

Summary
Pediatric Device Stakeholders Meetings
June 28, October 4 & 25, and November 1, 2004

In an ongoing effort to improve therapeutics and diagnostics for pediatric populations, the American Academy of Pediatrics (AAP), the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), the National Organization for Rare Disorders (NORD), the National Association of Children's Hospitals (NACH) and the Advanced Medical Technology Association (AdvaMed) hosted a series of four invitational meetings to discuss pediatric device availability and needs during the summer and fall of 2004.

An initial meeting was held on June 28, 2004, which served as the starting point to identify unmet pediatric device needs, barriers to addressing those needs, and possible mechanisms for increasing the availability of pediatric appropriate products. A series of three follow-up meetings (October 4, 25, and November 1) were then held that focused discussions on several specific areas: data collection/information sharing; administrative and regulatory issues; and market capacity and incentives. Other issues such as reimbursement and liability were touched on but not delved into sufficiently. It may be necessary to have an additional meeting/s to fully examine these and other important issues.

All four meetings included a diverse group of individuals committed to advancing devices for pediatric populations. Participants included pediatric surgeons, neonatologists, pulmonologists, cardiologists, biomedical engineers, device industry representatives, the Food and Drug Administration, the National Institutes of Health, and the Institute of Medicine. Perhaps the most significant outcome of the meeting was the clear recognition that children have medical devices needs that can differ considerably from adults across a broad range of illnesses, conditions, and subspecialties and the consensus that it is no longer a question of whether neonates, infants, children and adolescents need age- appropriate devices, but rather, how those needs can best be addressed.

It became evident through the discussions that finding effective solutions to improving the availability of pediatric devices raises complex issues, stemming from such factors as the continuing need to identify and prioritize unmet pediatric device needs; the variation in needs across pediatric subpopulations (neonates, infants, children, adolescents); children's growth and development as they relate to product design and manufacturing; the diversity of the device industry; the relatively quick evolution and short life-span of devices compared to drugs; high research and development costs vis-a-vis limited pediatric use; liability concerns for manufacturers and practitioners; intellectual property considerations; and reimbursement concerns. Additionally, for some devices, the pediatric version may be completely different device from that developed for the adult population. Among other factors, the pediatric version may require different pre-clinical models for testing and manufacturing set-up.

The intent of the meetings was to identify areas of agreement as well as to explore ideas that are viewed as important but where consensus has not yet been reached. The following summary is broken into *Consensus Items*: those action steps on which the group reached general agreement and *Outstanding Issues*, those on which the group did not reach agreement. Within each heading, categories of recommendations are identified and, where appropriate, assigned a proposed process to move the recommendations forward (e.g., legislative, administrative or non-government organization-led [NGO-led]). Lastly, there were two issues that were identified as important for future discussions: reimbursement and liability related to the use and development of pediatric devices. Because of time constraints and the lack of necessary expertise among the participants present, neither topic was discussed at any length during the meetings, although participants agreed that both deserve further consideration.

NOTE: The inclusion of a particular concept or action item on this list does not indicate an endorsement by any individual organization participating in the meetings. Further, examples of arguments in favor or in opposition to a particular concept should not be considered an exhaustive list.

CONSENSUS ITEMS:

National Institutes of Health (NIH) Support for Pediatric Device Development

- Require better coordination of existing support for pediatric device research and development across the Institutes, Centers and Divisions. *(legislative or administrative)*
- Designate a “point person” or office at the NIH to help innovators and physicians access existing funding for pediatric device development. *(legislative or administrative)*
- Designate funds for core and cross-cutting pediatric device research areas (e.g., development of materials that can grow as children do, safety of devices left in children long-term, etc.) that are unlikely to be undertaken by an individual device company. *(legislative or administrative)*

Survey of Pediatric Device Needs

- Develop a survey tool to assess pediatric device needs through major subspecialty organizations, as well as allied health professions (nurses, respiratory therapists), parents/families, vendors/home care agencies *(NGO-led)*.
 - Develop template of core questions with examples
 - Test in small number of organizations (e.g. 20)
 - Secure AHRQ assistance as needed
 - Work with other subspecialties groups to survey membership re: device needs
- Maintain ongoing inventory of pediatric device needs available on-line.
 - Need to address who would fund and maintain, e.g., FDA, Consortium, NGO, etc.

Food and Drug Administration (FDA) Device Processes and Expertise

- Provide explicit statutory authority to encourage FDA reviewers to allow the extrapolation of adult data to support a determination of pediatric safety and efficacy from adult data, as appropriate. *(legislative)*
- Develop a condensed “EZ” approval process with a 30 day fast track review for modifications to existing devices that need only minimal changes to be made appropriate for pediatric use. *(legislative or administrative)*
- Enhance/expand participation of qualified pediatric subspecialists on pre-IDE protocol evaluation and advisory panels. Strategies may include publicizing and encouraging the pediatric practitioner community to identify candidates. *(legislative, administrative and NGO-led)*
- Provide more and better training of FDA/industry/outside consultants regarding pediatric device needs. *(administrative)*
- Taking into consideration identified pediatric device needs, revise existing device guidance documents for specific device categories or create new guidance to encourage the development of pediatric information, where appropriate. Such guidance could also operate as an additional mechanism to communicate to companies about those device categories where pediatric devices are needed. *(administrative)*
- Improve online adverse event reporting documents (e.g. Medwatch) to encourage better collection of pediatric information. *(administrative)*
- Target audiences for education/training about how to improve pediatric device adverse event reporting, including physicians/CME, medical students, residents, risk managers, families/parents, outpatient/caregivers. *(NGO-led)*
- Urge FDA’s Combination Products office to promote a pediatric focus. *(administrative)*

OUTSTANDING ISSUES

Pediatric Device “Consortium” *(legislative)*

- Create and fund a non-profit Consortium to promote pediatric device development. Activities would include:
 - Nurturing innovation by connecting individuals with ideas with manufacturers
 - Providing “hands-on” mentoring and project management through the device continuum (e.g., product identification, prototype design, device development through marketing)
 - Connecting innovators/physicians to existing federal resources (FDA, NIH, SBA/Small Business Innovative Research grants, Department of Energy, Department of Education, NIST, NSF, AHCPR, VA)
 - Assessing scientific/medical merit of proposed device project
 - Assessing business feasibility and providing business advice
 - Provide assistance with prototype development
 - Provide assistance with post-market needs, (e.g., training, logistics, reporting)
- Establish a mechanism for feeding back to the NIH pediatric device contact point any identified pediatric device needs that the Consortium lacks sufficient funds to

address or those needs in which the Consortium has been unable to stimulate manufacturer interest.

- Would coordinate with FDA and companies to ensure that needed devices recommended by the consortium produce appropriate pediatric safety and effectiveness information, as determined by FDA review staff for a given pediatric product.
- Need to address funding source – possibly a mix of public and private funding. Participants agreed that funding for the Consortium should supplement, not supplant existing funding.
- Need to address intellectual property concerns and what to do when a need is identified but the originator company is not interested in modifying its device.

Ensuring that Pediatric Populations are Included in Therapeutic Advances (*legislative and administrative*)

Numerous participants noted that infants and children should share equally in the medical device advances that are available to adults. In an effort to include children in the initial stages of device development, a series of proposals were discussed:

- Create the presumption that certain devices will be appropriately studied and designed for pediatric use, following the model of the Pediatric Research Equity Act, which provides that if a drug or biologic occurs in the pediatric population, then that medication must be studied and formulated for pediatric use. PREA provides for waivers and deferrals and does not delay a medication from coming to the market for an adult population if the pediatric studies are not completed.
 - Could be focused on those devices most widely used by children, those requiring little modification, and/or those that represent a significant treatment or diagnostic advance
 - Concerns were raised that having to conduct additional pediatric testing or make design changes could be unfeasible or prohibitively expensive or could otherwise discourage a manufacturer from bringing a product to market. Concerns were also raised about the resource implications for FDA.
- Ensure that certain FDA device applications include a section to identify potential pediatric uses. Consider limiting to those devices requiring IDEs. (*legislative or administrative*)
- Formalize current FDA pediatric guidance process to ensure that pediatric use of devices is discussed in pre-approval product meetings. (*legislative or administrative*)

Modifications to the Humanitarian Device Exemption (*legislative*)

- Allow profit for pediatric, and potentially for adult, HDE devices. (While there was consensus that the profit should be explored, there was a difference of opinion about whether the profit should somehow be limited). Concerns were raised about potential “gaming” of the system, i.e., manufacturers using the HDE route to avoid a PMA submission, particularly where the potential off-label use of the product is significant. A proposal was made to address this concern by requiring companies to report the number of HDE approved devices shipped over the 4,000 limit. However, there was no

consensus on what enforcement mechanism or penalty should apply to those exceeding the limit.

- Eliminate or modify the requirement of IRB review of HDEs, based on the concern that it is inconsistent with HDEs being FDA-approved products and is confusing to IRBs, patients and insurers. Consider giving more guidance to IRBs, having review conducted by a national IRB, or eliminating the requirement entirely.
- Modify the current 4,000 population limit, either by
 - Raising the limit on population size to some number over 4,000, with appropriate justification
 - Setting a limit on population size on a device-by-device basis by applying an evidence-based/scientific framework (i.e., determining for each device the population below which a study to establish efficacy isn't feasible). On this option, the concern was raised that making such a determination for each HDE submitted would be labor/resource intensive for FDA.

Expanding the Existing Custom Device Provision for Small Pediatric Populations (legislative)

- Create a mechanism for legally shipping devices for small pediatric populations, i.e., in the range between the current custom device provision and HDE, for which manufacturers have little financial incentive to conduct pediatric safety and efficacy studies. Would address pediatricians' concerns about having to jerry-rig devices on case-by-case basis by providing the assurance that a device is constructed/engineered appropriately and consistently and would allow manufacturers to work directly with pediatricians to fulfill unmet device needs.
- No premarket review would be required. GMPs and design controls would apply and custom device files would be reviewed during scheduled FDA audits and inspections.
- Adverse event reporting (MDR) would apply.
- Would not require informed consent or IRB approval.
- Only modifications of existing adult devices (both 510K and PMAs), not entirely new pediatric devices, would be eligible.
- Raises the concern that devices would be legally available for pediatric use with no safety or efficacy information and without protections such as IRB approval and informed consent. Actual numbers of pediatric and other patients using the product, once on the market, for both on- and off-label use could be significantly higher than anticipated.
- Could require post-marketing gathering of information, but may only be of limited assistance given difficulty in reaching patients once devices are in use. Could link to the Consortium for post-marketing study.

Dissemination of Pediatric Information

- Disseminate any pediatric-relevant studies conducted as part of the approval process for general use devices. Need to address liability issues and usefulness of data to clinicians. (legislative)
- Pursue opportunities to gather and disseminate off-label use data for pediatric patients. (administrative)
- Consider including in a public forum (e.g., FDA website) that a company declined to do pediatric studies on a device identified by the Consortium process as a high

priority. *(legislative)* The concern was raised that this could be an infringement on intellectual property and proprietary information.

Postmarketing Surveillance and Reporting (Note that a congressionally-requested report from the IOM on this subject is expected in Spring 2005)

- Expand the current Medical Product Surveillance Network (MedSun) to create model program/s for adverse events (AE) reporting of in- and out-patient pediatric device use. Would require additional funding. *(legislative)*
- Expand the use of postmarketing studies as a possible avenue to collecting better information on use, adverse events, etc. related to pediatric populations. *(legislative or administrative)*

The importance of expanding knowledge about pediatric device use, including adverse events, through postmarketing surveillance and reporting was discussed at some length during the meetings. Solutions to improving the collection of and usefulness of postmarket data are complicated by such factors as the iterative nature of device development (i.e., a device may undergo several modifications or even become obsolete before a study is completed) and the difficulties in achieving manufacturer, physician and patient compliance/interest in completing or participating in such studies. However, there was a desire to explore this issue further.

- Explore inclusion of device tracking in electronic health records to ensure that primary care physicians can track device reactions/complications in patients who may have received subspecialty care. *(administrative)*

Protections for children in clinical trials

- Need better guidance to IRBs on assessing risk to children of participating in device trials. Should be included in any legislation to implement IOM recommendations from March 2004 report. *(administrative or legislative)*

Tax Incentives

- General interest in exploring tax incentives but no specific recommendations made.