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To: Food and Drug Administration
Center for Devices and Radiological Health

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Re: Possible Barriers to the Availability of Medical Devices
Intended to Treat or Diagnose Diseases and Conditions that
Affect Children; Request for Comments [Docket No. 2004N-
0254]



This letter is a response to the request for feedback concerning possible barriers to medical devices for children. Specific questions posed by the FDA and CDRH include:

1. What are the unmet medical device needs in the pediatric population? Are they focused in certain medical specialties and/or pediatric subpopulations?

As a pediatric cardiologist practicing for 15 years, I have been excited to see the recent strides made in studying and approving devices for children with various congenital heart defects. Nowadays, we can treat patent ductus arteriosus (PDA), secundum atrial septal defect, pulmonary and aortic valve stenosis, and occlude various vessels with devices or open them with balloon catheters or stents. Interestingly, however, many of the devices we use for catheter intervention/therapy involve off-label uses to deliver direct benefit for these children. The medical literature is replete with information regarding the use of "biliary" stents in the treatment of pulmonary artery stenosis, coarctation of the aorta, maintenance of ductal patency, and so forth. Likewise, embolization coils, initially released nearly 30 years ago for peripheral vessel occlusion, have been adapted for use in closing patent ductus arteriosus and even unusual abnormalities, such as surgical Fontan baffle leaks or intended fenestrations, as well as paravalvar leaks after prosthetic valve replacements. A device is now available for treatment of PDA for which it was designed and investigated. However, this device, the Amplatzer Duct Occluder, has been used in a variety of other vessel occlusions.

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While we now have a device designed for ASD and one for PDA closure, not all ASD's or PDA's have the same size or morphology. Most congenital heart defects have considerable variability in morphology and location. In other words, it is desirable to ultimately have the right tool for the job, rather than trying to adapt one device for all (i.e. trying to use the Amplatzer device to close every kind of PDA).

Another example of an unmet need is nonsurgical management of the neonatal PDA. In some cases, a large PDA needs to be closed, but currently existing materials and devices are not appropriate. Further, we are embarking on different ways to treat hypoplastic left heart syndrome, which will include implanting a stent to maintain patency of the ductus arteriosus. Some centers are using stents designed for adult problems (self-expanding or balloon expandable stents). The length and diameter of stents for our neonates is critical to achieve a good result. Covered stents hold tremendous interest for the benefit of our patients. Balloon angioplasty or stent implantation to treat coarctation really should involve either the primary use of a covered stent or the availability of a covered stent as a bailout in the event of an unexpected aortic rupture. Materials and stent designs particularly suited to these patients is essential. Drug-eluting stents are now available, but are designed for adults with coronary artery disease. As pediatric interventional cardiologists, we use what is available and adapt it the best we can to treat our patients and offer them the chance to avoid major surgeries. Ventricular septal defect devices are undergoing investigation, but different devices may be needed to treat the various types of VSD.

To summarize our current practice, we are involved in treatment of native defects (unoperated), residual/recurrent defects, palliative procedures that may bridge to further surgery, and are just beginning "hybrid" surgery (the use of endovascular catheter techniques with surgeon-assisted more direct cardiac access in the Operating Room).

2. What are the possible barriers to the development of the new pediatric devices? Regulatory? Clinical? Economic? Legal?

The overall lower volume/numbers in the pediatric population as compared to the adult population results in long time needed to enroll enough patients for any one device. Further, the variability of cardiac congenital defects, such as VSD, results in data that is less uniform. This often results in the need to extend the investigation even longer. Also, congenital heart disease itself entails a broad range of very different anatomic defects with vastly different physiologies.

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Therefore, one specific defect is not seen daily over and over again, as coronary artery disease is seen by adult cardiologists.

As for regulatory considerations, each new design modification has required a complete regulatory process, including a new clinical trial. An example is the Amplatzer Duct Occluder. It was investigated in sizes ranging from 5mm to 16 mm. However, the largest 2 sizes, 14 mm and 16 mm, were utilized in too few patients for them to be marketed after FDA approval of the device. The design is exactly the same, just that the larger two sizes were implanted in enough patients. This resulted in an additional trial sponsored by the manufacturer, but this study was terminated by the manufacturer because enrollment was so slow. Unfortunately, I had a patient who could have benefited from one of these larger devices. I was barely able to get by with the 12 mm device, but the smaller size created some concern about device embolization. A higher level of safety would have been achieved with the larger device.

Because of the low numbers in pediatrics, industry has been reluctant to invest in pediatric devices because of the small market. Some companies have made the effort and investment and hold a significant share of the pediatric market as a result.

3. What could FDA do to facilitate the development of devices intended for the pediatric population?

Any studies need to be done on as large a scale as possible in order to maximize patient enrollment. Larger centers with a track record of successful clinical trials and data submission should be included. The acceptable numbers for patient enrollment nationwide may have to be modified. For instance, if it takes 5-6 years to gather enough data with a device, but during the process, we discover that a modification to the device would improve its design, safety, and efficacy, then it takes another 5-6 years to complete a study of the modified device. So, in 12 years, we can provide the better device to many patients. In our current technology climate, this seems inordinately long to wait. Maybe decreasing the required enrollment number satisfactorily could shorten these studies to 2-3 years, at the longest.

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Given the increasing longevity for patients with congenital heart disease, maybe industry can be persuaded to invest in congenital heart disease and tailor devices for the anticipated needs of those patients. Some financial incentive for research and design by these manufacturers might prove to be effective.

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The time period from submission of PMA application to completion of data analysis and FDA market approval needs to be significantly shortened. This process adds another year to the entire process.

Finally, any one center should be allowed to be involved in several ongoing clinical trials for different devices intended for the same clinical situation/diagnosis. This allows the investigators to form their own opinions about different devices for the same job, thereby allowing them to remain unbiased but also streamline the medical understanding of which device works best in which situation. Likewise, the FDA should approve trials for different devices that serve the "same" purpose in order to expedite the understanding and improvement of device designs.

Naturally, this question is the hardest to answer, but hopefully, others in the FDA who know the workings of the government can use these suggestions to brainstorm as well. Thank you very much for the opportunity to provide these comments.

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