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May 9, 2014

Dr. Margaret A. Hamburg
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Commissioner Hamburg:

I write to inquire about the Food and Drug Administration's (FDA's) efforts to encourage the development of pediatric medical therapies and devices. When it comes to medical therapies and devices, children are not just small adults. Medical therapeutic devices for children must be appropriately sized, fit their unique physiology and accommodate the rapid growth that occurs during pediatric years. Additionally, children are not all homogenous; the needs of neonates differ greatly from those of toddlers and from those of older pediatric patients. Without appropriately tailored devices, physicians are forced to individually modify adult devices to serve the diverse and sophisticated needs of pediatric patients. These modifications can, in some situations, cause complications, and in other cases where modifications simply are not feasible, treatments must be delayed until the patient has reached an appropriate size to accept the device.

The lack of readily available and safe medical devices intended for the pediatric population led me to work on enacting the Pediatric Medical Device Safety and Improvement Act (PMDSIA) as a part of the Federal Drug Administration Amendments (FDAAA) of 2007, which was most recently reauthorized in 2012 as a part of the Food and Drug Administration Safety and Innovation Act (FDASIA). The pediatric device provisions of this law provide economic incentives for companies to develop devices for children with rare diseases, require the Food and Drug Administration (FDA) to track and compile information about potential pediatric uses of devices, and authorize continued funding for the Pediatric Device Consortia grant program, which helps facilitate the development, production, approval and distribution of devices intended for children.

Since enactment of the PMDSIA in 2007, the FDA has taken several actions to implement the law and improve pediatric devices, including awarding pediatric device consortia grants, most recently to seven consortia across the country. To understand fully the impact this law has had on the availability of reliable pediatric devices and FDA's progress in implementing provisions of the law, I respectfully request that you respond to the following questions no later than May 30, 2014.

1) For each year since the enactment of the pediatric medical device provisions of FDAAA, please indicate how many approved device applications have been labeled for use in pediatric populations. How does that number compare with each year in the five-year period prior to enactment of this law?

2) The pediatric device economic incentive provided for in FDAAA and FDASIA allows for device developers to earn a profit on Humanitarian Use Devices (HUD), devices that are intended for use in pediatric patients and that treat or diagnose a disease that affects fewer than 4,000 patients per year. These devices do not have to meet the same effectiveness requirements of a pre-market approval device, but they do have to submit a humanitarian device exemption (HDE) application, providing enough information to show that the device does not pose an unreasonable risk and demonstrating that there are no other comparable devices on the market. Once FDA approves an HDE, the device is considered authorized and can be legally marketed. However, because these devices are viewed as being "experimental" by private and public insurers, patients often have problems getting these devices paid for or reimbursed by their insurance plans. How has the FDA engaged with the Centers for Medicare and Medicaid Services (CMS), to ensure that they are aware that HDEs are FDA-authorized devices? Has the FDA engaged with the private payer community to educate them on these devices? If so, please explain. If not, why not?

3) Once FDA approves an HDE, the device is considered authorized and can be legally marketed. However, before an approved HDE device can be used in a patient, its use must first be approved and reviewed by an institutional review board (IRB). This additional IRB approval is typically not required of other FDA approved devices, since IRBs are typically responsible only for overseeing research and experimentation. Many clinicians have noted that the requirement for IRB approval can cause confusion and poses a significant barrier to increased access to HDE devices.

    a) Has the FDA evaluated whether the IRB review requirement poses a barrier to increased use of HDE authorized devices? If so, what did FDA find?

    b) In the absence of IRB review, is the FDA aware of other mechanisms that are available in institutions where HDEs are used that would be more appropriate to oversee the use of these devices? If so, what mechanisms has FDA evaluated and what did FDA conclude?

    c) Has the FDA evaluated whether instituting a requirement for extended post-market data collection would be useful for ensuring that these HDE devices are useful and continue to not pose unreasonable or significant risks to pediatric populations? If so, what was determined from this evaluation? If not, why not?

4) In 2007, section 515A(b) of FDAAA gave the Secretary authority to extrapolate adult data for pediatric patients and between pediatric subpopulations for purposes of supporting a determination of effectiveness for a device being used in pediatric patients, provided that the disease and the effects of the device are sufficiently similar in adults and pediatric patients.

The provision applies to both Humanitarian Use Devices (HUD) and Premarket Approval (PMA) devices reviewed by the agency. While the FDAAA provides explicit authority to extrapolate effectiveness data from adults to children, the law does not provide FDA with the authority to extrapolate safety data from adults to children.

a) When does FDA expect to publish guidance implementing Section 515A(b) of FDAAA?

b) For drugs, the FDA has determined that differences in the safety profiles between pediatric and adult populations preclude the extrapolation of safety information. Does the FDA believe it would be appropriate to extrapolate safety data from adults to children or within pediatric subpopulations for some or all medical devices? If so, please provide examples of circumstances and/or examples of PMA and HDE devices where the agency believes extrapolation of safety data is merited and why the agency would differ in its approach between drugs and devices.

c) Is the FDA aware of devices that have been approved by FDA for use in pediatric patients without the device ever being studied in pediatric patients? Is this scenario feasible under FDA's current authority?

5) In 2012, the FDASIA reauthorized the Pediatric Device Consortia (PDC) program for another five years. This program has great potential for promoting pediatric device development and getting new and innovative devices to market.

a) What impact has the PDC program funding had on private funding sources and venture capital?

b) Please describe how the establishment of the PDC program has resulted in the advancement of pediatric medical device development?

Thank you for your assistance and cooperation in responding to this request. Should you have any questions, please have your staff contact Dr. Avenel Joseph of my staff at 202-224-2742.

Sincerely,

Edward J. Markey

Edward J. Markey
United States Senator