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PEDIATRIC MEDICAL DEVICES SAFETY AND IMPROVEMENT ACT OF 2007

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Last September, Congress passed the Food and Drug Administration Amendments Act of 2007. Title III of that law, the Pediatric Medical Safety and Improvement Act, created new incentives, mandates, FDA authority, and funding with the aim of increasing the availability of devices for pediatric populations while assuring the safety and effectiveness of those devices. The purpose of this article is to situate this new law within the context of the problem it addresses, the general approach of medical device regulation in the United States, the complex problem the Title addresses, the regulatory solutions to the parallel problem for pediatric drugs, and stakeholder input.

In Part I, I will briefly discuss the history of the regulation of medical devices in the United States and the current general regulatory scheme for devices. In Part II, I will describe first the market failures that have resulted in the development of few medical devices intended for use in children. Second, I will discuss the ways Congress and the Food and Drug Administration (“FDA”) addressed the analogous problem in the drug context. Third, I will describe the ways Congress and FDA dealt with the problem in devices before the most recent legislation. In Part III, I will report stakeholder comments on the specific problems in the device arena that remained despite regulatory activity, including unmet needs, barriers, and their recommended solutions. In Part IV, I will briefly discuss FDA’s subsequent report to Congress, the Institute of Medicine’s report on problems and solutions regarding post-marketing surveillance of medical devices used in pediatric populations, and the Medical Device Innovation Initiative. Finally, in Part V, I will discuss the Pediatric Medical Device Safety and Improvement Act. First, I will recount briefly the Act’s legislative history. Second, I will describe the Title’s new mechanisms for increasing availability of pediatric devices. Third, I will conclude by

relating those mechanisms to the public comments, the Institute of Medicine's report, the goals of Congress, and the current regulatory scheme for encouraging the development of pediatric drugs.

PART I

1. History of the Regulation of Medical Devices

Regulation of medical devices has always lagged behind regulation of drugs.¹ While Congress authorized the national regulation of drugs in 1906, it did not provide for the regulation of devices until 1938.² Before 1938, government oversight of medical devices was left to the United States Post Office, which used its authority under mail fraud statutes to prosecute fraudulent medical device claims sent through the United States mail.³ When Congress strengthened the regulatory scheme for drugs in 1962, requiring premarket approval of each new drug for safety and effectiveness, medical devices were left to be governed by the pre-existing scheme.⁴ It was not until the Medical Device Amendments of 1976 that Congress gave FDA broad authority to regulate the safety and effectiveness of medical devices.⁵ Because the regulation of drugs and medical devices was contemplated separately, the resulting regulatory structure differs between the two.

2. The Current Regulatory Framework

¹ See Peter Barton Hutt, *A History of Government Regulation of Adulteration and Misbranding of Medical Devices*, 44 FOOD DRUG COSM. L.J. 99 (1989).

² *Id.* at 104.

³ *Id.* at 101.

⁴ *Id.* at 106.

⁵ *Id.* at 112.

Medical devices are diverse, from tongue depressors to artificial hearts to *in vitro* diagnostics.⁶ This range, in complexity, novelty, safety risk, and potential for benefit, is reflected in the FDA's regulation of medical devices. While nearly all new drugs must go through the same rigorous premarket approval process, new medical devices undergo different premarket processes depending on the risk to patients of their use or misuse.⁷ Since the 1976 Medical Device Amendments, FDA has regulated medical devices through this risk-based classification system. The riskier the device, the more oversight FDA extends.

(a) Class I

Class I devices, like tongue depressors, pose the least amount of risk and are subject to the lowest degree of regulatory control.⁸ Class I devices regulated through five "general controls:" (1) registration of entities involved in producing and distributing the device;⁹ (2) listing the medical device with FDA;¹⁰ (3) labeling the device with the name

⁶ FOOD & DRUG ADMIN., IS THE PRODUCT A MEDICAL DEVICE?, Feb. 28, 2002, <http://www.fda.gov/cdrh/devadvice/312.html>. A medical device is defined as, "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them; intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or; intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes." *Id.*, quoting Federal Food Drug & Cosmetic Act § 201(h), 21 USC 321(h).

⁷ FOOD & DRUG ADMIN., *supra* note 6.

⁸ FOOD & DRUG ADMIN., DEVICE CLASSES, Nov. 21, 2002, <http://www.fda.gov/cdrh/devadvice/3132.html>.

⁹ *Id.*

¹⁰ *Id.*

and place of business, intended use, and adequate directions for use;¹¹ (4) complying with good manufacturing practices as outlined by FDA regulation;¹² and (5) submission of premarket notification demonstrating that the device is substantially equivalent to, meaning at least as safe and effective as, a device already legally marketed.¹³ However, because of the low risk of Class I devices, most are exempt from one or both of the fourth and fifth requirements.¹⁴

(b) Class II

Class II devices, such as infusion pumps and power wheelchairs, carry more risk. FDA subjects most Class II devices to all general controls and a few “special controls,” which may include additional labeling requirements, performance standards, and postmarket surveillance.¹⁵ In keeping with the agency’s flexible approach to regulating devices, the special controls FDA requires depend on the nature of the device;¹⁶ a few Class II devices are even exempt from premarket notification of substantial equivalence.¹⁷

(c) Class III

¹¹ FOOD & DRUG ADMIN., LABELING REQUIREMENTS – GENERAL, Feb. 9, 2000, <http://www.fda.gov/cdrh/devadvice/331.html>.

¹² FOOD & DRUG ADMIN., GOOD MANUFACTURING PRACTICES (GMP) / QUALITY SYSTEM (QS) REGULATION, Jan. 28, 2004, <http://www.fda.gov/cdrh/devadvice/32.html>.

¹³ FOOD & DRUG ADMIN., PREMARKET NOTIFICATION 510(K), Nov. 1, 2006, <http://www.fda.gov/cdrh/devadvice/314.html>.

¹⁴ FOOD & DRUG ADMIN., *supra* note 8.

¹⁵ *Id.*

¹⁶ *E.g.*, FOOD & DRUG ADMIN., POSTMARKET SURVEILLANCE STUDIES, Aug. 29, 2007, <http://www.fda.gov/cdrh/devadvice/352.html#who>.

¹⁷ FOOD & DRUG ADMIN., MEDICAL DEVICE EXEMPTIONS 510(K) AND GMP REQUIREMENTS, May 6, 2008, <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpd/315.cfm>.

Class III devices, which include replacement heart valves and silicone breast implants, have the most potential for harm. They are “usually those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury.”¹⁸ Class III devices are generally subject to premarket *approval*, involving rigorous scientific assessment of the safety and effectiveness of the device for its intended use. However, in certain circumstances, even Class III devices can forgo the premarket approval process for the less intensive premarket notification.¹⁹

PART II

Both drug and device manufacturers are largely for-profit entities. Their ability to remain financially solvent depends largely on their ability to sell enough of their products at enough of a profit to support their business expenses, including research and development. As a result, when a disease population is too small, a condition too rare, market forces alone do not provide adequate incentive for manufacturers to develop therapeutic and diagnostic tools for those populations.

Children in need of medical products can be seen as a special case of the small market problem. Not only are there fewer children than adults generally, but children who need drugs and medical devices are even more rare. For example, heart disease is relatively common in adults, but congenital heart defects are very rare in children and

¹⁸ FOOD & DRUG ADMIN., *supra* note 6.

¹⁹ Because of an interesting historical compromise, Class III devices may gain market clearance through premarket notification only if the devices are substantially equivalent to Class III devices on the market before 1976. *Id.*

defects can vary considerably from child to child.²⁰ Moreover, because of differences in size, growth rate, metabolism, heart rate, activity level, and other biochemical differences, the drug, dosage, or device an infant needs is not the same as a 10-year-old, even if they have the same ailment. Thus, the pediatric market is more properly viewed as several submarkets, from neonatal to young adult, each potentially needing its own specialized device. The small market size not only reduces the potential sales of drugs or devices that could be sold; it also makes clinical trials more difficult to perform.

Pediatric medical researchers express frustration with the amount of time, energy, and financial resources required to enroll the number of pediatric patients in a clinical trial to test a device according to FDA's specifications. Because drugs and devices may be used, through not marketed, off-label, there is an overwhelming incentive to conduct trials in one population, write the label accordingly, and leave it to clinicians to prescribe it in other populations.

As a result, "for children, off-label use is the rule, not the exception."²¹ For drugs, this means "dosing down"²² a medication only tested in, and approved for, adult populations. Almost two-thirds of drugs prescribed for children are not labeled for their population;²³ nearly 80% of hospitalized children are given at least one drug for off-label

²⁰ Mullins, *infra* note 117, at 2.

²¹ *Ensuring Safe Medicines and Medical Devices for Children, Senate Committee on Health, Education, Labor, & Pensions*, 107th Cong. (2007) (testimony of Richard L. Gorman, MD, FAAP on behalf of the American Academy of Pediatrics), citing UNITED STATES GOVERNMENT ACCOUNTABILITY OFFICE, PEDIATRIC DRUG RESEARCH, GAO-07-557.

²² This common phrase can be seen, e.g., in Joanna K. Sax, *Reforming FDA Policy for Pediatric Testing: Challenges and Changes in the Wake of Studies Using Antidepressant Drugs*, 4 IND. HEALTH L. REV. 61 (2007).

²³ Gorman, *supra* note 21.

use.²⁴ For devices, this means “jury-rigging” an adult device, attempting to physically modify it to fit a child’s body and lifestyle.²⁵ However, there is little information, aside from anecdotes, to guide clinicians in these endeavors. Moreover, because children are not simply small adults, “dosing down” and “jury-rigging” are not always viable options. For example, children’s baseline respiratory rates are more rapid than adults, making artificial heart valves designed for adults unusable in children.²⁶

Thus, there are two main problems created by market failures in the pediatric drug and device arenas: (1) the dearth of drugs and devices specifically designed for pediatric populations, and (2) the lack of information on the appropriate pediatric use of drugs, through dosing, and devices, through physical modification. The next sections will show how Congress and FDA attempted to solve each of those problems.

1. The Drug Context

(a) The Orphan Drug Act and the Rare Diseases Act

In 1983, Congress began to tackle the first of these problems in the drug arena through the Orphan Drug Act. Congress has amended the Orphan Drug Act several times since, attempting to better tailor the incentives it provides to the statute’s purpose of

²⁴ *Id.*, citing Shah SS, Sharma VS, Jenkins KJ, Levin JE, *Off-label Drug Use in Hospitalized Children*, 161 ARCHIVES OF PEDIATRIC & ADOLESCENT MED., 282-290 (2007).

²⁵ *Programs Affecting Safety and Innovation in Pediatric Therapies: Hearings Before the Subcomm. on Health*, 110th Cong. (2007) (testimony of Diane Edquist Dorman Vice President of the National Organization for Rare Disorders), 1-19, 2.

²⁶ AM. PEDIATRIC SOC’Y & SOC’Y FOR PEDIATRIC RES., PEDIATRIC MEDICAL DEVICES: COMMENTS TO THE IOM, Aug. 23, 2004, http://www.aps-spr.org/Public_Policy/2004_Docs/CommentIOM20040823.htm.

making drugs available to Americans suffering from rare disorders.²⁷ In 2002, Congress supplemented these efforts with the Rare Diseases Act, which further supported research on diseases with small patient populations.²⁸ While these two statutes are not aimed specifically at pediatric populations, they have provided incentives and support for the development of pediatric drugs.

The Orphan Drug Act defines an “orphan drug” as either a drug²⁹ for a condition affecting fewer than 200,000 people in the United States, or one that would cost more to develop and make available than would be recovered from sales in the United States.³⁰ The Orphan Drug Act and the Rare Diseases Act, together, created a comprehensive scheme to promote the development of orphan drugs, through: (1) seven years market exclusivity; (2) a fifty percent tax credit for “qualifying clinical testing expenses,” including the human trials necessary to gain FDA approval; (3) the appropriation of grant funds for orphan drug research and clinical trials; and (4) assistance from FDA in designing the appropriate clinical trials. In addition, FDA used its authority granted by the Orphan Drug Act to encourage drug sponsors to use open clinical trial protocols to

²⁷ See Gary A. Pulsinelli, *The Orphan Drug Act: What's Right With It*, 15 SANTA CLARA COMPUTER & HIGH TECH. L. J. 299, 307-309 (1999).

²⁸ See Carl Rados, *Orphan Products: Hope for People With Rare Diseases*, FDA CONSUMER MAG., Nov.-Dec. 2003, http://www.fda.gov/fdac/features/2003/603_orphan.html.

²⁹ As defined in Federal Food Drug, & Cosmetic Act § 201(g), 21 U.S.C. § 321 (2004).

³⁰ FOOD & DRUG ADMIN., DEFINITION OF DISEASE PREVALENCE FOR THERAPIES QUALIFYING UNDER THE ORPHAN DRUG ACT, <http://www.fda.gov/orphan/designat/prevalence.html> (last visited, May 10, 2008). The second prong most closely maps onto the market problem Congress was aiming to address; indeed, the prevalence prong was not part of the original statute. The definition of “orphan drug” was expanded to include prevalence in the 1983 amendments, largely because the pharmaceutical response to the original Orphan Drug Act’s incentives was underwhelming. Gary A. Pulsinelli, *The Orphan Drug Act: What's Right With It*, 15 SANTA CLARA COMPUTER & HIGH TECH. L. J. 299, 307 (1999).

increase the availability of the drugs while still in the trial stage, and it established an Office of Orphan Product Development. The Rare Diseases Act subsequently established the Office of Rare Diseases within the National Institutes of Health (“NIH”). Altogether, the result is a regulatory scheme that aims to coordinate and support the research, development, and production of drugs for rare diseases.³¹

(b) The 1997 Food & Drug Administration Modernization Act

Still, the Orphan Drug Act and the Rare Diseases Act were not specifically aimed at solving the pediatric problems. The 1997 Food and Drug Administration Modernization Act (“The 1997 Act”) included the first incentives specific to research in pediatric populations. The 1997 Act began to address the lack of information about appropriate pediatric use of drugs marketed for adults, through offering drug sponsors six months of additional market exclusivity for voluntarily conducting pediatric studies that “fairly respond” to drug-specific FDA written requests for pediatric testing.³² As a result, over 125 products have adopted labeling addressing dosage, safety, and efficacy in children.³³ FDA estimated that the information gained through the pediatric exclusivity incentive, in addition to improving children’s lives, would save several million dollars per year, by reducing pediatric hospitalizations alone.³⁴ Heralded as “the most successful

³¹ Rados, *supra* note 27.

³² Written requests can originate in two ways. First, FDA can independently determine, through background research and review of the literature, that there is a public health need for a particular pediatric study to be conducted. Second, manufacturers can submit a proposal for a pediatric study, and FDA may consider that as a starting point for a written request if it believes the study presented in the proposal satisfies a public health need. *See supra* note 2.

³³ *Id.*

³⁴ FOOD & DRUG ADMIN, *infra* note 43.

pediatric initiative that [FDA] has participated in to date,”³⁵ the exclusivity incentive of the 1997 Act was reauthorized in the Best Pharmaceuticals for Children Act (“BPCA”) of 2002.

However, the incentive was far from perfect. First, it was both over- and underinclusive. The additional market exclusivity did not provide sufficient incentive to conduct pediatric clinical trials when the costs of the additional testing overwhelm the profits the additional period of exclusivity can provide. In other words, when a market is too small, six months of sales cannot financially support the investment of pediatric testing.³⁶ Conversely, the costs of pediatric studies could seem disproportionately small compared to the economic gains of the additional market exclusivity. This was particularly true with drugs that are widely used in adult populations; by undergoing the pediatric studies requested by FDA, manufacturers can hold off generic competition in the adult market while generating better information about pediatric use. A group of researchers in the Netherlands studying the impact of the pediatric exclusivity provision in the United States found that “[t]he distribution of [drugs granted pediatric exclusivity] closely matched the distribution of these drugs over the adult market, and not the drug utilization by children.”³⁷ Indeed, pediatric exclusivity was most frequently granted to

³⁵ *Hearing on Programs Affecting Safety and Innovation in Pediatric Therapies: Health Subcommittee of the Committee on Energy and Commerce of the U.S. House of Representatives*, 110th Cong. (2007) (statement of Rear Admiral Sandra Lynn Kweder, M.D.), available at <http://www.fda.gov/ola/2007/peds052207.html>.

³⁶ FOOD & DRUG ADMIN, *supra* note 44, at 13.

³⁷ *Programs Affecting Safety and Innovation in Pediatric Therapies: Hearings Before the Subcomm. on Health*, 110th Cong. (2007) (testimony of Peter Lurie, Deputy Director of Public Citizen’s Health Research Group, available at <http://www.citizen.org/publications/release/cfm?ID=7522>, citing Boots I, Sukhai RN, Klein RH, et al. *Stimulation programs for pediatric drug research – do children really benefit?*, EUROPEAN JOURNAL OF PEDIATRICS, Jan. 17, 2007. “The top three drug

drugs for depression and mood disorders, hypertension, elevated cholesterol, HIV, and pain – conditions that are common in adults.³⁸

At the time of the BCPA hearings in 2001, profits from the additional six months of market exclusivity could be several hundred million dollars or more, depending on the popularity of the drug in both the pediatric and the adult populations, while the costs to pharmaceutical companies of the pediatric studies requested by FDA were between one and seven million dollars.³⁹ This “windfall” to pharmaceutical manufacturers came at the expense of postponed generic competition,⁴⁰ which FDA estimated at a cost of \$13.9 billion over twenty years.⁴¹ This concern continued to be voiced through the 2007 hearings to reauthorize the BCPA.⁴²

Second, the exclusivity provision did not provide incentives to conduct pediatric research on drugs that no longer have patent protection or market exclusivity, such as older drugs already off-patent. For example, the pediatric exclusivity provision could not induce pediatric study of Albuterol inhalation solution, an off-patent drug prescribed for

categories granted pediatric exclusivity precisely matched (in category and sequence) the top three prescribing categories for adults, while none of the top three prescribing categories for children appeared in the top three for the granting of pediatric exclusivity.”
Id.

³⁸ *Id.*

³⁹ See, e.g., Rachel Zimmerman, *Child Play: Pharmaceutical Firms Win Big on Plan to Test Adult Drugs on Kids*, WALL ST. J., Feb. 5, 2001, at A1.

⁴⁰ E.g., *Hearings on Evaluating the Effectiveness of the FDA Modernization Act*, 107th Cong. 71–75 (2001) (testimony of Carole Ben-Maimon, President and CEO, Proprietary Research and Development, Barr Laboratories).

⁴¹ FOOD & DRUG ADMIN, *infra* note 43.

⁴² E.g., *Programs Affecting Safety and Innovation in Pediatric Therapies: Hearings Before the Subcomm. on Health*, 110th Cong. (2007) (testimony of Chairman Frank Pallone, Jr.), available at http://energycommerce.house.gov/Subcommittees/HE-Pallone/pallone_statement_rxdrugs_BPCA_PREA.pdf.

asthma to over 1.6 million patients under the age of 12.⁴³ Predictably, of the ten drugs most commonly prescribed to children, the six without market exclusivity had yet to be studied under the pediatric exclusivity program.⁴⁴

Third, the exclusivity program did not induce pediatric studies in the most vulnerable pediatric populations, particularly in the neonatal population. While pediatric research is generally more technically and ethically challenging than research in adults, research in neonatal populations is particularly hairy. In addition, safety concerns dictate that research in the neonatal population occur after research in older children. As a result, manufacturers that received the extra six months for the research in older pediatric groups had little incentive to undertake the additional testing.⁴⁵

Lastly, because the 1997 Act did not require pharmaceutical manufacturers to change their labeling in order to receive the additional market exclusivity, critics argued there was not sufficient incentive for manufacturers to actually disseminate the information learned by the pediatric studies. According to the United States General Accounting Office, it took manufacturers nine months on average, three months longer than the exclusivity extension, to agree upon a labeling change with FDA. At times, FDA found it particularly difficult to move manufacturers to disclose “unfavorable”

⁴³ FOOD & DRUG ADMIN., THE PEDIATRIC EXCLUSIVITY PROVISION: JANUARY 2001 STATUS REPORT TO CONGRESS (2001), at 37.

⁴⁴ These included Albuterol; Ampicillin injection, prescribed 639,000 times to patients under the age of 12 for infection; and Ritalin, prescribed 226,000 times to patients under the age of 6. All prescription prevalence figures are from 1994. *Id.*

⁴⁵ It should be mentioned that the 1997 Act did create the possibility for a second period of exclusivity to deal with this problem. However, according to FDA, “it is very limited in scope and to date [January 2001] no sponsor has utilized this option.” FOOD & DRUG ADMIN., *supra* note 44, at iii.

results on drug labels.⁴⁶

In sum, the market exclusivity incentive is systematically biased toward newer, on-patent drugs with large non-pediatric markets. And, without a link between exclusivity and labeling, there is little incentive for pharmaceutical companies to disseminate unfavorable information uncovered during pediatric testing. In other words, the incentive does not directly align with the goal of generating information on those drugs most utilized by children and making that information available to their health care providers.

(c) The Best Pharmaceuticals for Children Act of 2002

The BPCA addressed some, though not all, of these issues. Generally, it added new mechanisms for further research and development of pediatric drugs and dissemination of information regarding the safety and efficacy of drugs used in the pediatric population. First, it required FDA and NIH to generate a prioritized list of drugs whose safety and effectiveness in pediatric populations should be assessed. This list includes drugs that are off-patent and without market exclusivity⁴⁷ in addition to new drugs.⁴⁸ If a sponsor of a drug on the list declines to conduct the additional studies, FDA can then request contract proposals from third parties, including universities, federally funded programs, and even individuals.⁴⁹

⁴⁶ U.S. GEN. ACCOUNTING OFFICE, PEDIATRIC DRUG RESEARCH: SUBSTANTIAL INCREASE IN STUDIES OF DRUGS FOR CHILDREN, BUT SOME CHALLENGES REMAIN (2001) (testimony of Janet Heinrich), at 10.

⁴⁷ The 1997 Act required FDA to develop a similar list, which the agency generated in 1998. But without the ability to enroll third parties to conduct studies drug sponsors, most off-patent drugs on this list were not studied. *Supra* note 2.

⁴⁸ I.e., those drugs approved through the application process described in section 505(j) of the Federal Food, Drug, and Cosmetic Act. 42 U.S.C. § 284m(a).

⁴⁹ 42 U.S.C. § 284m(b)-(c).

Second, the BPCA outlined a process for assuring the timely dissemination of information, both for drugs on the list described in the previous paragraph and other new drugs that “the Secretary determines...information relating to [its] use...in the pediatric population may produce health benefits in that population.”⁵⁰ Data generated pursuant to the Act must be submitted in the form of a report to NIH and FDA, and that report will be publicly available.⁵¹ The BPCA also dictated a timeline for negotiating labeling changes and resolving any related disputes, giving FDA’s authority here more of a bite. If manufacturers refuse to adopt the final set of recommended labeling changes for a particular drug, the FDA may deem that drug misbranded and commence enforcement actions accordingly.⁵²

Third, the BCPA gave a nod to the problem of little research in the neonatal population, by explicitly naming “neonates” as a pediatric age group.⁵³ However, this acknowledgement was of minimal impact, since neonatal research still had to come after research in older pediatric populations, and it was still the case that only one clinical investigation in pediatric populations was required to gain the additional exclusivity.

Fourth, the BCPA established several structural mechanisms for coordination between industry and government and to assist the implementation of the Act. It created a private, non-governmental Foundation of Pediatric Research at the NIH to enhance collaboration efforts among researchers in academia, industry, and non-profits. Among other tasks, the Foundation is to assist the funding of pediatric studies for drugs on the

⁵⁰ 21 U.S.C. § 355a(b).

⁵¹ 42 U.S.C. § 284m(c); 21 U.S.C. § 355a(j).

⁵² 42 U.S.C. § 284m(c); 21 U.S.C. § 355a(i).

⁵³ 21 U.S.C. § 355a.

FDA/NIH prioritized list.⁵⁴ It also set up two new government entities within the FDA, the Office of Pediatric Therapeutics and the Pediatric Advisory Committee. The Office of Pediatric Therapeutics is the pediatric hub within the Office of the Commissioner at the FDA. It is “responsible for coordination and facilitation of all activities of the Food and Drug Administration that may have any effect on a pediatric population or the practice of pediatrics or in an other way involve pediatric issues.”⁵⁵ Among other tasks, the Office for Pediatric Therapeutics houses the Pediatric Advisory Committee.⁵⁶ The Pediatric Advisory Committee advises FDA on pediatric research, priorities in pediatric therapeutics, and pediatric research ethics.⁵⁷ For example, the Pediatric Advisory Committee is called upon to help resolve any labeling change disputes between FDA and a manufacturer.⁵⁸ The Pediatric Advisory Committee also has authority to conduct post-marketing safety review of all therapeutics with pediatric exclusivity and make recommendations regarding labeling and additional areas for investigation.⁵⁹

Other specific provisions of BCPA, as well as how it relates to other legislation, can be found elsewhere.⁶⁰

(d) The Pediatric Research Equity Act

In 2003, Congress passed another law relating to pediatric therapeutics, the Pediatric Research Equity Act (“PREA”). While the BCPA mainly relied on incentives

⁵⁴ 42 U.S.C. § 290b.

⁵⁵ 21 U.S.C. § 393a.

⁵⁶ See FOOD & DRUG ADMIN., OFFICE OF PEDIATRIC THERAPEUTICS, <http://www.fda.gov/oc/opt/default.htm> (last visited, May 17, 2008).

⁵⁷ Pub. L. 107-109 § 14, 115 Stat. 1419 (2002).

⁵⁸ 42 U.S.C. § 284m(c); 21 U.S.C. § 355a(i).

⁵⁹ *Supra* note 2.

⁶⁰ Lauren H. Breslow, *The Best Pharmaceuticals for Children Act of 2002: The Rise of the Voluntary Incentive Structure and Congressional Refusal to Require Pediatric*, 40 HARV. J. ON LEGIS. 133-192 (2003).

and structural support to facilitate pediatric research, the PREA allowed FDA to require drug sponsors to conduct pediatric research in certain circumstances.⁶¹

i. PREA's historical background

Even before the 1997 Act, FDA was concerned with the nearly universal absence of pediatric information for drugs prescribed off-label to children. In 1994, FDA issued a rule requiring manufacturers to adjust their labels to explicitly address whether drugs had been tested for safety and effectiveness in children.⁶² FDA hoped this would induce manufacturers to voluntarily conduct the much needed research in pediatric populations. Instead, more than half of the drug labels that were changed simply added the sentence, “Safety and effectiveness in pediatric patients have not been established.”⁶³ Struck by the lack of response, FDA proposed a new rule requiring manufacturers to evaluate the safety and effectiveness of any new or currently marketed drug or biological product that is “likely to be used in a substantial number of pediatric patients [which FDA set at 50,000] or would provide a meaningful therapeutic benefit to pediatric patients over existing treatments.”⁶⁴ Believing the pediatric exclusion provisions of the 1997 Act insufficient, FDA continued the rulemaking process and issued a final rule, known as the “Pediatric Rule,” in December of 1998.⁶⁵

After passage of the BPCA in 2002, the Bush administration suspended the Pediatric Rule, letting the incentives of the new law stand alone. Democratic leadership

⁶¹ *Supra* note 2. Also unlike BCPA, PREA applies to both new drug applications (“NDAs”) and biologic license applications (“BLAs”).

⁶² Regulations Requiring Manufacturers to Assess the Safety and Effectiveness, 63 Fed. Reg. 66,631-66,672 (Dec. 2, 1998).

⁶³ *Id.*

⁶⁴ *Id.*

⁶⁵ *Id.*

attacked this move, arguing the importance of the Pediatric Rule in assuring safe pharmaceuticals for children, and the Administration subsequently reversed the suspension.⁶⁶ However, later that year, the United States District Court for the District of Columbia determined that the Pediatric Rule exceeded FDA's regulatory authority.⁶⁷ Again, supporters of the Pediatric Rule were outraged, this time asking Congress to step in.⁶⁸ In response, Congress enacted PREA, essentially codifying much of the Pediatric Rule.⁶⁹

ii. PREA's mechanics

Under PREA, all applications to the FDA for a new active ingredient, indication, dosage form, dosing regimen, or route of administration *must* include an assessment of “the safety and effectiveness of the drug or the biological product for the claimed indications in all relevant pediatric subpopulations.”⁷⁰ They must also include information that “support[s] dosing and administration for each pediatric subpopulation for which the drug or the biological product has been assessed to be safe and effective.”⁷¹

While PREA only applied to new applications, the provisions were retroactive, meaning

⁶⁶ See Breslow, *supra* note 60.

⁶⁷ Ass'n of Am. Physicians and Surgeons, Inc. v. Food & Drug Admin., 226 F.Supp.2d 204 (D.D.C., 2002).

⁶⁸ See Breslow, *supra* note 60, at 187, citing Laura Meckler, *U.S. Court Rejects Efforts to Test Drugs On Children: The Decision Means Companies Don't Have to Study Adult Medicines Often Given to Children*, PHIL. INQUIRER, Oct. 20, 2002, at A7. “The Director of Public Policy at the Elizabeth Glaser Pediatric AIDS foundation characterized the ruling as ‘a devastating setback to children’s health in this country,’ promising that ‘[t]here’s going to be a lot of additional enthusiasm and energy behind this [legislation] as a result of the ruling.’” *Id.*

⁶⁹ FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: HOW TO COMPLY WITH THE PEDIATRIC RESEARCH EQUITY ACT, Sept. 12, 2005, <http://www.fda.gov/cber/gdlns/pedreseq.htm>. For a broader discussion of PREA, see Sax, *supra* note 21, at 70-71.

⁷⁰ FOOD & DRUG ADMIN., *supra* note 69.

⁷¹ *Id.*

it covered any “new” application submitted starting in 1999.⁷²

(e) 2007 Reauthorization

The BCPA and PREA were up for reauthorization in 2007, as both were scheduled to sunset in that year. In the House and Senate committee hearings, the “carrot-and-stick”⁷³ approach the two created received repeated praise from industry, patient groups, and FDA – and clamoring calls for reauthorization. They argued that regulatory scheme created by BPCA and PREA has generated invaluable information about drugs in pediatric populations, though the lack of information about pediatric therapeutics remains staggering.⁷⁴ In September of 2007, both laws were reauthorized as Titles IV and V of the Food and Drug Administration Amendments Act of 2007.⁷⁵ The 2007 bill was passed by unanimous consent in the Senate and by an overwhelming 405 to 7 in the House.⁷⁶

2. *The Device Context*

(a) Safe Medical Devices Act

As with the general regulation of devices, legislation to induce the development of medical devices for the treatment and diagnosis of rare conditions lagged behind and generated different regulatory outcomes. In 1990, seven years after the Orphan Drug Act

⁷² *Id.*

⁷³ *E.g., Subcommittee on Health Hearing: Programs Affecting Safety and Innovation in Pediatric Therapies*, 107th Cong. (2007) (statement of Frank Pallone, Jr., Chairman, Subcommittee on Health, House Committee on Energy and Commerce).

⁷⁴ Elizabeth Glaser Pediatric AIDS Foundation, Public Comment on 2004N-0254 (Aug. 20, 2004), 1-7.

⁷⁵ Food and Drug Administration Amendments Act of 2007, Pub. Law No: 110-85 (2007).

⁷⁶ Open Congress, *Prescription Drug User Fee Amendments of 2007*, (Sept. 27, 2007), <http://www.opencongress.org/bill/110-h3580/show>.

of 1983, Congress passed the Safe Medical Devices Act. While the Orphan Drug Act's primary goal was to encourage the production of more "orphan drugs," the Safe Medical Devices Act's main purpose was to establish a series of post-marketing controls. Yet, it did authorize FDA to adopt special approval mechanisms for devices intended to help treat or diagnose very rare conditions, defined as "affect[ing] or...manifested in fewer than 4,000 individuals in the United States per year."⁷⁷

Still, it was not until 1996 that FDA promulgated regulations to effect these provisions.⁷⁸ Devices intended to for these small populations are called humanitarian use devices ("HUDs"), and the special approval mechanism authorized is a humanitarian device exception ("HDE"). Devices with an HDE were exempt from having to demonstrate effectiveness during the premarket approval process. To receive an HDE, a drug sponsor only had to show need, safety, and a favorable risk-benefit ratio: (1) that the device would not be otherwise available on the market and no comparable device exists, (2) that the device "will not expose patients to an unreasonable or significant risk of illness or injury" and (3) "the probable benefit" of using the device "outweighs the risk of injury or illness of its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment."⁷⁹

The HDE mechanism attempted to reduce the cost of bringing a device to market through eliminating the cost of meeting FDA's regulatory hurdle of showing effectiveness. However, to prevent manufacturers from abusing the new incentives, they

⁷⁷ FOOD & DRUG ADMIN., HUMANITARIAN DEVICE EXEMPTION (HDE): REGULATION QUESTIONS AND ANSWERS; FINAL GUIDANCE FOR INDUSTRY, July 18, 2006, <http://www.fda.gov/cdrh/ode/guidance/1381.html>.

⁷⁸ INSTITUTE OF MEDICINE (*hereinafter* "IOM"), SAFE MEDICAL DEVICES FOR CHILDREN 39-40 (2006). The current version of these regulations is 21 C.F.R. § 814 (2007).

⁷⁹ Federal Food Drug, & Cosmetic Act § 520(m), 21 U.S.C. § 360j(m) (2004).

were not allowed to make a profit off of their HUDs; they could recoup only “the costs of research and development, fabrication, and distribution of the device.”⁸⁰

According to a 2004 FDA report, the agency reviews approximately 5-10 HDEs annually.⁸¹ By October 2007, forty-four HDEs had been approved.⁸² Of note here, the very first device to receive an HDE was a fetal bladder stent, a life-saving pediatric device.⁸³

The differences between the ways Congress addressed the similar problem of small patient populations in drugs and devices here are striking. Orphan drug status can be granted to drugs for conditions with less than 200,000 patients, while an HDE can only be granted to a device for a condition with less than 4,000 patients. Sponsors of orphan drugs are not restricted as to their ability to make a profit, unlike sponsors of HUDs. Orphan drugs receive seven years of market exclusivity; HUDs receive no additional market exclusivity. Yet, orphan drugs are subject to the same safety and effectiveness standards as other drugs, while HUDs are exempt from showing effectiveness, a lower regulatory burden. While some of the differences may speak to the differences between the two kinds of medical products, others may speak more to differences in political landscape, statutory structure, historical regulatory norms, and legislative priorities.

(b) Medical Device User Fee and Modernization Act of 2002

⁸⁰ *Id.*

⁸¹ FOOD & DRUG ADMIN., REPORT TO CONGRESS: BARRIERS TO THE AVAILABILITY OF MEDICAL DEVICES INTENDED FOR THE TREATMENT OR DIAGNOSIS OF DISEASES AND CONDITIONS THAT AFFECT CHILDREN (Oct. 2004).

⁸² FOOD & DRUG ADMIN., HUMANITARIAN USE DEVICES, Nov. 24, 2003 [sic], <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/HDEInformation.cfm#2>.

⁸³ Cook Group Incorporated, Public Comment on 2004N-0254 (Aug. 13, 2004), 1-5, 2.

In 2002, Congress directly addressed pediatric medical device issues for the first time through the Medical Device User Fee and Modernization Act (“MDUFMA”). MDUFMA contained many important provisions relating to the regulation of medical devices generally, including, as its name suggests, the authority for FDA to collect user fees. MDUFMA’s provisions relating specifically to pediatric medical devices included the following. First, it declared that no user fees could be collected on applications for use in pediatric populations.⁸⁴ Second, it required pediatric expertise on premarket approval panels when appropriate.⁸⁵ Third, it gave FDA 270 days to issue guidance concerning “the type of information necessary to provide reasonable assurance of the safety and effectiveness of medical devices intended for use in pediatric populations;” and “protections for pediatric subjects in clinical investigations of the safety or effectiveness of such devices.”⁸⁶ Lastly, it required FDA to employ the Institute of Medicine to conduct a study evaluating the existing postmarket surveillance of medical devices used in pediatric populations.⁸⁷

(c) 2004 FDA Guidance

On July 24, 2003, FDA published a draft guidance document to comply with its Congressional mandate.⁸⁸ FDA solicited input from stakeholders through the public comment process.⁸⁹ On May 14, 2004, the agency issued non-binding recommendations,

⁸⁴ Medical Device User Fee and Modernization Act of 2002, Pub. L. 107-250 (2002), at § 738(a)(1)(A)(v).

⁸⁵ *Id.* at § 210.

⁸⁶ *Id.* at § 213.

⁸⁷ *Id.* at § 212.

⁸⁸ FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY AND FDA STAFF: PREMARKET ASSESSMENT OF PEDIATRIC MEDICAL DEVICES, May 14, 2004, at 1.

⁸⁹ It received three comments. One asked about assuring the agency aimed to determine least burdensome approach for achieving its goals. The remaining comments largely

which, at the time this paper was written, were still the pre-marketing guidelines for industry put forward on FDA's website.⁹⁰

In its guidance document, FDA defined four pediatric subpopulations to guide research and labeling of new devices: (1) newborn or neonate, from birth to one month old; (2) infant, older than one month to two years old; (3) child, older than two years to twelve years old; and (4) adolescent, older than twelve to twenty one years old.⁹¹ FDA also listed several factors for researchers to consider when developing devices and planning clinical trials in pediatric populations: "height, weight, growth and development, disease or condition, hormonal influences, anatomical and physiological differences from the adult population, activity and maturity level, [and] immune status."⁹²

FDA reaffirmed that its flexible approach to medical device oversight would continue to apply in the pediatric context, proposing that "the amount and type of evidence" required to demonstrate the safety and effectiveness of a pediatric device would depend on an array of device-specific features, including "the nature of the device, what is already known about the product in the adult population (if relevant), what is known or can be extrapolated about the device to the pediatric population, and the

centered on implications of the proposed upper age limit of children; the proposed guidance had extended that age to 21, while other legal standards set that age at 18. *Id.* at 3.

⁹⁰ Available at www.fda.gov/cdrh/MDUFMA/guidance/1220.pdf.

⁹¹ *Id.* at 4. FDA identified three other subpopulations: low birth weight (newborns less than 2.5Kg), very low birthweight (newborns less than 1.5Kg), and preadolescent (from 11 to 13 years). "Although these pediatric subpopulations are not included in [the main four], device labeling and clinical studies should address, as applicable, any issues that pertain to these or other pediatric subpopulations, such as low birth weight newborns."

Id. at 5.

⁹² *Id.* at 6.

underlying disease or condition being treated.”⁹³ In some cases, FDA might not require clinical trials at all. In others, adult population data might suffice, perhaps with limited supplemental safety data in pediatric populations. FDA also indicated that for some devices, data could be extrapolated from one pediatric age ground to another, while for others, FDA might require safety and effectiveness data in every targeted pediatric subgroup.⁹⁴ To assure appropriate study design, FDA recommended individual sponsors discuss their specific clinical trial plans with the FDA reviewing division.⁹⁵

FDA’s guidance addressed labeling specifically as well. In general, medical device labels must include a description of the device; indications, including the target populations; contraindications, warnings, and precautions; adverse events; summary of clinical trial data; and instructions for use.⁹⁶ For devices intended for use in pediatric populations, FDA recommended sponsors consider patient size (i.e., “weight, height, body mass, or surface area”), the implications of pediatric development and growth, variations in body habitus, unique pediatric pathophysiologies, and behavioral and psychosocial factors, among other factors.⁹⁷

Finally, FDA reiterated the ethical issues inherent in pediatric research and the special protections FDA regulations require.⁹⁸ Because children have been identified as a particularly vulnerable population for research, FDA reminded sponsors of the agency’s already existing regulations outlining the safeguards required for research in pediatric

⁹³ *Id.*

⁹⁴ *Id.* at 7-9.

⁹⁵ *Id.* at 8.

⁹⁶ FOOD & DRUG ADMIN., LABELING: REGULATORY REQUIREMENTS FOR MEDICAL DEVICES (1989), available at <http://www.fda.gov/cdrh/dsma/470.pdf>.

⁹⁷ *Id.* at 10-11.

⁹⁸ *Id.* at 15-20.

populations. Those regulations address issues of “informed consent, assent, permission, financial remuneration, direct benefit, and minimal risk.”⁹⁹

While many patient groups, researchers, and device manufactures commended FDA for drafting guidance on pediatric medical devices, the document was not universally lauded. For example, the American Academy of Orthopaedic Surgeons was “concerned about defining all patients greater than 12 years of age to 21 years of age as adolescents,” because doing so seemed to brush over clinically important biological transitions, such as skeletal maturity, which occurs for females at approximately 14 and males at approximately 16.¹⁰⁰

(d) Medical Devices Technical Corrections Act of 2004

While FDA was composing this guidance document, Congress enacted a second law with provisions addressing pediatric medical devices. The Medical Devices Technical Corrections Act was signed into law in April 2004, one month before FDA issued the May 14, 2004 draft guidance document described above. The explicit purpose of the Medical Devices Technical Corrections Act was to “make technical and clarifying corrections” to MDUFMA; at least in its Senate Bill form, the new Act left the “underlying substance” of MDUFMA “unchanged” and was estimated to cost nothing to taxpayers.¹⁰¹

Nevertheless, the new law did add a requirement that the Secretary of Health and Human Services to provide a report to Congress on why there are so few appropriate therapeutic and diagnostic devices for children and what could be done to solve the

⁹⁹ *Id.*; see 21 C.F.R. Part 50.

¹⁰⁰ American Academy of Orthopaedic Surgeons, Public Comment on 2004N-0254 (Aug. 20, 2004), 1-9, 3.

¹⁰¹ REPUBLICAN STUDY COMMITTEE, LEGISLATIVE BULLETIN, March 9, 2004.

problem.¹⁰² Congress gave the Secretary 180 days from the enactment of the law to do so.¹⁰³ By October 2004, FDA generated the Congressionally mandated report,¹⁰⁴ which will be discussed below.

PART III

Again, FDA solicited public comment on unmet medical device needs for pediatric populations, barriers to the development of such devices, and ways the FDA could better facilitate that development.¹⁰⁵ FDA also incorporated discussions from a June 28, 2004 meeting hosted by the American Academy of Pediatrics, the Elizabeth Glaser Pediatric AIDS Foundation, the National Organization for Rare Disorders, and the National Association of Children's Hospitals.¹⁰⁶ Here, I will go through those comments and discussions to demonstrate the breadth and depth of the current needs, barriers, and potential solutions, as articulated by stakeholders.

1. Unmet needs

The needs raised at the June stakeholder meeting fell into three categories: (1) pediatric indications for which no device is available, (2) pediatric indications for which an adult device is being used off-label, and (3) pediatric indications for which a device is available but does not meet the needs of a specific population.¹⁰⁷ These general

¹⁰² Medical Device User Fee and Modernization Act of 2002 (MDUFMA), 107th Cong. (2004), P.L. 107-250.

¹⁰³ *Id.*

¹⁰⁴ FOOD & DRUG ADMIN., *supra* note 81.

¹⁰⁵ This time, FDA received 25 comments. FOOD & DRUG ADMIN., Possible Barriers to the Availability of Medical Devices Intended to Treat or Diagnose Diseases and Conditions that Affect Children: Request for Comments, 69 Fed. Reg. 34374-75 (June 21, 2004).

¹⁰⁶ *Id.*

¹⁰⁷ *Id.*

categories were also reflected in the public comments FDA solicited from clinical groups, health care providers, academic researchers, and medical device manufacturers. As one clinician remarked, “most devices which are used in the pediatric/congenital cardiac population are used ‘off label’ as ‘hand-me-downs’ of devices approved for humans, but only for *adult* humans.”¹⁰⁸ Even when there are devices designed for children, those devices are few and out of date. Texas Children’s Hospital, the largest pediatric hospital in the United States, reported the lack of appropriately sized devices and the lack of choice among devices that are appropriately size.¹⁰⁹ The American Academy of Orthopedic Surgeons lamented “the lack of available innovative products...caus[ing] [pediatric orthopedic surgeons] to utilize devices that have been virtually unchanged for the past forty years.”¹¹⁰

Many commentators evidenced the above issues by describing the concrete needs of specific patient groups, from the practices of pediatric cardiology, pulmonology, nephrology, orthopedics, and general surgery.¹¹¹ The American Society for Pediatric Nephrology (“ASPN”) discussed the lack of sufficiently small catheters for pediatric patients with renal failure and volume tubing for children on dialysis; ASPN reported that the smallest catheters available were too large for some infants and the smallest volume tubing available required too large of a percentage of an infant’s blood to go through the dialysis circuit at any given time.¹¹² As another example, the American Thoracic Society highlighted the need for pediatric breathing algorithms for non-invasive positive pressure

¹⁰⁸ Mullins, *infra* note 117, at 2.

¹⁰⁹ Goldstein, *infra* note 129, at 2.

¹¹⁰ American Academy of Orthopaedic Surgeons, *supra* note 100, at 2.

¹¹¹ FOOD & DRUG ADMIN., *supra* note 96, at 9.

¹¹² American Society for Pediatric Nephrology, Public Comment on 2004N-0254 (Aug. 25, 2004).

ventilators; available machines were tailored to an adult inhalation/exhalation cycle, which has a different pacing than a child's.¹¹³ Many clinical groups specifically pointed out, again, the acute lack of devices for neonates and infants, as the smallest and most vulnerable groups within pediatric populations.¹¹⁴

2. Barriers to developing pediatric medical devices

Three types barriers were mentioned: (a) the lack of communication and coordination identifying pediatric device needs and potential solutions, (b) the technological challenges of creating devices for growing children, and (c) the limited profitability of pediatric medical devices.

(a) Lack of communication and coordination

First, researchers, device manufacturers, and clinician groups believed that device needs for pediatric patients were going unmet, in part, because of a lack of awareness and understanding of those needs. For example, the American Pediatric Society and the Society for Pediatric Research wrote, “the lack of availability of appropriately designed and studied pediatric devices appears to be based in part on a lack of understanding of need and importance of devices for children.”¹¹⁵ Both manufacturers and clinical groups saw a lack of communication among themselves, in particular, as a key barrier to addressing pediatric medical device needs.¹¹⁶ Without better coordination, the needs pediatric clinicians see at the bedside can go unnoticed by those who develop and make devices available in the market. In fact, AdvaMed, an industry group representing

¹¹³ American Thoracic Society, Public Comment on 2004N-0254 (Aug. 20, 2004), 1-4, 3.

¹¹⁴ *Id.*; *supra* note 103.

¹¹⁵ American Pediatric Society & Society for Pediatric Research (“APS/SPR”), Public Comment on 2004N-0254 (Aug. 20, 2004), *available at* http://www.aps-spr.org/Public_Policy/2004_Docs/CommentFDA20040820.htm.

¹¹⁶ E.g., AdvaMed, Public Comment on 2004N-0254 (Aug. 20, 2004), 1-14, 3.

manufacturers of medical devices, diagnostic products, and medical information systems, who together manufacture almost ninety percent of the health care products purchased in the United States, refused to respond directly to FDA's request for input on unmet needs. Instead, AdvaMed called upon pediatric specialty groups, those "involved in the treatment of pediatric populations," to identify, prioritize, and communicate to manufacturers the needs they see in their practices.¹¹⁷

At least one clinician believed that manufacturers are hesitant to communicate with pediatricians or facilitate communication among physicians, because of liability concerns. The off-label use of adult devices in children is not per se illegal, but off-label marketing is and can be followed by hefty sanctions. Thus, if a manufacturer discusses with clinicians the pediatric use of a device approved only in adults or a potential modification of a device approved only for use in adults, the manufacturer could fear being subject to an FDA enforcement action for illegally marketing a non-approved product. As a result, manufacturers shy away from open communication with physicians regarding off-label use, "much less supporting educational meetings and/or seriously discussing new products."¹¹⁸

(b) Technological challenges

Second, manufacturers raised the technological difficulties of developing pediatric medical devices, particularly in comparison to adult devices, as a barrier to pediatric device development. These include the limited applicability of devices intended for long-term use because of children's dynamic rate of change in size and shape of

¹¹⁷ *Id.*

¹¹⁸ Charles E. Mullins (Professor of Pediatrics, Baylor College of Medicine and Medical Director Emeritus, Cardiac Catheterization Laboratories, Texas Children's Hospital), Public Comment on 2004N-0254 (Aug. 18, 2004), 1-6, 3.

anatomy; constraints in choice of materials because of children’s susceptibility to certain physical and chemical agents and children’s metabolic and hormonal changes; and technical challenges in anticipating the “lifetime burden of exposure to agents.”¹¹⁹

(c) Limited profitability

Third, and by far the most common barrier mentioned in comments solicited by FDA, the limited profitability of pediatric medical devices because of the market size, was viewed, also most commonly, as the most serious challenge to their availability.¹²⁰ Again, pediatric populations are small, diverse, and dispersed, particularly in comparison to the adult market. Often, the costs of research and development, manufacturing, and distribution cannot be recouped, given the size of the patient base. In addition to the problems identifying needs and the technological challenges – each creating financial as well as practical barriers to pediatric device development – several other factors exacerbate the limited profitability problem, including: (i) regulatory requirements, (ii) perception of increased liability, (iii) relative impotence of patent protections, (iv) reimbursement difficulties, (v) the structure of the medical device industry, and (vi) lack of outside funding.

i. Regulatory requirements

Meeting regulatory requirements takes considerable time and money, particularly in the pediatric arena. The American Academy of Orthopaedic Surgeons complained generally about the “complex regulatory burdens on device and product development” and commented that manufacturers choose to conduct studies outside of the US to avoid

¹¹⁹ AdvaMed, *supra* note 116, at 5.

¹²⁰ E.g., mentioned by AAAAI, *infra* note 173; Kong, *infra* note 155; Bindon, *infra* note 138, at 2; Cook Group, *supra* note 83, at 2.

FDA's burdensome regulatory scheme.¹²¹ One researcher remarked that the "disproportionate" amount of time and money spent on the regulatory process stifles innovation.¹²²

1) Getting enough human subjects

Because the patient population for any given pediatric device is small and can be "scattered across the country,"¹²³ investigators have difficulty generating a large enough population of pediatric participants to satisfy FDA criteria to conduct a clinical trial.¹²⁴ In other words, "[the] small patient base means it is well nigh impossible to build up clinical trial numbers to compare to, say, coronary trials [in adults]."¹²⁵ The requirements for randomized controlled trials can be particularly difficult. The Spina Bifida Association of America observed that the call for a randomized controlled trial, by itself, could create enough of a disincentive to conduct medical device research in pediatric patients as to be prohibitive.¹²⁶ For example, the need for a placebo arm hinders already difficult recruitment, because very few parents are willing to risk their children receiving the control.¹²⁷

2) Time

A corollary to the difficulty recruiting patients is the length of time needed to enroll enough patients to conduct a trial on any single device. Completing large scale

¹²¹ American Academy of Orthopaedic Surgeons, *supra* note 100, at 3.

¹²² Michael Tynan (Emeritus Professor of Paediatric Cardiology, Kings College, London), Public Comment on 2004N-0254 (July 12, 2004), 1-3, 2.

¹²³ Cook Group, *supra* note 82, at 2.

¹²⁴ American Academy of Orthopaedic Surgeons, *supra* note 100.

¹²⁵ Tynan, *supra* note 121, at 2.

¹²⁶ Spina Bifida Association of America, Public Comment on 2004N-0254, (Aug. 18, 2004), 1-3, 2.

¹²⁷ AAAAI, *infra* note 173.

studies like those that are standard in the adult population was characterized as “impossible” to do “in a reasonable time frame.”¹²⁸ During the lengthy process, devices are “frequently” improved, making the device or the procedure easier and safer. However, those improvements cannot be incorporated into the ongoing trial; the improved device must be subjected to a new trial, at the threat of “severe penalties for the sponsor/manufacturer.”¹²⁹

3) Need for multi-center collaboration

If a device sponsor is willing to conduct the requisite trials, a multi-center collaboration is often necessary to find enough patients and do the trial in a reasonable amount of time.¹³⁰ This raises costs in multiple ways. First, coordination among centers is not free. Developing trusted relationships among hospitals takes time and resources. Second, contract negotiations among the various centers can be expensive.¹³¹ Even with multiple institutions on board, it can still take a long time to enroll sufficient patients, and the rigidity of the clinical trial model in the face of ongoing, iterative improvement of the investigational device is still a barrier.

4) Ethical issues with randomized controlled trials

Some commentators objected to using randomized controlled trials, which they perceive as FDA’s gold-standard, arguing that “no knowledgeable and/or moral person can require that a child...who happen [sic] to be ‘randomized’ to the ‘short straw,’ be

¹²⁸ Larry Latson (Chairman of Pediatric Cardiology and Medical Director of Center for Pediatric and Congenital Heart Diseases, Children’s Hospital at the Cleveland Clinic), Public Comment on 2004N-0254 (July 19, 2004), 1-3, 2.

¹²⁹ Mullins, *supra* note 117, at 5, providing four examples.

¹³⁰ *Id.* at 2; Stuart L. Goldstein (Associate Professor of Pediatrics, Baylor College of Medicine and Medical Director, Renal Dialysis, Texas Children’s Hospital), Public Comment on 2004N-0254 (Aug. 13, 2004), 1-2.

¹³¹ Goldstein, *supra* note 129.

subjected to the additional [mental and physical] trauma and risks of the [control].”¹³²

For example, obesity is increasingly prevalent in children, paralleling adults, yet the kind of surgery most successful in adults is not well tailored to children. The manufacturer of the device used in that surgery wrote that the best currently available surgery for children with obesity is so dangerous that conducting a randomized trial comparing a child’s version of the new device to the one in current use would be unethical.¹³³

5) Other available data FDA generally does not consider

Meanwhile, other data exist that FDA arguably could use instead of or as a supplement to new trials in the United States. Those include: (1) data from small independent studies,¹³⁴ (2) off-label data, and (3) data from overseas.¹³⁵ One can see why FDA would hesitate to accept these data; small independent studies and data from overseas may not be of sufficiently high standards, and accepting off-label data might encourage off-label marketing.

In addition, some researchers expressed concern over the “potential” for FDA to ignore its own guidance concerning the use of literature evidence and population evidence in lieu of prospective clinical studies.¹³⁶ Regardless of whether FDA would, in reality, ignore its own guidance here, the fact that major stakeholders believe the agency might suggest, at best, uncertainty about the regulatory requirements, which carries a

¹³² Mullins, *supra* note 117, at 2.

¹³³ “Randomizing LAP-BAND with gastric bypass would be unethical in an investigational study.” Inamed Corporation (“Inamed”), Public Comment on 2004-0254 (Aug. 20, 2004), at 8.

¹³⁴ AAAAI, *infra* note 173.

¹³⁵ Mullins, *supra* note 17, at 3.

¹³⁶ *Id.* at 9. This concern over predictability was raised by clinicians’ groups as well, e.g., American Academy of Orthopaedic Surgeons, *supra* note 100, at 8, which said that the unpredictability of regulatory requirements increases costs of development to the point where it “has aided in the financial demise of some manufacturers”

price tag for companies deciding whether to develop pediatric devices. At worst, it suggests a breakdown in communication and trust between FDA and the individuals it serves and regulates.

6) Institutional Review Board review

One professional association characterized Institutional Review Board (“IRB”) review of clinical studies for pediatric devices as “excessively stringent.”¹³⁷ More common was the concern that IRBs are uncertain about how they should consider pediatric devices that have an HDE, namely, whether they should treat HUDs as approved or investigational.¹³⁸

7) The approval process

The expertise and attitude of FDA officials were criticized, as were the speed and standards used for FDA approval. For example, one researcher wrote that “devices are currently often evaluated by people who have so little knowledge about the current state of the field that they are paralyzed from effective action.”¹³⁹ Another wrote that FDA adopts an adversarial and distrustful attitude towards industry, evidenced by threats of “extreme” fines and possibly “the destruction of a company” for “perceived ‘deviations.’”¹⁴⁰

One manufacturer wrote that while FDA approval takes the same amount of time for devices intended for use in children as for adults, the IDE process takes longer

¹³⁷ American Academy of Orthopaedic Surgeons, *supra* note 96, at 4.

¹³⁸ Latson, *supra* note 127, at 3; AdvaMed, *supra* note 116, at 8. FDA does have guidance on this topic. FOOD & DRUG ADMIN., HUMANITARIAN DEVICE EXEMPTION (HDE) REGULATION QUESTIONS AND ANSWERS; FINAL GUIDANCE FOR INDUSTRY, available at <http://www.browardhealth.org/workfiles/irb/HumanDeviceExemption.PDF>.

¹³⁹ Latson, *supra* note 127, at 3.

¹⁴⁰ Mullins, *supra* note 117, at 3.

because pediatric trials are more expensive to set up and take longer to complete, as discussed above.¹⁴¹ Other commentators thought FDA added to the length of time with “considerable regulatory foot-dragging,” which they perceived to evidence an “[apparent fear] to commit to full approvals.”¹⁴²

Many comments expressed that FDA holds a double standard for children and adults. Possibly because children are viewed as a more vulnerable population, FDA requests randomized controlled trials for devices intended for use in children when “no such trials may have been required for approval of the indication for adults.”¹⁴³

Comments expressed the belief that FDA overestimates the risk of pediatric medical devices and requires more documentation and evidence than it would for a parallel adult device.¹⁴⁴ As one manufacturer wrote, “FDA [can emphasize] possible risks, rather than known benefits, of technologies already applied to adults, and on restricting access rather than working with manufacturers to provide safe but earlier access.”¹⁴⁵

8) HDE program

Of far greater concern than IRB confusion over how to handle an HDE device were the requirements for receiving an HDE. The 4000 patient limitation and the limitation on profit were widely considered “significant disincentives to using the program.”¹⁴⁶ Only small volume devices fall into the humanitarian use classification, and

¹⁴¹ Adele Bindon (Regulatory Affairs Engineer, Fisher & Paykel Healthcare Ltd.), Public Comment on 2004N-0254 (no date), 1-4, 2.

¹⁴² Mullins, *supra* note 117, at 3, providing examples.

¹⁴³ Inamed, *supra* note 133, at 8.

¹⁴⁴ Bindon, *supra* note 138, at 2.

¹⁴⁵ Inamed, *supra* note 133, at 9.

¹⁴⁶ AdvaMed, *supra* note 116, at 8.

without any possibility for profit, manufacturers will not sponsor HUDs, as one professional society put it, “absent a corporate display of altruism.”¹⁴⁷

ii. Perception of increased liability

Device manufacturers hesitate to conduct research on pediatric populations for fear of liability from a bad outcome.¹⁴⁸ Manufacturers worry pediatric device litigation would be more emotional and lead to higher awards,¹⁴⁹ creating financial and reputational risk. One researcher reported that liability insurance can account for 30% of the cost of a medical device.¹⁵⁰ The heightened liability risk could extend to health care practitioners, institutions, and industry, chilling research.¹⁵¹

iii. Relative impotence of patent protections

Because of the nature of medical devices, patent protections are frequently successfully challenged or designed around by competitors. Device patents are usually not held for the device as a whole, but for a particular design attribute or material, making it easier for a manufacturer to copy a competitor’s device without infringing on that competitor’s patent.¹⁵² As an illustration, according to one manufacturer, several companies hold competing patents on pacemakers – all with the same intended use and population.¹⁵³ In addition, some devices are frequently improved upon and updated, rendering the original patent protection worthless.¹⁵⁴ For example, “new medical surgical

¹⁴⁷ Sandra Watkins (President of the American Society for Pediatric Nephrology), Public Comment on 2004-0254 (Aug. 25, 2004), 1.

¹⁴⁸ Goldstein, *supra* note 129.

¹⁴⁹ E.g., AdvaMed, *supra* note 116, at 7.

¹⁵⁰ Rosenbloom, *infra* note 157, at 2.

¹⁵¹ Inamed, *supra* note 133, at 10.

¹⁵² AdvaMed, *supra* note 116, at 4.

¹⁵³ *Id.*

¹⁵⁴ Inamed, *supra* note 133, at 10.

devices quickly become obsolete.”¹⁵⁵ As a result, the market exclusivity incentive that is so successful in drugs is ill suited to many devices.

iv. Reimbursement difficulties

The lack of insurance reimbursement was reported in several comments.¹⁵⁶ First, some pediatric patients, such as those with congenital heart problems, are systematically underinsured or non-insured.¹⁵⁷ Second, CPT codes do not exist for many procedures involving pediatric medical devices.¹⁵⁸ Third, medical device companies are smaller than drug companies in general, and thus do not have the resources or expertise to negotiate coverage, coding, and payment with every payer.¹⁵⁹ Thus, even when insurance will reimburse pediatric use of medical devices, reimbursement is not infrequently below cost, causing physicians and hospitals to take an income loss in order to provide them to their patients.¹⁶⁰

These issues are exacerbated by the fact that the confusion seen within IRBs in dealing with HDEs is also present among insurers. Insurers are uncertain whether HUDs should be considered approved, and covered, or as investigational, and not covered.¹⁶¹ In fact, some insurance companies refuse to pay for humanitarian use devices because FDA has not deemed them effective,¹⁶² threatening to defeat the purpose of the HDE

¹⁵⁵ Dorman, *supra* note 18, at 2.

¹⁵⁶ E.g., Patricia Tierney (school nurse), Public Comment on 2004N-0254 (Aug. 24, 2004).

¹⁵⁷ Mullins, *supra* note 117, at 5.

¹⁵⁸ Phillip Kong (Children’s Hospital Boston), Public Comment on 2004N-0254 (July 19, 2004), 1-3.

¹⁵⁹ AdvaMed, *supra* note 116, at 7.

¹⁶⁰ Arian Rosenbloom (University of Florida College of Medicine), Public Comment on 2004N-0254 (Aug. 25, 2004).

¹⁶¹ Latson, *supra* note 127, at 2,

¹⁶² AdvaMed, *supra* note 116, at 9.

regulatory scheme. One manufacturer summarized this by saying, “reimbursement systems have not kept pace with regulatory processes for HUDs.”¹⁶³

iv. Structure of the medical device industry

As mentioned above, medical device companies are generally smaller than drug companies; they are also generally younger and differently structured. Medical devices, compared to pharmaceuticals, have shorter life cycles and lower barriers to entry.¹⁶⁴ Most device companies are set up to produce one or several particular devices and are financed by venture capitalists. As a result, the risk they can take on is lower than drug companies; they do not have streams of profits from other products to off-set the heightened risk of developing, researching, and distributing pediatric devices. The “overly burdensome statutory or regulatory mandates can easily overwhelm both the financial and human resource capabilities of small device companies.”¹⁶⁵ Even the rare large device manufacturer, that has the capital to spend on a pediatric device and the stability to take the risks involved, most likely does not have the appropriate facilities to produce the small quantities needed for pediatric patients; its facilities are generally built to produce large quantities of a device.¹⁶⁶

v. Lack of outside funding

One solution to market failures is to provide other, non-market mechanisms for funding. However, there is little available funding for researchers to conduct device

¹⁶³ *Id.*

¹⁶⁴ Inamed, *supra* note 133, at 10.

¹⁶⁵ AdvaMed, *supra* note 116, at 4.

¹⁶⁶ *Id.* at 8.

research in pediatric populations outside the industry context,¹⁶⁷ at least little that most stakeholders seemed aware of.

3. *Recommendations*

The stakeholders' recommendations addressed the specific problems they saw by drawing upon the current regulatory scheme of devices, the existing regulatory mechanisms for pediatric drugs, as well as unique changes targeted at what they viewed as unique problems. Here, I divide those recommendations into recommendations on (a) facilitating coordination, (b) improving the regulatory process, (c) modifying clinical trial standards, (d) accepting other types of data, (e) creating new positive incentives for development, and (f) miscellaneous issues.

(a) Facilitating coordination

Many comments included recommendations to facilitate communication among the different players in the medical device field,¹⁶⁸ particularly between clinicians and industry.¹⁶⁹ Some suggested creating and providing continuing support for multi-center collaborative networks to ease clinical research, specifically pediatric recruitment.¹⁷⁰ Others recommended integrating medical devices into the agenda of the OPT and PAC.¹⁷¹ Another idea was for FDA to use the exemption of pediatric devices from user fees to generate a system to identify and track the use of devices in children, both on and

¹⁶⁷ Spina Bifida Association of America, *supra* note 125, at 2.

¹⁶⁸ AdvaMed, *supra* note 116, at 10.

¹⁶⁹ *Id.*

¹⁷⁰ Cook Group Inc., *supra* note 82, at 3. Texas Children's Hospital recommended using the ppCRRT registry as a model. Goldstein, *supra* note 129.

¹⁷¹ American Thoracic Society, *supra* note 112, APS/SPR *supra* note 114.

off-label.¹⁷² “Such a system could be used, for example, for FDA to identify devices that require only slight modifications or minimal additional testing to obtain a pediatric indication and to communicate the necessary data requirement to the manufacturer.”¹⁷³

(b) Improving the regulatory process

In thinking of ways to encourage testing on pediatric populations and subpopulations, recommendations looked toward PREA. Professional societies suggested establishing a presumption that all devices with indications in pediatric populations, regardless of whether they are manufactured for adults, should be designed for and tested in pediatric populations.¹⁷⁴ Like PREA, that presumption would be rebuttable, “tak[ing] into account feasibility, ethical and ethical concerns, and the public health interest in not delaying the development of devices for adults.”¹⁷⁵ To address the lack of incentives for device sponsors to conduct further research in pediatric populations once a device is approved, “have device manufacturers pay a portion of profits to fund studies on the use of these devices with other medications, or in other age groups.”¹⁷⁶

Comments also included recommendations for more subspecialty input in the regulatory process. For example, FDA could assure pediatric cardiac device applications are evaluated by pediatric cardiologists, with the idea that individuals of special expertise can “reasonably interpret...less clear and voluminous data.”¹⁷⁷ Because of their understanding of current practice, special experts may be better suited to

¹⁷² American Thoracic Society, *supra* note 112, at 4.

¹⁷³ *Id.*

¹⁷⁴ *Id.*, at 3-4.

¹⁷⁵ APS/SPR, *supra* note 114.

¹⁷⁶ American Academy of Allergy, Asthma, & Immunology, Public comment on 2004N-0254 (Aug. 19, 2004), 1-2, 2.

¹⁷⁷ Latson, *supra* note 127, at 3.

“define...criteria for device performance that would at least equal current practice,” potentially reducing the level and type of evidence necessary to gain approval.¹⁷⁸ One group even provided a list of organizations of pediatric cardiologists who could be willing to provide that expertise without conflicts of interest.¹⁷⁹

Third, further recommendations aimed at adding clarity and uniformity to the regulatory process. One suggestion was for FDA to fund an independent, centralized IRB to reduce the costs of conducting multicenter trials, both in the sheer administrative task of bringing a study before several IRBs and in the uncertainty and coordination problems when local IRBs vary their specific requirements.¹⁸⁰ Another was for FDA to increase predictability by providing more guidance on pediatric submissions, both in general¹⁸¹ and for individual companies trying to determine the likelihood of approval.¹⁸² FDA was asked to eliminate its perceived double standard between their approval processes for adult and pediatric devices.¹⁸³

Fourth, several public comments requested a decrease in the amount of time spent during the review process. Stakeholders expressed frustration with the additional year

¹⁷⁸ Latson, *supra* note 127, at 3.

¹⁷⁹ Those include: Congenital Heart Committee of the Society of Catheterizations and Interventions, the Pediatric Committee of the American College of Cardiology and the Cardiology Section of the American Academy of Pediatrics. This commenter argued that they would likely not have conflicts of interest, because pediatric congenital cardiologists involved in development of devices are salaried and in academic institutions. Mullins, *supra* note 117, at 5.

¹⁸⁰ Rosenbloom, *supra* note 157, at 2.

¹⁸¹ Bindon, *supra* note 138, at 3.

¹⁸² Latson, *supra* note 127, at 3.

¹⁸³ Bindon, *supra* note 138, at 3.

the premarket approval process can add.¹⁸⁴ For example, the American Academy of Orthopaedic Surgeons recommended FDA adopt international consensus standards to decrease the net amount of time a device has to spend in premarket review globally.¹⁸⁵ The device manufacturer Fisher & Paykel Healthcare, Ltd. recommended FDA cut down on premarket review time by allowing manufacturers to submit a *de novo* 510(k) without having to go through the NSE Class III determination first.¹⁸⁶ Fisher & Paykel also recommended FDA accept online applications for pediatric submissions and provide expedited 510(k) review for a fee.¹⁸⁷ In exchange for a more streamlined review process, FDA could mandate more rigorous and longer-term post-marketing activities.¹⁸⁸ Alternatively, or in addition, FDA could use labeling to add caveats to devices that went through an expedited review.¹⁸⁹

Fifth, AdvaMed recommended fast-tracking the coverage decisions by the Center for Medicare and Medicaid Services (“CMS”) in addition to expediting FDA review.¹⁹⁰ It also thought that FDA and CMS could provide an incentive similarly powerful to pediatric exclusivity in the drug context by expediting the FDA and CMS processes for

¹⁸⁴ Mark H. Hoyer (Director of Cardiac Catheterization and Interventional Cardiology at Riley Hospital for Children and Associate Professor of Clinical Pediatrics at Indiana University School of Medicine), Public Comment on 2004N-0254 (July 14, 2004), at 3.

¹⁸⁵ American Academy of Orthopaedic Surgeons, *supra* note 100, at 6.

¹⁸⁶ Bindon, *supra* note 138, at 3.

¹⁸⁷ *Id.* at 4.

¹⁸⁸ Latson, *supra* note 127, at 3.

¹⁸⁹ “When issues that affect risk can be addressed through labeling modifications (i.e., user qualifications, indications and contraindications, training, warnings) this method should be used. It will facilitate earlier access to important technology.” Inamed, *supra* note 133, at 11. One might wonder whether allowing manufacturers to “label away” the clinical questions that are expensive, time consuming, or both would provide manufacturers a disincentive to ever conduct the necessary trials to answer them. Perhaps such a liberal labeling policy could be balanced by readily requiring more post-marketing research.

¹⁹⁰ AdvaMed, *supra* note 116, at 10.

“the related adult indications of a pediatric device or for the adult indication of another device manufactured by the same company when there is no corresponding adult indication related to the pediatric device or if the adult device is already on the market.”¹⁹¹

(c) Modifying clinical trial standards

Several comments addressed ways to alter FDA’s clinical trial requirements, including relaxing the required enrollment numbers,¹⁹² developing new standards for efficacy,¹⁹³ and creating a mechanism for allowing improvements to investigational devices without requiring a new study.¹⁹⁴

Specifically, several comments recommended FDA take a more flexible approach to clinical trials for pediatric medical devices, tailored to the specific condition or subpopulation.¹⁹⁵ For example, American Academy of Allergy, Asthma, & Immunology recommended allowing studies in infants and young children to proceed without placebo arms.¹⁹⁶ AdvaMed recommended FDA using its discretion to waive informed consent for certain studies.¹⁹⁷ One pediatric cardiologist recommended adopting different process for promising new technologies for extremely rare heart defects.¹⁹⁸

It is interesting to note here the tension between the benefits of flexibility, tailoring premarketing approval to each specific device, condition, and affected population, and bright-line rules, which add simplicity, uniformity, and predictability. As

¹⁹¹ *Id.*

¹⁹² Hoyer, *supra* note 181.

¹⁹³ AAAAI, *supra* at 173, at 2.

¹⁹⁴ Mullins, *supra* note 117, at 6.

¹⁹⁵ E.g., Inamed, *supra* note 133, at 10-11.

¹⁹⁶ AAAAI, *supra* at 173, at 2.

¹⁹⁷ AdvaMed, *supra* note 116, at 13.

¹⁹⁸ Mullins, *supra* note 117, at 5-6.

previously mentioned, FDA’s approach to regulating medical devices is flexible, certainly more flexible than its approach to regulating drugs. Yet stakeholders’ comments indicate they believe FDA’s premarket approval scheme for pediatric devices both lacks sufficient simplicity, uniformity, and predictability, and lacks sufficient flexibility. Given the wide variety of recommendations on both, it is not surprising that regulatory solutions that best balance the two are not obvious.

(d) Accepting other types of data

One device manufacturer based in New Zealand requested FDA more readily accept trials from the European Union, Canada, Japan, and other developed countries with “recognized” regulatory controls for medical devices, and work with device sponsors to design their international trials according to FDA requirements.¹⁹⁹ Other device manufacturing groups recommended FDA utilize historical data, published data from off-label use, and clinical data from patient files²⁰⁰ when the patient population is prohibitively small, along with “appropriate safeguards to ensure against abuse by manufacturers.”²⁰¹

(e) Creating new positive incentives for development

i. Mimicking the Orphan Drug Act

A minority of comments wanted Congress to extend the regulatory scheme of the orphan drug act to pediatric medical devices.²⁰² However, the orphan drug incentives

¹⁹⁹ Bindon, *supra* note 138, at 3.

²⁰⁰ AdvaMed lamented that this data was not available to manufacturers because of informed consent concerns. AdvaMed, *supra* note 116, at 12.

²⁰¹ Cook Group, *supra* note 82, at 4.

²⁰² E.g., Goldstein, *supra* note 129, at 2.

work largely because of the effectiveness of the patent extension, a regulatory lever that would probably not work, at least not as uniformly well, in the device context.²⁰³

ii. HDE improvements

Many stakeholders gave recommendations for improving the HDE program. The most popular recommendation was to lift the profit restriction for HUDs intended for use in pediatric patients.²⁰⁴ AdvaMed recommended lifting the restriction on the required number of patients as well.²⁰⁵ Note, however, that this would mean that device manufacturers would never have to prove effectiveness for devices intended for use in children, at least not during the premarket process. Some organizations had more modest proposals, such as allowing manufacturers to collect profits on devices exceeding \$250,²⁰⁶ and increasing the threshold number of patients to some unspecified number.²⁰⁷

iii. Financial incentives to industry

Many comments argued that providing manufacturers with financial incentives to invest in researching, designing, and producing pediatric devices could be effective.²⁰⁸ The American Thoracic Society suggested Congress consider creating grants or providing guaranteed loans to small companies for the research and development of pediatric devices.²⁰⁹ It also recommended Congress provide financial support for developing prototypes and conducting clinical trials through a network.²¹⁰ Other comments

²⁰³ See *infra* text, at 36.

²⁰⁴ E.g., American Thoracic Society, *supra* note 112, at 4.

²⁰⁵ AdvaMed, *supra* note 116, at 12.

²⁰⁶ American Academy of Orthopaedic Surgeons, *supra* note 100, at 6.

²⁰⁷ Cook Group, *supra* note 83, at 3.

²⁰⁸ E.g., Hoyer, *supra* note 181.

²⁰⁹ American Thoracic Society, *supra* note 112, 4.

²¹⁰ *Id.*

recommended tax credits to manufacturers,²¹¹ an incentive used in the drug context, as discussed above. Some stakeholders here thought tax credits should be applicable to any research a manufacturer conducts associated with pediatric devices.²¹²

Several reinforced the importance of the exemption from user fees that sponsors submitting devices applications with pediatric indications currently enjoy.²¹³ One manufacturer recommended FDA reduce user fees for all medical device submissions, arguing that any added fees are resources that could be spent on pediatric innovation.²¹⁴

iv. Financial incentives to non-profit organizations

The representative from Boston Children’s Hospital recommended Congress provide product development funding to programs like Boston’s own Pediatric Product Development Institute (“PPDI”).²¹⁵ PPDI, and programs like it, ideally engage in risky early stage development, where a company may be less likely to get involved, and then partner with companies to take promising ideas to market.²¹⁶ One academic suggested providing funding for innovative investigators “with breakthrough ideas who may not have a “research track record.”²¹⁷ AdvaMed recommended increased funding from

²¹¹ American Academy of Orthopaedic Surgeons, *supra* note 100, at 8.

²¹² AdvaMed, *supra* note 116, at 14.

²¹³ Inamed, *supra* note 133, at 11; AdvaMed, *supra* note 116, at 14.

²¹⁴ Inamed, *supra* note 133, at 11. This approach could make sense if manufacturers could shift unpaid user fees to the development of pediatric medical device, but simply reducing user fees generally does not seem to provide a specific incentive to create more pediatric medical devices. Moreover, with less revenue flowing into FDA, the agency may be less able to quickly process pediatric device submissions, potentially reducing the availability of new devices for pediatric populations.

²¹⁵ Kong, *supra* note 155, at 1.

²¹⁶ *Id.*

²¹⁷ Rosenbloom, *supra* note 157.

relevant institutes of the NIH for the research and development of specific medical devices.²¹⁸

v. Identifying current sources of funding and suggesting others

One manufacturer believed it would be helpful for FDA to identify existing grant programs to help link pediatric device researchers who need funding with funding sources.²¹⁹ In doing so, FDA could suggest new programs to Congress if those it identifies are not sufficient.²²⁰

(e) Miscellaneous issues

Comments touched on several other issues, including off-label use, liability, and reimbursement.

i. Off-label use

Relating to the comments that off-label use was the rule rather than the exception, recommendations included remarks that allowing these devices to be used off-label is “essential.”²²¹ On a less extreme end, device manufacturers requested more guidance on the consequences of using or advertising a device off-label in the pediatric context.²²²

ii. liability

Most comments did not provide recommendations about liability concerns, and one even stated that improving the problems associated with liability concerns is “not

²¹⁸ Those institutes include the National Institute of Child Health and Human Development and the National Institute for Biomedical Imaging and Bioengineering, among others. AdvaMed, *supra* note 116, at 11.

²¹⁹ Cook, 4.

²²⁰ *Id.*

²²¹ Latson, *supra* note 127, at 2.

²²² Bindon, *supra* note 138, at 4.

feasible...[because you can't take] lawyers out of the equation."²²³ Nevertheless, one manufacturer did suggest using legislation to reduce the liability risk associated with pediatric medical devices.²²⁴

iii. Reimbursement

In the same vein as the recommendations that CMS speed its review of pediatric medical devices, comments recommended engaging insurance companies to more rapidly approve the reimbursement of pediatric devices.²²⁵

Manufacturers also cautioned against requiring pediatric labeling for devices because of the potential effect on reimbursement. Requiring pediatric labeling could render the pediatric use of devices on the market with general labeling off-label, and thus ineligible for reimbursement. This could both hurt patients directly, by reducing the affordability of those devices, and indirectly, in the form of lost revenues by manufacturers who then have less capital to invest in new research and development opportunities.²²⁶ In addition, Advamed warned that required labeling could put device manufacturers out of business because of the additional data or testing for pediatric indications that labeling for those indications would require. Again, fewer manufacturers could translate into fewer devices available for pediatric patients.²²⁷

PART IV

1. FDA's Report to Congress

²²³ Rosenbloom, *supra* note 157.

²²⁴ Inamed, *supra* note 133, at 11.

²²⁵ Latson, *supra* note 127, at 3.

²²⁶ Advamed, *supra* note 116, at 9.

²²⁷ *Id.*

In FDA's October 2004 report to Congress, which summarized the comments it received, FDA refused to make any concrete policy recommendations. "HHS conclude[d] that it is premature to recommend any substantive policy changes, including administrative and legislative changes."²²⁸ Notwithstanding the detailed comments FDA received by knowledgeable stakeholders, FDA determined that "the complexity of the issues and the wide range of perspectives" compelled them to call for "further study...to determine the scope of unmet needs, the potential barriers to bringing new pediatric devices to market, and the most promising solutions to addressing these unmet needs."²²⁹

2. *The Institute of Medicine's Report*

The Institute of Medicine ("IOM") generated a 457 page report on the adequacy of postmarketing surveillance of medical devices used in pediatric populations.²³⁰ Postmarketing surveillance includes activities to understand the safety and effectiveness of medical devices already on the market, through post-market testing or adverse event reporting, and the steps taken to respond to any safety concerns revealed.²³¹ The goal of

²²⁸ FOOD & DRUG ADMIN., *supra* note 80, at 20.

²²⁹ *Id.* at 18.

²³⁰ IOM, *supra* note 76. IOM's specific tasks were to examine: "(1) the U.S. Food and Drug Administration's monitoring and use of adverse reaction reports, registries, clinical studies, and other postmarket surveillance activities; (2) the adequacy of FDA's monitoring of commitments for further clinical studies made by manufacturers at the time of approval of specific devices; (3) the adequacy of postmarket surveillance studies to evaluate how children's active lifestyles may affect failure rates and longevity for implanted devices; and (4) the length of postmarket surveillance studies of implanted devices, including whether studies continue long enough to evaluate the impact of children's growth and development given the expected length of time that a child will have an implant. The committee was not asked to evaluate FDA's premarket review of medical devices or to assess barriers to the development of medical devices to meet children's special needs." *Id.* at 3.

²³¹ *Id.* at 85.

FDA's postmarketing surveillance efforts, according to IOM, should be to create an "objective, trustworthy, and effective" program that balances eliminating unsafe devices on the market with promoting innovation and stimulating product improvement.²³² While this paper has focused on premarketing regimes, the IOM report was influential in the subsequent Congressional action.²³³

At the time IOM issued its report, FDA had in place few postmarketing activities uniquely addressing at the pediatric use of medical devices.²³⁴ IOM noted several deficits in FDA's approach to postmarketing surveillance, both for devices in general and for pediatric population use in particular, and provided corresponding recommendations. IOM characterized FDA's monitoring of postmarketing studies and the lack of public access to their findings and methods as "the most obvious deficits in FDA's performance."²³⁵ IOM was also struck by the lack of FDA authority to hold premarket clearance conditional on a commitment to postmarket study, especially because clearance is a lower premarket bar. In addition, IOM noted that FDA was only authorized to require postmarket study for up to three years. In thinking about the pediatric population, this could be too soon for developmental consequences of a particular device used in children to manifest.²³⁶ Other observations of IOM included the "incomplete or inaccurate" adverse event reporting and the lack of a centralized point of responsibility within FDA to handle pediatric medical device issues.²³⁷

²³² *Id.* at 5.

²³³ See *infra* text, 54-55.

²³⁴ IOM, *supra* note 76, at 73.

²³⁵ *Id.* at 6.

²³⁶ *Id.* at 7.

²³⁷ *Id.* at 8-10.

IOM generated eighteen recommendations.²³⁸ Some recommendations were for FDA internally; some were directly for industry, professional, academic, or patient groups, or a combination of those; many were for collaboration and coordination among FDA, other government agencies, and industry, professional, academic, and patient groups; and some were for Congress. For example, IOM called upon FDA establish a centralized point of responsibility within the Center for Devices and Radiological Health²³⁹ to address pediatric issues. It also called upon “children’s hospitals and other user facilities” to establish similar centralized points of responsibility for monitoring and responding to device safety concerns. As another example, IOM recommended FDA promote the development and uptake of a common device coding system to help link data on use and outcomes.²⁴⁰ As a third example, IOM suggested FDA collaborate with NIH, the Agency for Healthcare Research and Quality (“AHRQ”), and “other research funding agencies and interested parties” to develop “a research agenda and priorities for the evaluation of the short-and long-term safety and effectiveness of medical devices used with growing and developing children.”²⁴¹

IOM made two recommendations specifically to Congress. First, it called upon Congress to mandate FDA create a system for monitoring and publicly reporting relevant information about postmarket studies.²⁴² Second, it recommended Congress allow FDA to require postmarket studies as a condition of clearance on certain categories of devices

²³⁸ *Id.* at 11-15.

²³⁹ The Center for Devices and Radiological Health is the center within the FDA that addresses device issues. *See* CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, <http://www.fda.gov/cdrh/index.html> (last visited May 16, 2008).

²⁴⁰ *Id.* at 14.

²⁴¹ *Id.* at 15.

²⁴² *Id.* at 13-14.

and allow FDA discretion to require postmarket studies beyond three years when appropriate.²⁴³

3. Medical Device Innovation Initiative

Meanwhile, in May 2006, before Congress acted on the above recommendations and reports, FDA announced the Medical Device Innovation Initiative. Recognizing the rapid advance of technology and the corresponding potential for “medical devices that will challenge existing paradigms and revolutionize the way treatments are administered,” FDA decided to launch an initiative to facilitate this innovation and update its review process for such devices. While this initiative was not focused on pediatric medical devices, FDA did mention devices for pediatric populations as the kinds of innovative devices the initiative would address.²⁴⁴

PART V

1. In the House and Senate

On March 8, 2007, Democratic Senator Chris Dodd from Connecticut introduced S. 380, the Pediatric Medical Device Safety and Improvement Act of 2007. This legislation set out to both improve incentives for the development of devices for children and provide FDA with greater authority to assure the safety of new devices once on the

²⁴³ *Id.* at 15.

²⁴⁴ FOOD & DRUG ADMIN., THE CENTER FOR DEVICES AND RADIOLOGICAL HEALTH’S MEDICAL DEVICE INNOVATION INITIATIVE, May 22, 2006, <http://www.fda.gov/cdrh/ocd/mdii.html>.

market.²⁴⁵ On March 13, Congressmen Edward Markey, a Democrat from Massachusetts, and Mike Rogers, a Republican from Michigan, introduced companion legislation in the House.²⁴⁶ Congressman Markey likened the need for pediatric medical devices to car seats: “Just as kids need car seats in the car while adults are fine with seat belts, kids need medical devices that are designed to work for them and keep them safe.”²⁴⁷

On March 27, 2007, Senator Dodd chaired a Health, Education, Labor and Pensions (HELP) Committee hearing entitled, “Ensuring Safe Medicines and Medical Devices for Children.” The hearing addressed the reauthorizations of BCPA and PREA in addition to the new Pediatric Medical Device and Improvement Act. As often happens when drug and device legislation are considered together, the drug provisions seemed to have taken the limelight. Of the five individuals testifying before the committee, only two mentioned the Pediatric Medical Device and Improvement Act. The House’s Energy and Commerce Subcommittee on Health held a similar hearing “on Programs Affecting Safety and Innovation in Pediatric Therapies.”²⁴⁸ The bills seemed, at least from the public statements of members of the House and Senate reviewed for this article, to have been well-supported. By September of 2007, the House version was incorporated into

²⁴⁵ *Senator Dodd Introduces Legislation to Help Develop Safer Medical Devices for Children*, Mar. 9, 2007, <http://dodd.senate.gov/index.php?q=node/3770/print>.

²⁴⁶ *Congressmen Markey and Rogers Introduce Bipartisan Legislation to Help Develop Safer Medical Devices for Children*, Mar. 13, 2007, http://markey.house.gov/index.php?option=com_content&task=view&id=2680&Itemid=141.

²⁴⁷ *Id.*

²⁴⁸ *Hearing on Programs Affecting Safety and Innovation in Pediatric Therapies: Health Subcommittee of the Committee on Energy and Commerce of the U.S. House of Representatives*, 110th Cong. (2007).

the Food and Drug Administration Amendments Act of 2007, along with BCPA and PREA.²⁴⁹ As previously stated, the legislation passed easily in both chambers.

2. *The Mechanics of the Act*

Informed by FDA's 2004 report, recommendations from the IOM, and its own hearings, Congress used the new act to create several modifications to the pre-existing regulatory scheme for pediatric medical devices. First, it required the Secretary of Health and Human Services to track and report new devices used in pediatric populations, mandating that certain device applications and protocols include the number of pediatric patients affected with "the disease or condition that the device is intended to treat, diagnose, or cure" and a description of the targeted pediatric subpopulations.²⁵⁰ Second, it expressly permitted FDA to accept adult data to "support a determination of a reasonable assurance of effectiveness in pediatric populations" and to extrapolate data from one pediatric subpopulation to another, when appropriate.²⁵¹ Second, it lifted the prohibition against making profits on HUDs when they are intended for use in pediatric populations and labeled for use in pediatric patients.²⁵² Third, it required FDA to issue guidance for IRBs on evaluating HDE applications.²⁵³ Recall that each of these was widely recommended by public stakeholders. Congress also provided that the Comptroller General assess the impact of lifting the ban on making profits off of HUDs

²⁴⁹ GovTrack.us, H.R. 3580: Food and Drug Administration Amendments Act of 2007, <http://www.govtrack.us/congress/bill.xpd?bill=h110-3580> (last visited May 16, 2008).

²⁵⁰ *Supra* note 73, at §515(a).

²⁵¹ *Supra* note 73, at §5159A(b).

²⁵² *Id.* at § 303(a). This incentive is not retroactive; HUDs on the market before the passage of this legislation are still prevented from making profits. *Id.*

²⁵³ *Supra* note 73 at §303(c).

intended for use in pediatric populations, and submit a report with that assessment to the House and Senate by January 1, 2012.²⁵⁴

Fourth, a twist on one of IOM's recommendation to FDA, Congress gave the Secretary of Health and Human Services, in consultation with FDA, NIH, and AHRQ, 180 days to present Congress "a plan for expanding pediatric medical device research and development," including improving FDA's clearance and approval processes for pediatric medical devices and evaluation of their short- and long-term safety and effectiveness.²⁵⁵

Fifth, in response to nearly universally articulated concerns over coordination and lack of outside funding, Congress authorized \$6 million per year for the next four years to go towards demonstration grants to nonprofit consortia to "facilitate the development, production, and distribution of pediatric medical devices."²⁵⁶ Those consortia are to coordinate with NIH and FDA, and each must provide an annual report to the Secretary of Health and Human Services.²⁵⁷ Sixth, Congress required FDA to "designate a contact point or office to help innovators and physicians" find funding sources for research on pediatric medical devices, mirroring one of the public comments. And, picking up on the recommendations of multiple stakeholders, Congress expressly included medical devices as part of the purview of the Office of Pediatric Therapeutics and the Pediatric Advisory Committee.²⁵⁸

Finally, Congress followed IOM's advice and gave FDA the authority to require postmarket surveillance as a condition of approval or clearance for certain devices and to

²⁵⁴ *Supra* note 73 at §303(b).

²⁵⁵ *Supra* note 73 at §304(b).

²⁵⁶ *Supra* note 73 at §305(c)-(d).

²⁵⁷ *Id.*

²⁵⁸ *Id.* at §306.

order postmarket surveillance for certain class II and class III devices, and to order, when “necessary,” over 36 months of postmarket surveillance for devices that are “expected to have significant use in pediatric populations.”²⁵⁹

3. *Congress’s Policy Choices*

Given all the viewpoints discussed in this paper, it does seem that the Congressional action picked up on most of the largest themes addressed by many individuals in many sectors. While I will not go through each observation and recommendation here to show which were incorporated and which were not, I will highlight certain policy choices embedded in the new law and discuss their potential impact.

First, Congress refrained from increasing the size of the patient population necessary for a device to qualify for an HDE. Many stakeholders, particularly in industry and research, recommended policy makers remove what they perceived as an “arbitrary” line.²⁶⁰ However, few, if any, stakeholders who recommended increasing the cap named a larger number that would be less arbitrary. As previously mentioned, some stakeholders wanted the limitation to be eliminated. Still, Congress could have set the number at the same number for orphan drugs, 200,000 patients. This number may be arbitrary as well, but there could have been an applicable rationale for its use in the drug context. Perhaps Congress believed eliminating the prohibition on profits would provide sufficient incentive without increasing the patient cap, or perhaps it wanted to see what lifting one restraint would do to the market before lifting another. It should be remembered that

²⁵⁹ *Id.* at §522(2)(a).

²⁶⁰ FOOD & DRUG ADMIN., *supra* note 80, at 10.

orphan drugs are not exempt from the effectiveness requirement, and so perhaps Congress felt more comfortable having a higher limit in that context, where children are not being exposed to devices whose effectiveness has not been shown. This illustrates a main tension of the HDE scheme, balancing the importance of making devices available against assuring those devices are effective.

Second, Congress decided to enhance non-market funding for devices solely through appropriating grants for non-profit consortia, and not through providing direct financial aid to industry, as some industry representatives would have liked. While it might not be surprising that Congress felt more comfortable funding non-profit organizations than for-profit ones, it may be surprising that Congress did not require those consortia to coordinate with industry, but only with FDA and NIH. Perhaps policy makers believed they were already “funding” industry through allowing them to make a profit off of HUDs. Because of the possibility for profit, industry should have the incentive to make itself informed of any promising devices or ideas for devices that the consortia may develop. However, given the common complaint that industry currently lacks mechanisms for linking with non-profit research and clinicians, and the fact that pediatric devices are not large profit-makers, it remains to be seen how well idea-exchange will flow between the non-profit consortia and device manufacturers. While Congress did require FDA to provide a point person to help “innovators” identify funding, this is not the same as creating a mechanism for those who practice medicine or conduct research to interact with those who can manufacture and produce those devices.

Similarly, the “plan for expanding pediatric medical device research and development,” mandates that the Secretary of Health and Human Services coordinate

with FDA, NIH, and AHRQ. While many stakeholders, and the IOM, recommended the development of such a plan, most explicitly recommended non-government stakeholders should be involved. For example, AdvaMed was adamant that clinicians should help define the priorities for pediatric medical devices, since they know what their patients most need. Even IOM recommended a slew of non-government actors that should be brought to the table. Here, not only was industry left out, but so were clinicians, patient advocates, academics, professional organizations, and other non-profit entities.

Perhaps Congress believed the Secretary would involve at least some of those stakeholders anyway and wanted to leave the particular groups to the Secretary's discretion. Perhaps Congress believed that the public comment process FDA facilitated in order to generate its congressional report and Congressional public hearings provided sufficient non-government input, or that the government employees at FDA, NIH, and AHRQ include sufficient representation from at least some of those stakeholder groups. Perhaps because of the short time-frame on delivering the plan, Congress did not want to overburden the secretary by forcing the involvement of more viewpoints. Yet, Congress could have simply extended the time-frame.²⁶¹

Fourth, the Congressional authorization to require a commitment to postmarketing study as a condition of approval or clearance is similar to what was recommended by some industry players. Yet, it was explicitly argued against by the Medical Device Manufacturers Association when the bill was being considered by the Senate:

²⁶¹ Perhaps the law's authors wanted to see results quickly and move forward on solving the problem, thinking that even if the plan is not the very best, FDA, NIH, and AHRQ together are sufficiently informed and capable to produce a plan that is very good. Or, perhaps there were more self-interested political motivations for moving quickly, such as the upcoming 2008 elections.

“By permitting FDA to “condition” approval or clearance on postmarket surveillance, FDA could prevent a manufacturer from marketing a device, for its approved or cleared indications, until the manufacturer agreed to conduct potentially burdensome and expensive studies on unapproved pediatric uses of the device. As a result, the [provision] may deter manufacturers from developing medical devices that may have a potentially significant pediatric use. A manufacturer may decide during the initial approval or clearance process, to contraindicate its device for use in pediatric populations to avoid being subject to burdensome and costly postmarket surveillance.”²⁶²

Hopefully, FDA will not use its new authority to require “burdensome and expensive studies;” indeed, as mentioned above, FDA is only authorized to require those studies when “necessary.” Yet one can assume that this new requirement would create a disincentive to produce pediatric devices, first because of the added expense of the required trials and second because of the potential uncertainty over whether a given device’s approval or clearance will be subject to such a commitment. The size of the disincentive is unclear; it could be negligible. Nonetheless, the project of device, and drug, regulation, particularly for small markets, is to balance assuring a device or drug is safe and effective with providing sufficient profit incentive to developing helpful, and potentially life-saving, devices and drugs. Where to fall on that balance is a difficult policy choice, and, as seen throughout this paper, setting the incentives accordingly can be even more challenging. MDMA here argues that some devices will not be produced with this extra regulatory burden, and it may be right. Yet, it is also true that FDA, and the public, could have a greatly increased understanding of which devices on the market are helpful, which ones are dangerous, which require monitoring, and which need further study.

²⁶² *Hearing on the Reauthorization of the Medical Device User Fee and Modernization Act Before the House Energy and Commerce Subcommittee on Health (2007)* (testimony of Kelvyn Cullimore, on behalf of the Medical Device Manufacturers Association).

Lastly, the particular tracking mechanism Congress chose is interesting. It is simple to implement, but is likely not as robust as what IOM had in mind for postmarketing surveillance. This tracking mechanism could help FDA and Congress see what kinds of new devices are becoming available for children over time, and it may help identify which conditions and which subpopulations, if any, are receiving more or less attention by manufacturers. Importantly, it could also help gauge the impact of future Congressional or regulatory action. For example, if Congress did choose to increase the size of the patient population for which an HDE can be granted, any subsequent increase in the volume of pediatric devices going to market could be observed. However, the tracking mechanism cannot, by itself, identify areas where there is underdevelopment or overdevelopment of devices. In other words, it cannot provide a normative baseline to compare the numbers it generates; it cannot tell Congress where the numbers should be. Moreover, because the tracking mechanism is being put in place along with the other potentially market-altering initiatives Congress passed in this act, it cannot directly track their impact. For example, the impact of the \$6 million appropriation for research cannot be measured using this mechanism, because corresponding numbers from before the appropriation was granted are not available.

Nevertheless, given the relatively low implementation cost of the tracking system, the amount of information it can provide, even just for measuring the impact of future initiatives, is likely worthwhile.

4. Regulatory Actions So Far

On October 10, 2007, FDA established an internal committee to deal with pediatric

medical device issues, the Pediatric Review Committee (“PeRC”).²⁶³ FDA was scheduled to issue guidance for IRBs on the evaluation of HUD applications, as Congress mandated, on March 3, 2008.²⁶⁴ However, there appears to be no evidence this was done, at least from the guidance available on the FDA website.²⁶⁵ As far as the research plan Congress mandated, the Secretary placed NIH at the lead, so FDA is currently “supporting” NIH in that endeavor.²⁶⁶ From FDA’s public information, it seems this plan is also yet to be completed.²⁶⁷

5. *A Final Comparison to Drugs*

Because of historical differences in regulation and because of differences in the kinds of things devices and drugs are and the characteristics of the industries that produce devices and drugs, the regulatory schemes for encouraging the development of drugs and devices for pediatric populations are also different. Both require post-market surveillance and both are now linked under the same coordinating office at the FDA. While the drug regulations rely primarily on market exclusivity, the device regulations provide incentives through reducing premarket regulatory hurdles. Both use federal funding to support research, at least among non-profit researchers, though drug regulation provides

²⁶³ U.S. FOOD & DRUG ADMIN., IMPLEMENTATION OF THE FOOD & DRUG ADMINISTRATION AMENDMENTS ACT OF 2007, (last visited May 16, 2008), http://www.fda.gov/oc/initiatives/advance/fdaaa/implementation_chart.html.

²⁶⁴ *Id.*

²⁶⁵ The guidance on FDA’s website, which is usually up to date, is from 2004. The pediatric medical devices website was last updated February 23, 2006 (*see* timestamp on <http://www.fda.gov/cdrh/pediatricdevices/index.html>), so either little has been done since 2006 or the particular set of webpages dealing with pediatric medical devices has not been updated.

²⁶⁶ FOOD & DRUG ADMIN., *supra* note 218.

²⁶⁷ *Id.*

more financial incentives to industry.

Here, my project is not to show whether drug regulation is better or more appropriate than device regulation, or the other way around. Instead, I hope to show how a similar problem of pediatric innovation has been addressed in two different ways, how the two schemes have evolved over time, and how the different regulatory tools and incentives chosen affect the other kinds of tools and incentives required to achieve the policy goal. Similarly, through the description of the public comments in the device context, I hoped to demonstrate that different stakeholders who agree on the goal – here, of increasing availability of pediatric devices – can have differing, but more often similar, views on how to achieve a policy end. In addition, through an in depth discussion of the stakeholder views and the subsequent legislation, I aimed to provide a sense of the breadth and complexity of the issues and an illustration of how Congress addressed that complexity through generating a set of new provisions.

It remains to be seen how the Pediatric Medical Device Safety and Improvement Act will work towards achieving its goals. The problem of pediatric markets is a difficult one, raising interesting questions of which legislative and regulatory levers best achieve the policy goals, given the realities of the industries, health care system, and patient populations in need.