obtain coverage and reimbursement decisions. Private insurers typically follow the lead of CMS with respect to coverage and reimbursement for adult devices. This lack of reimbursement uncertainty adds significantly to the costs of pediatric device development and discourages investment in pediatric devices. To address reimbursement challenges, we propose the following:

- Require **Medicaid** to cover all pediatric device trials with a 90% federal match. Currently, Medicare covers routine patient care costs associated with medical device trials in the Medicare population for both Category A and Category B devices and will cover the device costs for Category B investigative devices.<sup>4</sup>
- Provide **Medicare** reimbursement for pediatric devices based on safety and early effectiveness data and continue reimbursement while companies collect additional data to demonstrate effectiveness. Companies would be required to demonstrate progress on the ongoing data collection effort. While these devices are still being studied, they would be limited to use in children's hospitals.
- To ensure there is a single entity for initial coverage and reimbursement decisions related to pediatric devices, **Medicare** should be required to provide three to five years of Medicare coverage for pediatric devices with a requirement that by the end of the three- to five-year period, CMS must make a coverage recommendation that Medicaid must follow. Currently, CMS refuses to make these determinations because Medicare does not cover children except for children designated chronically disabled.
- Establish a Center for Medicare & Medicaid Innovation (CMMI) grant program to help fund development and reimbursement of pediatric devices for new pediatric device innovations. While these devices are being studied, they would be limited to use in children's hospitals.

### ***National Institutes of Health (NIH)-Related Proposals***

AdvaMed recommends that data on unmet pediatric device needs be methodically collected and prioritized including the number of patients with a particular disease or condition, current treatment and diagnostic options, and health outcomes including whether there are related basic research questions that need to be answered. FDA started this process with its *UnMet Medical Device Needs for Patients with Rare Diseases* but it lacks the necessary detail needed to take critical next steps. The National Institute of Child Health and Human Development (NICHD) could help facilitate this data collection. Collection of pediatric device needs data can assist in prioritization of basic research or device development activities that could be conducted by NIH,

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<sup>4</sup> See FDA Guidance entitled: *FDA Categorization of Investigational Device Exemption (IDE) Devices to Assist the Centers for Medicare and Medicaid Services (CMS) with Coverage Decisions*. The guidance defines Category A devices (Experimental): 42 CFR 405.201(b): "...a device for which 'absolute risk' of the device type has not been established (that is, initial questions of safety and effectiveness have not been resolved) and the FDA is unsure whether the device type can be safe and effective." The guidance also defines Category B devices (Nonexperimental/investigational): 42 CFR 405.201(b): "...a device for which the incremental risk is the primary risk in question (that is, initial questions of safety and effectiveness of that device type have been resolved), or it is known that the device type can be safe and effective because, for example, other manufacturers have obtained FDA premarket approval or clearance for that device type."

thus reducing overall device development costs and enhancing commercialization opportunities and technology transfer for interested stakeholders such as device manufacturers or pediatric device consortia. NIH should also assist in the identification and development of appropriate clinical and/or surrogate endpoints. NIH should engage the appropriate pediatric and pediatric subpopulation clinical experts to assist in development of clinical and/or surrogate endpoints. Creation of an NIH Office of Orphan and Pediatric Diseases could greatly facilitate the conduct and coordination of data collection, and establishment of priorities and research needs. The Pediatric Device Consortia network, each of which are housed at major pediatric clinical centers, are well positioned to conduct such unmet need studies.

### ***Opposition to Pediatric Device Development Mandates***

During the public meeting, there were suggestions that perhaps one solution to promote pediatric device development issues would be to provide FDA with the authority to mandate that device companies develop pediatric devices, presumably when an adult device already exists that could treat a disease or condition in the pediatric population. It was pointed out that this has worked well in the pharmaceutical space where the Best Pharmaceuticals for Children Act (BPCA) provides incentives in the form of marketing exclusivity to companies to voluntarily conduct pediatric studies. BPCA has been paired with the Pediatric Research Equity Act (PREA), which requires drug companies to assess the safety and effectiveness of certain products in pediatric patients. These proposals ignore the basic differences between drug and device markets and drug and device development. Device markets, and even more so, the pediatric device market, is significantly smaller and more fragmented than drug markets with fewer so-called “blockbusters.” As a result, device companies have significantly reduced capacity, financial and otherwise, to respond to mandates like those included in PREA for the drug industry. The vast majority of device companies are small. Even the largest device companies are a collection of small device companies with each division within the larger corporation required to stand on its own and be independently viable. A mandate of this nature could further reduce development in the pediatric device space.

It should also be noted that the BPCA incentive, which extended patents for companies that voluntarily conduct pediatric drug studies, is largely ineffective in the device environment. In most cases, there are many ways to develop device therapies for different pediatric diseases and conditions. As a result, patents, although good for protecting a single device approach, may not protect from other device approaches for the same population or disease. Therefore, patent extension in devices is not as beneficial as it is for pharmaceuticals. In addition, most devices are Class I and II 510(k)s (approximately 5,000 devices) whose commercial success is not dependent upon a patent.

There are other challenges associated with device development that do not exist for drugs. As noted above, pediatric populations are typically broadly and geographically dispersed, and few in number. As a result, one has to open many sites to recruit a small number of patients within the targeted subpopulation. It is costly to open and manage many investigational sites. As just one example, one company incurred costs of \$15 million for a 40-person pediatric study at 15 sites.

In addition, because of the iterative nature of device innovation, the average life-cycle for many devices may be as short as 18 months. In many instances, relatively small populations receive each generation of the device. Sometimes the first-generation device is never marketed at all. As a result, device companies may have a small market and a relatively short time from which to recoup the resources spent on pediatric product development, including the conduct of a clinical trial(s) where required. Moreover, for many pediatric devices, any mandate and related patent extension would also have to factor in the significant costs associated with the development, clearance or approval, and maintenance of quality manufacturing and related quality systems and recordkeeping for many different sizes of devices to accommodate different pediatric age groups. In short, given these factors—factors that in many cases are not applicable in the pharmaceutical space – it is not clear that patent extension would play the same beneficial role, especially given the short life-cycles of devices. Furthermore, patents would have to be continually renewed to have any beneficial effect at all.

As noted by Dr. Josh Makower in a 2010 Institute of Medicine (IoM) report, “The medical device innovation system is fragile and extremely sensitive to changes in the cost of innovation which is substantial.”<sup>5</sup> We believe a mandate of this nature to develop pediatric devices would introduce significant costs into the entire device innovation ecosystem while ultimately providing little benefit to pediatric populations. It will also act to further discourage investors from participating in the device market. In short, patent extension might provide limited benefit for a very few devices in the real-market but we believe its effects would likely be more harmful than beneficial to the device sector.

## Conclusion

In conclusion, thank you for the opportunity to provide our comments on this important topic. AdvaMed is committed to working with all stakeholders to ensure that children have access to safe and effective medical devices in a timely fashion. Please don’t hesitate to contact me if I can help answer any questions.

Sincerely,

/s/

Tara Federici  
Vice President  
Technology and Regulatory Affairs

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<sup>5</sup> See IOM (Institute of Medicine) 2010. Public Health Effectiveness of the FDA 510(k) Clearance Process: Balancing Patient Safety and Innovation: Workshop Report. Washington, D.C.: The National Academies Press.