THE BEST PHARMACEUTICALS FOR CHILDREN
ACT AND THE PEDIATRIC RESEARCH EQUITY
ACT—HELPING OR HURTING
AMERICA'S CHILDREN?

Lisa Jerles*

INTRODUCTION

In 2000, an eleven-year-old child came into Lucile Packard Children’s Hospital at Stanford, located in Palo Alto, California.¹ The girl had inflammatory bowel disease² but was admitted because she was experiencing severe backaches and difficulty sleeping. The doctors found that the steroids she had been taking to alleviate the stomach pain had weakened her bones, causing two vertebrae to collapse. Her doctor determined that she needed a drug to improve her bone density but at the time, there was no drug that had been approved in pediatric patients. This doctor was forced to prescribe a medication only approved for use in adults and adjust the medication to a dose that seemed appropriate for an eleven-year-old girl. Fortunately, there were no adverse side effects and the girl responded well to the treatment. However, this situation is an example of a larger problem—a dearth of prescription drugs, devices and other therapies approved for use in children.

In response to problems like this one and in an effort to improve the quality and quantity of pharmaceuticals available to children, the federal government took steps to improve the effectiveness, safety and availability of drugs for children by compelling drug companies to test their products on children. The 2002 Best Pharmaceuticals for Chil-

* J.D., 2008, Benjamin N. Cardozo School of Law; B.A. 2001 Barnard College. Lisa would like to thank the Children’s Brain Tumor Foundation for providing her with the inspiration to explore this topic. She also wishes to thank her husband Todd, her parents and brother, Jesse, for their endless love, support and guidance, not only with this Note, but with all of her undertakings.

¹ This story was adapted from Krista Conger, What Would Goldilocks Do?, STAN. MED. MAG. (Summer 2005), available at http://mednews.stanford.edu/stanmed/2005summer/kids-drugs.html.

dren Act\(^3\) and the Pediatric Research Equity Act of 2003\(^4\) were passed with these intentions.\(^5\) However, the laws were riddled with problems—namely an expiration date in late 2007. With such a short period of enactment, it was unclear whether the statutes could have a meaningful effect on the need for drugs approved for pediatric use. However, on September 27, 2007, President Bush signed the Food and Drug Administration Amendments Act of 2007 which, among other things, reauthorized both acts for five more years.\(^6\) In addition, the Act created the Pediatric Medical Device Safety and Improvement Act\(^7\) which, for the first time, provides incentives to device manufacturers to create products that specifically meet the needs of pediatric patients.

This Note will first examine the two federal statutes that mandate pediatric testing, their history and how they have affected the availability, safety and efficacy of pharmaceuticals in treating children. Next, this Note will look at the challenges to pediatric testing that make pediatric testing undesirable for pharmaceutical companies. This Note will also explore the shortcomings of the initial legislative measures and discuss whether the new legislation, including the addition of the Pediatric Medical Device Safety and Improvement Act, succeeds in remedying these problems.

I. Best Pharmaceuticals for Children Act

The Best Pharmaceuticals for Children Act of 2002 ("BPCA 2002") was passed to address the concern that, in 2001, only twenty percent of prescription medications were tested and approved for use in children.\(^8\) This concern stemmed from the fact that dosing children with medication tested on adults and then adjusted for children solely according to their lower body weight is problematic. For example, children's bodies metabolize certain medications differently than adults and

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\(^5\) See BPCA 2002, supra note 3 (the purpose of BPCA was to "to improve the safety and efficacy of pharmaceuticals for children"); PREA 2003, supra note 4 (the purpose of PREA was to "require certain research into drugs used in pediatric patients").  
\(^7\) Id.  
some drugs may have different adverse side effects in children than in adults. In addition, the lack of age-appropriate formulations, such as liquid forms for children who cannot yet swallow drugs in pill form, make it difficult to administer medication to children. Because most drugs are not specifically designated for children, doctors often prescribe drugs to children "off label" without formally testing them on younger patients. In response to this practice, both the Senate and the House of Representatives proposed legislation to encourage pharmaceutical companies to test existing drugs on pediatric audiences.

BPCA 2002 was passed after the Food and Drug Administration Modernization Act ("FDAMA") expired at the end of 2001. FDAMA provided for pediatric exclusivity—six months of marketing exclusivity for pharmaceutical companies who respond to the Food and Drug Administration's ("FDA") requests to conduct pediatric studies. In addition, FDAMA authorized the FDA to develop a list of already approved drugs for which additional information concerning use in children would be useful—this list is known as the Pediatric List. The FDA found that this pediatric exclusivity provision had "done more to generate clinical studies and useful prescribing information for the pediatric population than any other regulatory or legislative process to date," so upon its expiration, Congress enacted the BPCA 2002.

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9 Id. The drug Cyclosporine was approved for adults to counter organ rejection following transplants. The drug was then used in children without testing and without the same success. Researchers eventually discovered that children metabolize Cyclosporine much faster than adults, therefore needing more frequent dosing. See Inst. of Med. of the Nat'l Acad., Ethical Conduct of Clinical Research Involving Children 27 (2004) [hereinafter Ethical Conduct of Clinical Research].

10 Ethical Conduct of Clinical Research, supra note 9, at 67. See also BPCA, Background of the Act, http://bpca.nichd.nih.gov/about/background/index.cfm (last visited October 31, 2006), for a list of problems and difficulties that have discouraged the testing of drugs in pediatric populations.


12 For more information about the dangers of off-label prescriptions, see infra Part III.


BPCA 2002 made several changes to the FDAMA, most significantly, eliminating the Pediatric List.\textsuperscript{18} According to the FDA, the Pediatric List was eliminated because it was resource intensive, and diverted resources from other needed work on pediatric drugs. The list also did little to prioritize effectively which drugs should be studied in children. Finally, the priority list created the mistaken impression on the part of some drug manufacturers that only those drugs on the list could qualify for the pediatric incentive.\textsuperscript{19}

Instead, the FDA first researches existing drugs to determine if “information relating to the use of a new drug in the pediatric population may produce health benefits in that population.”\textsuperscript{20} If the FDA finds a drug suitable, the patent holder receives a written request to conduct a pediatric study.\textsuperscript{21} If the holder agrees to perform the pediatric study within a specified time frame, the holder is awarded an additional six months of market exclusivity.\textsuperscript{22} The intention of the statute is to incentivize these patent holders to complete the pediatric studies.\textsuperscript{23}

If the patent holder does not wish to conduct the study, the FDA refers the study to the Foundation for the National Institute of Health (“FNIH”) for funding.\textsuperscript{24} The National Institute of Health division with the appropriate expertise will work with the National Institute for Child Health and Human Development to develop a request for proposal.\textsuperscript{25} These proposal requests solicit entities with expertise in conducting pediatric clinical trials, such as universities and hospitals, to make a bid to undertake the trials that the manufacturer does not wish to conduct.\textsuperscript{26} Funding for these studies comes from the FNIH and industry or private individuals who donate to the FNIH.\textsuperscript{27} According to the most recent

\begin{itemize}
  \item \textsuperscript{20} 21 U.S.C. 355a.
  \item \textsuperscript{22} Id.
  \item \textsuperscript{23} S. Rep. No. 107-79.
  \item \textsuperscript{26} Id.
  \item \textsuperscript{27} The Act in Action, supra note 24.
\end{itemize}
figures, FNIH has allocated approximately $3.5 billion for these types of studies.28

In addition, BPCA 2002 created a similar system for drugs that are no longer under patent.29 Under BPCA 2002, the Secretary of the Department of Health and Human Services ("the Secretary") works with the National Institute of Health ("NIH") to create a list of these drugs, considering "(A) the availability of information concerning the safe and effective use of the drug in the pediatric population; (B) whether additional information is needed; (C) whether new pediatric studies concerning the drug may produce health benefits in the pediatric population; and (D) whether reformulation of the drug is necessary."30 The Secretary then awards contracts to qualified institutions such as universities, hospitals and laboratories to conduct pediatric studies concerning one or more of the drugs identified on the list.31

The Food and Drug Administration Amendments Act of 2007 ("FDAAA"), enacted the Best Pharmaceuticals for Children Act of 2007 ("BPCA 2007")32 which reenacted the original act for an additional five years with a few minor changes. Most significantly, BPCA 2007 does not allow pharmaceutical companies to make last minute applications to the FDA in order to keep exclusivity.33 Under BPCA 2002, pharmaceutical companies could submit pediatric test results right before patent expiration.34 While the FDA reviewed the results, the companies were granted a grace period of exclusivity.35 If the pediatric test results were accepted, a company then received an additional six months of exclusivity per the statute.36 Thus, even if the results were rejected, a company could still squeeze out a few extra months of exclusivity while the FDA reviewed the results of pediatric studies. The new rule eliminates this grace period and also lengthens the amount of time the FDA has to review pediatric test results from ninety days to 180 days.37 In this way,

28 Id.
29 The FDA found that six out of ten drugs most often prescribed for children were off-patent. S. Rep. No. 107-79, at 2 (2001).
31 Id. § 284m(b).
33 Id.
34 BPCA 2002, supra note 3.
35 Id.
36 Id.
37 BPCA 2007, supra note 32.
BPCA 2007 tightens the FDA's control over pharmaceutical companies circumventing the system in order to gain a few more months of exclusivity so they can generate profits that would otherwise be lost if the patent were to expire.

II. PEDIATRIC RESEARCH EQUITY ACT OF 2003

BPCA 2002 sought to increase the amount of research performed on drugs administered to children. By extending market exclusivity, Congress hoped to incentivize drug merchants to test products on pediatric patients. In addition, the federal government funds testing on drugs for which extended market exclusivity is not applicable. The federal government's initial involvement in this arena proved successful; however, Congress still felt that the FDA needed authority to mandate pediatric testing because voluntary testing provided for under BPCA 2002 was not sufficient. Thus, Congress passed the Pediatric Research Equity Act of 2003 (“PREA 2003”).

On December 2, 1998, the FDA published a regulation known as the “Pediatric Rule,” asserting its authority to compel drug companies to engage in pediatric testing. However, the American Association of Physicians and Surgeons, the Competitive Enterprise Institute, and Consumer Alert challenged the Pediatric Rule in federal court. The plaintiffs claimed that the Pediatric Rule exceeded the FDA's statutory authority and that the Rule's promulgation was “arbitrary and capricious.” On October 17, 2002, a U.S. District Court invalidated the Pediatric Rule, holding that the FDA lacked statutory authority to promulgate the regulation. The FDA pointed out that “drug manufacturers, who are those most affected by the Pediatric Rule, are not complaining about the requirements.” However, the court rejected that argument, pointing out that:

38 BPCA 2002, supra note 3.
39 Id.
40 Id.
42 Id.
43 PREA 2003, supra note 4.
46 Id. at 205.
47 Id. at 222.
In so arguing, the FDA misses the point. This court does not pass judgment on the merits of the FDA’s regulatory scheme. The Pediatric Rule may well be a better policy tool than the one enacted by Congress; it might reflect the most thoughtful, reasoned, balanced solution to a vexing public health problem. The issue here is not the Rule’s wisdom. Indeed, if that were the issue, this court would be a poor arbiter indeed. The issue is the Rule’s statutory authority, and it is this that the court finds lacking.

In response, Congress enacted PREA 2003, concluding that it was necessary to grant this authority to the FDA because of “the particular importance of pediatric drug labeling.”

PREA gave the FDA the authority to mandate pediatric testing retroactive to April 1, 1999. In addition, the Act mandated pediatric testing in all drugs and biological products not yet approved by the FDA. However, the FDA is required to give a full or partial waiver of the pediatric testing requirement in certain cases: where the FDA finds pediatric studies are impossible or highly impractical; where there is evidence strongly suggesting that the product would be ineffective or unsafe in certain or all pediatric age groups; where the product will not offer a meaningful therapeutic benefit over existing treatments for pediatric patients; where the product is not likely to be used by a substantial number of pediatric patients; or where the absence of ade-

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49 Id.
50 S. REP. NO. 108-84.

This legislation responds to the court’s holding by providing FDA new statutory authority to require pediatric assessments. The authority granted by the legislation tracks many elements of the former Pediatric Rule to ensure that the progress produced by the incentive and the Pediatric Rule will continue. There is a compelling basis for providing FDA such authority because of the importance of ongoing pediatric research. At the same time, the legislation establishes clear limitations on the new authority to require pediatric assessments to ensure that the unique needs of the pediatric population continue to be met by the co-existence of the incentive and the mandate.

Id. 51
51 PREA 2003, supra note 4.
52 Id.

53 A full waiver means that the patent holder does not need to provide any pediatric data. A partial waiver only applies to a particular pediatric age group or age groups. S. REP. NO. 108-84 (2003). A full waiver will only be granted for select cases. For example, a waiver will be granted if a drug treats a condition like prostate or breast cancer that does not occur in children. See Conger, supra note 1.

54 For example, if the number of such pediatric patients is so small or geographically dispersed, the FDA might grant a waiver. S. REP. NO. 108-84.
quate labeling specifically for pediatric populations would not pose significant risks to pediatric patients.\textsuperscript{55}

For drugs and biological products already approved and in the marketplace, under PREA 2003, the FDA could only mandate pediatric testing after asking the manufacturer to conduct research voluntarily.\textsuperscript{56} If the manufacturer agreed, the drug received six months of market exclusivity pursuant to BPCA 2002; if the manufacturer refused, the FDA referred the product to the FNIH for funding in the process outlined in greater detail above.\textsuperscript{57}

FAAA enacted the Pediatric Research Equity Act of 2007 ("PREA 2007"), which reenacted PREA 2003 for an additional five years with some modifications.\textsuperscript{58} PREA 2007 requires a pharmaceutical company to produce more documentation in order to receive a waiver for pediatric testing.\textsuperscript{59} The new law also removes the provision outlined above that allowed the FDA to mandate pediatric testing only after asking the manufacturer to conduct the testing voluntarily.\textsuperscript{60} This new power gives the FDA broader authority to mandate pediatric testing. PREA 2007 also requires the FDA to conduct two outside studies with the Institute of Medicine and the Government Accountability Office to assess the effectiveness of the law in the coming years.\textsuperscript{61} These changes strengthen the FDA's role in mandatory pediatric testing of pharmaceuticals and other therapeutics.

III. CHALLENGES OF PEDIATRIC TESTING

Several challenges to pharmaceutical testing are exclusive to children. One important factor is the length of time that it takes to complete a clinical trial. Since children are constantly growing, the effects of a particular treatment are not always immediate and often require extensive follow-up.\textsuperscript{62} Long-term studies are often extremely expensive, lead-

\textsuperscript{56} Id.
\textsuperscript{57} See supra Part I.
\textsuperscript{59} Id.
\textsuperscript{60} Id.
\textsuperscript{61} Id.
\textsuperscript{62} See ETHICAL CONDUCT OF CLINICAL RESEARCH, supra note 9, at 82 (Cranial radiation was often used to prevent the spread of leukemia to a child's central nervous system. However, latent effects were eventually discovered "including impaired intellectual function, profound neuroendocrine abnormalities, and second central nervous system malignancies, ultimately re-
ing sponsors to resist funding the follow-up. In addition, children grow at a rapid pace, so their responses to certain treatments can change as the tests are being conducted. Another problem with long-term studies is that people move, including both child subjects and the researchers conducting the studies, which can make follow-up logistically impossible. Thus, the length of time needed to conduct a proper clinical trial in pediatric subjects can be challenging for researchers, making it difficult for them to achieve reliable results regarding the safety or effectiveness of a particular treatment in these young patients.

Another challenge to pediatric testing is the relatively small population of potential test subjects. With children accounting for only 24.6% of the United States population, it is hard to find enough children to participate in studies. In addition, the size of this country makes it nearly impossible to confine the study to a particular geographic area as children with a specific condition are likely spread across the country. With only a small number of participants, studies may not be able to generate statistically reliable information concerning the effectiveness of a drug relative to a control group or a placebo. This practical challenge, coupled with the challenges of keeping up with a child’s rapid development during a clinical trial, further complicates pediatric testing.

A third challenge in pediatric testing is that children often react differently to certain treatments than adults with the same condition. Since most pediatric testing starts with research already done on adults, doctors often discover, through disastrous results, that certain drugs do not yield identical results in children. Some drugs are simply difficult...
to administer to children.\textsuperscript{71} For example, many adult intravenous medicines, if converted into the appropriate dose for an infant, would be too small to measure into a clinical syringe.\textsuperscript{72} Other drugs are absorbed differently by children and can therefore have different effects.\textsuperscript{73} Children have larger skin surface per pound of weight than adults and therefore absorb more of a topical drug than necessary.\textsuperscript{74} With a topical steroid, this difference can inhibit growth in children.\textsuperscript{75} Other drugs can simply metabolize differently in children due to developmental changes that have not yet occurred.\textsuperscript{76} For example, antihistamines may sedate adults, but can produce hyperactivity in children.\textsuperscript{77} Thus, physicians beginning to test drugs that are already approved for adult usage for use in children often find that what they know about a particular drug can do more harm than good for their patients.

A fourth challenge to pediatric testing is the companies’ concern about liability and adverse public relations consequences.\textsuperscript{78} While medical investigators are required to obtain informed consent from parents or children before enrolling the child in a clinical trial,\textsuperscript{79} they are prohibited from asking patients to give up their legal rights in any informed consent document.\textsuperscript{80} This concern discourages companies from testing in children because if a child dies during a clinical trial and a lawsuit ensues, jury awards can be very high.\textsuperscript{81} One pharmaceutical company, Pfizer, has faced lawsuits concerning the safety of the antidepressant Zoloft in treating depression in children.\textsuperscript{82} In one instance, the Miller

countries, pediatric deaths have been associated with local formulations of acetaminophen containing diethylene glycol.

\textsuperscript{71} \textit{Id.} at 68.  
\textsuperscript{72} \textit{Id.}  
\textsuperscript{73} \textit{Id.} at 69.  
\textsuperscript{74} \textit{Id.}  
\textsuperscript{75} \textit{Id.}  
\textsuperscript{76} \textit{Id.} at 71.  
\textsuperscript{77} \textit{Id.}  
\textsuperscript{78} \textit{Id.} at 62.  
\textsuperscript{79} See, \textit{infra} Part IV.  
\textsuperscript{80} 21 C.F.R. § 50.20 (2006).  
\textsuperscript{82} Jonathan Mahler, \textit{The Antidepressant Dilemma}, \textit{N.Y. Times Mag.}, Nov. 21, 2004, at 59.
family of Overland Park, Kansas, sued Pfizer when their thirteen-year-old son committed suicide after he had taken Zoloft. Although the Millers lost, the suit did gain media attention, raising awareness about the potential dangers of mixing children and antidepressants. When a child dies as a result of a clinical trial, this tragedy tugs at the heartstrings of the American public and raises public awareness of these problems. Negative publicity of this kind could taint a company’s image and hurt profitability.

A final challenge to pediatric testing is the prohibitive costs associated with dealing with the four problems mentioned above. There are two types of costs associated with clinical trials: first, patient care costs, which are often borne by either the patient or the patient’s insurance company and generally are not factored into the costs of undertaking a clinical trial; second, research costs, such as the costs of data collection management, compensation for physicians and nurses, and laboratory testing, which are borne by the company. Taken together, the average cost to develop a new drug, according to most recently available statistics, was $802 million.

83 Id. While Matt Miller was not involved in a clinical trial, his family’s lawsuit is similar to the types of lawsuits faced by drug companies when clinical trials go awry. See also Gardiner Harris, Student, 19, in Trial of New Antidepressant Commits Suicide, N.Y. TIMES, Feb., 12, 2004, at A30. Traci Johnson, 19, committed suicide after participating in a clinical trial for the drug that would later be released in the marketplace as Cymbalta. Id.
84 Mahler, supra note 82.
85 Groopman, supra note 81.
86 ETHICAL CONDUCT OF CLINICAL RESEARCH, supra note 9, at 61:

The commercial value of various . . . options for children . . . may not be enough to offset the costs of developing them. Even for relatively common childhood conditions, the numbers of potential research participants may be small and thus require more study sites and additional costs for coordination. Development costs may also be increased because more time is required per patient to complete study procedures . . . . The widespread off-label prescription and use of drugs for children tend to further diminish the incentives to finance pediatric research on drugs that are already approved for use in adults.

Id.
88 Id.
These costs only increase when developing preventive, diagnostic and therapeutic options for children because of the factors outlined above, such as geographical barriers and negative publicity. Such trial costs often exceed the profitability of children's medicine in the marketplace. Thus, there is no financial incentive for companies to test their products on children. In addition, doctors and nurses require more time for child patients because children are, by nature, fidgety and difficult to control, further increasing costs. Also, the number of potential child research participants is relatively small compared to adults, even for relatively common conditions, requiring additional study sites across the country, adding additional costs for coordination and execution of the study. In light of these challenges, Congress enacted BPCA 2002 and PREA 2003.

IV. BPCA 2002 AND PREA 2003 FACE THESE CHALLENGES

All of the barriers described above discourage pharmaceutical companies from developing drugs and other therapeutics for use in pediatric audiences. From the manufacturer's perspective, it is easier and more cost-effective to simply allow doctors to prescribe their drugs off-label. There were also several problems with BPCA 2002 and PREA 2003 that made it relatively easy for pharmaceutical companies to avoid complying with these laws.

Even with BPCA 2002 and PREA 2003 legislation in place, positive results did not occur quickly. Because trial testing takes so long and because BPCA 2002 and PREA 2003 were enacted for a relatively short period of time, drug makers could easily drag their feet, delaying testing as long as possible or taking longer to initiate and complete testing, in the hopes that the legislation would not be reenacted. Even companies that had already begun pediatric testing took advantage of the fact that pediatric testing takes such a long time to complete. The statute that mandated testing lasted only four years, and it is likely that the tests would require more time for completion. This disparity highlights the need to keep legislation in place. As costs of pediatric clinical trials

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90 See Ethical Conduct of Clinical Research, supra note 9, at 80.
91 Id. at 61.
92 National Center for Health Statistics Highlights, Health, United States, 2005, http://www.cdc.gov/nchs/data/hus/hus05.pdf#highlights. According to the NCHS, in 2004, 24.9% of the population was under the age of 18. Id.
93 See Conger, supra note 1; see also, infra Part VII.
continue to rise, federal legislation is becoming the only incentivizing device for companies to test on children.

BPCA 2002 and PREA 2003 also contained a significant number of loopholes that allowed companies to manipulate the law to their advantage. For example, under the old laws, a company could apply for pediatric exclusivity by presenting the FDA with results of pediatric testing days or weeks before patent expiration. The FDA had ninety days to review the materials and during this time the company was granted a *de facto* exclusivity period pending the FDA’s decision. As a result, a company whose patent was expiring could effectively extend its patent by presenting the FDA with inadequate testing just before patent expiration. Even if the testing was ultimately rejected for the additional six months of market exclusivity, the company would retain market exclusivity during the ninety-day period that the FDA had to review the application.

Another problem with BPCA 2002 and PREA 2003 is that the laws did not mandate the testing of devices. Devices designed specifically for children are particularly important in pediatric care. While it is at least feasible for a doctor to prescribe medication to a child off-label, devices often need to be sized to the child patient in order to work properly. Since many diseases are treated with devices either in conjunction with or in lieu of medicine, this gap in the statutory mandates regarding medical treatment for children and young adults was particularly worrisome. Clearly, Congress agreed. Title III of the FDAAA created the Pediatric Medical Device Safety and Improvement Act of 2007. The details of this Act will be discussed in greater detail in Part VII, *infra*. While BPCA 2002 and PREA 2003 sought to improve the way drugs and other therapeutics were made available to children, both acts were riddled with problems that had negative impacts on the very children they were designed to protect.

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95 For more on the need for medical devices developed exclusively for pediatric audiences see *infra* Part VI.

96 See FDAAA, supra note 6; see also discussion supra Part VI.C.
V. Industry Growth under BPCA 2002 and PREA 2003

Despite clear problems with the BPCA 2002 and PREA 2003, this country has seen positive changes in the way children are perceived in the health care industry since their enactment, suggesting that these statutes are working and again should be reenacted upon expiration. Sales of pediatric prescription products are expected to increase 6.2% annually and surpass $46 billion by 2009 as a result of BPCA and PREA.97 Pharmaceutical manufacturers, motivated by the patent extensions granted under these statutes, have begun seeking approval for pediatric use for appropriate products already approved for use in adults.98 As a result of increased profits, there have been many positive developments in pediatric drug availability.

For example, in 2006, the United States partnered with eleven European countries and Canada to conduct the world's largest clinical trial aimed at treatment for a rare type of bone cancer most commonly seen in children and young adults.99 The collaboration hopes to recruit 1,400 patients over the next few years and currently has 335 patients participating in the trial.100

In 2003, the FDA approved FluMist, a nasal spray flu vaccine.101 The drug was tested on both children and adults and ultimately approved only for children over five years old because of an elevated incidence of asthma and wheezing in vaccinated children under that age.102 The vaccine was, however, tested on younger children despite the fact that it was not ultimately appropriate for that age group, a sign that companies are complying with the legislation.103 In recent months, FluMist, manufactured by MedImmune, received FDA approval for a

97 Eric Ladley, Safety, Economics Converge: Children and Pharmaceutical Manufacturers Have Benefited From the FDA Measure Granting Exclusivity to Products That are Successfully Tested for Children, MED AD NEWS, May 1, 2006, at 1.
98 Conger, supra note 1.
100 Id.
102 Id.
103 Id.
refrigerated version of the same nasal vaccine.\textsuperscript{104} MedImmune has conducted more than 40 clinical trials with children as young as six weeks, showing that FluMist is safe and effective,\textsuperscript{105} another strong indicator that children are getting greater access to drugs and other therapies.

Clinicaltrials.gov, a website run by the NIH, allows users to search for available clinical trials using a variety of criteria, including particular conditions or age groups.\textsuperscript{106} A search for clinical trials being funded by pharmaceutical companies currently recruiting children under eighteen yielded 801 results as of January 2007.\textsuperscript{107} Many of these clinical trials are for drugs already approved for adult use\textsuperscript{108} such as Erbitux (Cetuximab), a drug approved by the FDA in February 2004 for treatment of colorectal cancer that has spread to other parts of the body.\textsuperscript{109} The drug’s manufacturer, ImClone, and the drug distributor, Bristol-Myers Squibb, are currently recruiting children between the ages of one and eighteen in order to study the maximum tolerated dose of Erbitux in pediatric and adolescent patients with refractory solid tumors.\textsuperscript{110} Another example is Abilify (Aripiprazole), an oral anti-psychotic drug approved by the FDA in June 2006 for use in adults with Bipolar Disorder.\textsuperscript{111} Bristol-Myers Squibb and Otsuka America Pharmaceutical are currently recruiting autistic children between the ages of six and seventeen to test the drug’s effectiveness in reducing serious behavioral

\textsuperscript{105} Id.
\textsuperscript{107} Id. (search conducted Jan. 14, 2007).
\textsuperscript{109} Id.
problems in autistic children and adolescents. These studies are only some examples of the many clinical trials currently underway to test drugs already approved for use in adults.

However, while clinical trials available to children have significantly increased, the number of studies conducted by pharmaceutical companies that are currently recruiting children is highly misleading. A search of Clinicaltrials.gov for pharmaceutical companies currently recruiting children yielded a clinical trial currently underway to test a particular type of chemotherapy treatment for men with prostate cancer. It is unclear why these results do not get filtered out, but it appears that some companies, in this instance, Johnson & Johnson, do not put proper age filters into their listing. This phenomenon is not limited to clinical trials currently recruiting subjects. For example, a clinical trial began in 2001 “to evaluate the addition of Herceptin to standard chemotherapy treatment of patients newly diagnosed with operable breast cancer.” It is unlikely that children would be appropriate test subjects for this clinical trial. In addition, some trials may recruit pediatric subjects but conduct tests on all patients with a particular condition rather than solely on children. Thus, it is difficult to ascertain

117 For example, there are many studies, both ongoing and completed, testing new therapies for HIV and AIDS. While the companies do recruit patients of all ages, it is unclear how many
the true number of clinical trials that pharmaceutical companies are currently running and that actively recruit children.

While drug companies are starting to test already developed drugs on pediatric audiences, there is little development of drugs specifically designed for children. Instead, as demonstrated by the U.S. government's clinical trial database, pharmaceutical companies more often test the effects on children for drugs that have already been approved for use in adults. By testing those drugs, the drug companies stand to benefit from additional months of market exclusivity. Thus, they have little incentive to develop drugs specifically for children since this practice is less profitable than simply testing already approved drugs on children.

Testing already existing drugs on a pediatric population is one way to improve the availability of drugs to children, but a strong need for companies to develop therapies specifically for children still exists. In the area of devices, this need is particularly clear. For example, The New Yorker reported the story of a pregnant woman whose baby had a malformed heart and was admitted to the Children's Hospital in Boston in March 2004. The baby needed an operation to enlarge a hole in the heart, but no company has developed a catheter appropriately sized for such a small child. Doctors performed the surgery using a balloon and catheter designed for an adult, but the balloon ruptured during the procedure and the catheter was large and cumbersome when used on such a tiny patient. Complications of this kind could have been avoided with the use of properly sized devices, but with only a small amount of children requiring this surgery every year, the development is unlikely to occur.


118 Groopman, supra note 81 ("It seems unlikely that either private industry or the government will ever take the initiative in creating therapies specifically designed for children.").


120 See supra Part III.

121 See Groopman, supra note 81.

122 Id.

123 Id.

124 Id.

125 See id.
There has been a significant increase in the number of medical therapies available for children, yet there is still a shortage of drugs and other therapies designed specifically for children. Even under the revised BPCA 2007 and PREA 2007, this shortage will still be a problem because the market exclusivity promised by BPCA and PREA incentivizes manufacturers to test drugs already approved for adults rather than develop new drugs for children; in the long run, those drugs will make more money for manufacturers because during the longer period of market exclusivity, the manufacturers can still sell the drug to adult audiences, thereby maximizing profit. Since drugs manufactured for children tend to be less profitable, companies have less incentive to develop drugs and devices that only children can use, despite the market exclusivity promised by these legislative measures. While testing existing drugs on pediatric audiences is a positive step, Congress should consider offering further incentives for companies to develop new drugs designed specifically for pediatric audiences.

VI. PROBLEMS ARISING IN PEDIATRIC CLINICAL TRIALS

A. Informed Consent

With new incentives and rules compelling companies to test their products on children, companies must now shift gears in order to comply with these laws; moving away from developing drugs solely for adults toward actively peddling their products to children and their parents. With this shift, families, rarely equipped with any medical knowledge, are forced to determine whether participation in research trials will help or hurt their children, placing a significant burden on both parents and children. Pediatric testing can help a child afflicted

126 Cf. id. (discussing how the new medical therapies have not been properly researched on children).
127 Cf. id. ("[T]he hospital interviews the clinical staff about medical gaps that need to be filled.").
128 See supra Part III.
129 MedscapeWire, Pediatric Clinical Trials are on the Rise as New Law Goes Into Effect, Aug. 9, 2000, http://medoffice.medscape.com/viewarticle/412078 (last visited Jan. 21, 2007) (discussing how "[m]any more parents will be approached by physicians, asking for permission to enroll their children in drug trials.").
130 See id.
131 At a certain age, a child has the capacity to make voluntary and informed decisions. However, that exact age is often disputed by medical professionals. See e.g., ETHICAL CONDUCT OF CLINICAL RESEARCH, supra note 9, at 146–47. For the purposes of this Note, the author will examine how the decision to participate in pediatric testing is made by the family as a whole.
with a particular condition, but this testing also allows doctors and researchers to learn more about how a particular condition manifests itself in children. Thus, while pediatric testing can benefit a child, some children will undoubtedly experience some level of harm from the testing, because drug use in pediatric patients is sometimes either ineffective or harmful. These risks make the decision whether to participate in pediatric trials extremely challenging.

As legislation requires pharmaceutical companies to test their products on a pediatric audience in the face of the challenges outlined above, it is important that the FDA closely monitors this testing to ensure that the testing is always conducted without exploiting the children or their families. The process by which parents and children must consent before a child is allowed to take part in a clinical trial is an important check. In order to participate in a clinical trial, children and parents must sign a consent form, which serves to protect the pharmaceutical company and the research institution from liability. However, language in the form may not induce families to waive their legal rights, nor release the laboratory, pharmaceutical company, doctors or other hospital staff from liability due to negligence. In addition, physicians are required to secure what is called “informed consent” from the patients. Informed consent is

the process whereby a physician informs a patient about the risks and benefits of a proposed therapy or test. Informed consent aims to provide sufficient information about the proposed treatment and any reasonable alternatives that the patient can exercise autonomy in deciding whether to proceed. . . . Most general guidelines require patients to be informed of the nature of their condition, the proposed procedure, the purpose of the procedure, the risks and benefits of the proposed treatments, the probability of the anticipated risks and benefits, alternatives

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132 See id. at 129-30.
133 Id. at 60.
134 Id. at 149-50.
135 Id. at 150.
137 The idea of informed consent was addressed in Salgo v. Stanford, 154 Cal. App. 2d 560 (1957). While in Salgo, the patient was undergoing clinical treatment and not research treatment, the federal government has mandated that clinical trial subjects must also give informed consent. Informed consent documents must comply with the regulations set forth in 21 C.F.R. 50.20, 21 C.F.R. 50.25(a) and 21 C.F.R. 50.25(b).
to the treatment and their associated risks and benefits, and the risks and benefits of not receiving the treatment or procedure.\[138\]

While the goal of informed consent is both to prevent liability and ensure the subjects’ awareness of the risks and benefits of the procedure, consent is often obtained in haphazard ways. Such imprecision leaves patients with no real understanding of the procedure to which they consented.\[139\] Asking the patient to paraphrase the information yielding informed consent before signing the form improves the quality of the doctor-patient discussion and improves the likelihood that the obtained consent is actually informed.\[140\]

In order to help parents and children understand informed consent, government agencies and non-profit organizations offer advice to parents and children regarding the issue of informed consent. The act of signing a waiver can be daunting for many families. The most comprehensive government-run website on this topic is Clinicaltrials.gov, which offers a detailed question-and-answer section including a description of informed consent.\[141\] Other government agencies also post information regarding informed consent on their websites. For example, the National Cancer Institute’s website offers these families guidance on informed consent and children’s ability to assent to participate in studies.\[142\] In addition to providing background information and details about relevant laws, the site offers tips for parents and guardians.\[143\] Non-profit organizations such as St. Jude’s Children’s Research Hospital\[144\] and Children’s Cause for Cancer Advocacy\[145\] also offer information and advice online about clinical trials. These resources are

\[142\] National Cancer Institute, Children’s Assent to Clinical Trial Participation, http://www.cancer.gov/clinicaltrials/understanding/childrensassent0101/allpages#2c726b4e-4160-4179-ae3a-5801788b98ba (last visited Jan. 21, 2007).
\[143\] Id.
important, as many parents and children turn to the Internet after diagnosis in order to learn more about their condition.\textsuperscript{146}

B. Payment Incentives

Payment incentives are the main types of incentives medical investigators offer to children and their families for participation in drug research. Payments are grouped into four categories: (1) reimbursements for direct research-related expenses; (2) compensation for the time and inconvenience of participating in research; (3) appreciation payments to thank the child for participation; and (4) incentives to encourage enrollment.\textsuperscript{147} Payments made either to the parent or directly to the child present ethical problems. There is virtually no opposition to reimbursement and compensation payments which help eliminate the financial obstacles that may prevent participation in a research study.\textsuperscript{148} However, compensation payments alone are often not enough to garner participation and companies resort to appreciation and incentive payments. There is no data publicly available regarding the amounts of the appreciation and incentive payments that pharmaceutical companies do make to families.\textsuperscript{149} Few companies conducting clinical trials actually have written guidelines concerning payment of research subjects.\textsuperscript{150} This deficiency leads these organizations to rely on "rules of thumb,"\textsuperscript{151} rather than specific formulas to calculate payment or to recognize when payment may be unethical.\textsuperscript{152} This ambiguity results in an ethical dilemma that is only heightened through legislation that has essentially forced pharmaceutical companies to test on children.

If investigators make appreciation and compensation payments to the parent, this incentive might encourage parents to enroll their chil-

\textsuperscript{147} David Wendler, et al., The Ethics of Paying for Children's Participation in Research, 141(2) J. PEDIATRICS 166, 167 (2002).
\textsuperscript{148} See id. For example, if a parent has to take time off from work in order to bring a child to and from the doctor conducting the trial, this type of compensation ensures that financial strain will not result in the removal of a child from the study.
\textsuperscript{149} Id. at 168 (discussing a ban on disclosure of payments).
\textsuperscript{151} Id.
\textsuperscript{152} Id.
Children in clinical trials. This is not to say that parents will necessarily be malicious in their motives, but rather that there are cases where financial gain to a family eclipses the risks involved in participation, turning informed consent into purchased consent. This possibility has the greatest impact on poorer families who are more likely to need the money. These parents may unconsciously inflate the benefits of participation and/or minimize the risks of participation. Thus, proper safeguards must prevent undue influence on parents and promote the best interests of the child. The American Pediatric Society and Society for Pediatric Research recommend that parents not receive any payment other than the reimbursement of expenses.

If payments are made to the children, there is a concern that a minimal payment made to a parent might seem larger to a child or teenager, driving them to consent to a particular procedure. The Committee on Drugs of the American Academy of Pediatrics recommends that payments directly to children be made after the study is completed to ensure participation is voluntary. Payment should not be mentioned to the child until the study's completion to further ensure voluntariness of participation. The American Society of Pediatrics and the Society for Pediatric Research agrees, recommending that in order to prevent bribery, any payment to a child research subject be “no more than a ‘thank you gift’ that is clearly understood to be because they are helping others.”

These concerns are compounded by federal laws mandating that pharmaceutical companies test their products on children. With signifi-

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153 Id.; see also Committee on Drugs, Guidelines for the Ethical Conduct of Studies to Evaluate Drugs in Pediatric Populations, 92 PEDIATRICS 286, 293 (1995) [hereinafter Guidelines for Ethical Conduct].
156 Guidelines for Ethical Conduct, supra note 153, at 293.
158 Wendler, supra note 147, at 167.
159 See Guidelines for the Ethical Conduct, supra note 153, at 293.
160 Id.
161 American Pediatric Society & Society for Pediatric Research Statement before the Institute of Medicine, supra note 157.
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cant challenges to pediatric testing already hindering the process, it is logical for drug companies to turn to financial incentives in order to complete the trials that are mandated by federal law. However, while the federal government does statutorily mandate the testing of drugs on children, it is remarkably silent on the issue of payment for participation. Federal regulations require that researchers obtain informed consent:

[Un]der circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

In this informed consent, federal law requires a "statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled." However, the same statute requires researchers to inform a subject of "[t]he consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject" which would logically include the loss of any promises of payment upon completion of the study.

Currently, the institutional review board ("IRB") of each pharmaceutical company oversees the payment process as part of its review of all research activities mandated by federal law. However, IRBs are not given any mandates concerning implementation of these payments.

162 See supra Part III.
164 Id. § 46.116(a)(8).
165 Id. § 46.116(b)(4).
166 45 C.F.R. § 46.109 (2008). This section requires that "[a]n IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy." The statute also requires IRBs to oversee the process of securing informed consent of test subjects. Id.
The FDA offers only guidelines on how to properly offer payment for participation in research.\textsuperscript{167} According to the FDA, payment to research subjects for participation in studies is not considered a benefit, but rather a recruitment incentive which should be used when health benefits to subjects are remote or non-existent.\textsuperscript{168} The FDA recommends that the amount and schedule of intended payments be presented to the IRB at the time of initial review so that the IRB can ensure that none of these measures are coercive or present undue influence.\textsuperscript{169} The FDA also recommends that credit for payment accrue as the study progresses and should not be contingent upon completion of participation.\textsuperscript{170} However, it is permissible for IRBs to withhold payment until the time that subjects would have completed the study had they not withdrawn.\textsuperscript{171}

While the FDA guidelines are helpful, they have not been updated since the inception of the laws that require pediatric testing.\textsuperscript{172} Given the difficulties of pediatric testing, it is likely that more companies have turned to financial incentives to encourage participation.\textsuperscript{173} However, companies are doing so without proper, updated guidance from the federal government. While a host of articles in medical journals attempts to guide the community in navigating these murky waters,\textsuperscript{174} there is nothing firmly in place to ensure that the statutorily mandated need to conduct research on young people does not eclipse children's safety. Since BPCA 2007 and PREA 2007 require drug companies to perform tests, the companies would likely benefit from some federal guidance on how to compensate children and their families in a manner that the government finds appropriate, rather than simply relying on the intuition and personal judgment of company executives. Since the federal government has shown a willingness to regulate in this area,\textsuperscript{175} addi-

\textsuperscript{167} See U.S. Food and Drug Administration, Information Sheets Guidance for Institutional Review Boards and Clinical Investigators available at http://www.fda.gov/oc/ohrt/irbs/toc4.html (last visited Jan. 9, 2007). This Information Sheet was last updated in 1998, long before BPCA and PREA were enacted. See id.

\textsuperscript{168} Id.

\textsuperscript{169} Id.

\textsuperscript{170} Id.

\textsuperscript{171} Id.

\textsuperscript{172} See supra note 167.

\textsuperscript{173} There is little data on the specific types of payments.

\textsuperscript{174} See e.g., Wendler, supra note 147.

\textsuperscript{175} See e.g., 45 C.F.R. § 46.116 (2008) (general requirements for informed consent).
tional legislation specifically concerning payment of test subjects would not be extreme.

C. Disclosure of "Bad" Results

Since the pharmaceutical industry is a for-profit industry, the cost associated with pediatric clinical trials has caused these companies to find ways to comply with the statutes without putting themselves at great financial risk. One major problem that came about as a result of BPCA 2002 and PREA 2003 is a lack of data disclosure where the results of a trial are negative. When there are negative results in clinical trials, companies are reluctant to make those findings public. In 2004, the Pharmaceutical Research Manufacturers of America created a voluntary database for the results of marketed drugs. To supplement this attempt to gain transparency, the New England Journal of Medicine requires that, for a study to be published in the journal, the trial must be registered with a public clinical trial registry. In addition, the International Committee of Medical Journal Editors requires registries to publish negative clinical trial results. However, these measures alone are not enough to guarantee that negative clinical trial results are made available to the public. For example, propofol, a sedative commonly used in adults, was, for some time, administered to children in lower doses. However, some children who took propofol developed a lethal buildup of acid in their blood. In 2001, the company that created the drug, AstraZeneca, issued a letter to American pediatricians disclosing the results of the pediatric trial: of two hundred and twenty-two young patients who received propofol, twenty-one died, while in contrast only four of the hundred and five patients died when given standard sedatives.

A barrage of negative publicity brought the data disclosure problems to the forefront. The controversy surrounding antidepressant use in children and teenagers prompted several Senators to introduce the Fair Access to Clinical Trials Act ("FACT Act") on February 28, 2005. At the time the FACT Act was introduced, only three of the

176 Lisa J. Bain, Crossroads in Clinical Trials, 2(3) NEURORx 525, 526 (July 2005).
177 Id.
178 Id.
179 Groopman, supra note 81.
180 Id.
181 Id.
fifteen studies conducted on pediatric use of antidepressants showed that the drug worked on children.\textsuperscript{183} Those three studies were also the only ones published in medical journals.\textsuperscript{184} In a hearing conducted by the House Committee on Energy and Commerce Subcommittee on Oversight and Investigations on September 9, 2004, the committee questioned why the FDA and seven drug companies failed to warn doctors and patients that most antidepressants had not proven to be effective in treating children\textsuperscript{185} at a time when one in six children in the United States was taking some type of prescription antidepressant.\textsuperscript{186} The FACT Act was introduced in response to these hearings.\textsuperscript{187}

The proposed FACT Act requires that the FDA expand the Clinicaltrials.gov database to create a national databank of information accessible to the public.\textsuperscript{188} The proposed databank would consist of a clinical trial registry and a clinical trial results database.\textsuperscript{189} The clinical trial registry database would be accessible to patients and health care providers seeking information about ongoing clinical trials for serious or life-threatening diseases and conditions.\textsuperscript{190} The FACT Act also calls for a database of all publicly and privately funded clinical trial results, regardless of the outcome, which would be accessible to the scientific community, health care practitioners, and members of the public.\textsuperscript{191} The FACT Act would also require the FDA to make internal drug approval


\hspace{1cm}\textsuperscript{184} Id.

\hspace{1cm}\textsuperscript{185} Gardiner Harris, Lawmaker Says F.D.A. Held Back Drug Data, N.Y. Times, Sept. 10, 2004, at A22 [hereinafter Harris, F.D.A. Held Back Drug Data] (“The F.D.A.’s lack of cooperation with the committee in obtaining relevant and responsive information in a timely fashion on a matter that involves the safety of our children leaves me wondering whether this is sheer ineptitude or something far worse,” (quoting Rep. Joe Barton)).


\hspace{1cm}\textsuperscript{188} Fair Access to Clinical Trials Act, supra note 182.

\hspace{1cm}\textsuperscript{189} Id.

\hspace{1cm}\textsuperscript{190} Id.

\hspace{1cm}\textsuperscript{191} Id.
and safety reviews publicly available.\textsuperscript{192} The Act would apply to clinical trials for drugs, biologics and medical devices, and would require all trials to be registered in the database to obtain approval from an IRB in the United States.\textsuperscript{193} This process would allow for increased transparency, prohibiting drug companies from only publishing positive results.\textsuperscript{194} It would also make both doctors and patients more aware of treatment options and the risks associated with each of those options so that both parties could make better decisions regarding treatment choices.

The FACT Act first came to being in February 2005, and was referred to the Senate Committee on Health, Education, Labor and Pensions, but no further action was taken on the bill.\textsuperscript{195} On June 30, 2005, the FACT Act was revived in the House of Representatives by Rep. Henry Waxman, one of the members of the Subcommittee on Oversight and Investigations which oversaw the September 2004 hearings.\textsuperscript{196} That bill was referred to the House Energy and Commerce Subcommittee on Health and no further action was taken on it.\textsuperscript{197}

On August 3, 2006, the Enhancing Drug Safety and Innovation Act\textsuperscript{198} was introduced, a modification of the FACT Act. Title III of the bill would establish a clinical trials registry and results database.\textsuperscript{199} Unlike in the FACT Act, other types of intervention trials, such as devices, procedures, and behavioral interventions, would not be included in the database.\textsuperscript{200} Under Title III, the public must be able to search both the registry and the results database by categories and the results database must contain the name of the drug studied, its approval status, and significant safety information.\textsuperscript{201} Under this Act, the information submitted to these databases must include non-promotional summary in-

\begin{footnotesize}
\item[192] Id.
\item[193] Id.
\item[197] Legislative Updates: Access to Clinical Trial Information, supra note 195.
\item[199] Legislative Updates: Access to Clinical Trial Information, supra note 195.
\item[200] Id.
\item[201] Id.
\end{footnotesize}
formation. Again, the bill was referred to the Senate Committee on Health, Education, Labor and Pensions but no further action has been taken since August 2006.

Laws like the FACT Act and the Enhancing Drug Safety and Innovation Act should be revived and enacted as they will make important changes to the current clinical trials process, increasing the transparency of clinical trials and drug research by forcing companies to publish results that showed either negative effects or simply that the drug was ineffective in pediatric audiences. This transparency will allow parents and children to make more informed decisions about treatment options. These types of laws are particularly important in the face of BPCA 2007 and PREA 2007 because, while the laws require drug companies to conduct research on pediatric audiences, the companies are not currently required to publish the results. Since publishing negative results would inevitably lead to heightened scrutiny from the FDA and a likely decrease in sales, pharmaceutical companies will not voluntarily publish any data that will call the drug's efficacy into question. Thus, Congress must enact laws like these in order to ensure that the drugs prescribed for children are safe and effective; otherwise, the purpose of BPCA and PREA will be undermined.

As more clinical trials are testing drugs and other therapies on children, some pharmaceutical companies are cutting costs in order to satisfy this statutory mandate while still making a profitable product. In a typical clinical trial testing on adults, a company first studies how differ-

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202 Id.
203 Id.
204 Representative Henry Waxman made this point clear in his testimony at the September 9, 2004 hearing conducted by the House Committee on Energy and Commerce Subcommittee on Oversight and Investigations. Rep. Waxman stated:

So I think what we have to be concerned about is we have given this pediatric exclusivity in order to encourage the studies for children, but the companies are using that only to get a longer patent time or monopoly time over the drug that they are selling to adults, and they are not making the results of their studies that aren't positive known.


205 This likely effect became clear in the September, 2004 hearings. See Harris, F.D.A. Held Back Drug Data, supra note 185 ("The hearing comes in the midst of a growing controversy about not only the safety of antidepressant therapy in children but also the drug industry's longtime tendency to suppress the results of clinical trials that might undermine the sales of their drugs.").
ent drugs are absorbed and metabolized before testing for effectiveness.\textsuperscript{206} However, to lower costs, many drug companies combine these two steps in clinical trials involving children.\textsuperscript{207} As a result, children often remain in a clinical trial for a longer period of time leading many children and their families to turn down enrollment.\textsuperscript{208} Thus, many of these clinical trials are conducted with a low number of test subjects, allowing \"[a] drug company [to] satisfy the law without generating meaningful data about how to prescribe its drug for children.\textsuperscript{209}\" In order to fix this problem, these laws mandating pediatric testing should contain provisions compelling pharmaceutical companies to conduct trials yielding more reliable results.

This cost-cutting problem manifests itself in other ways as well. Due to the significant cost of undertaking clinical trials, pharmaceutical companies lobbied for the sunset clause causing these statutes to expire at the end of 2007.\textsuperscript{210} While the statute was reenacted, it was again only given a five-year term. Some drug manufacturers rely on the looming expiration dates as an excuse to delay testing and prolong clinical trials in pediatric audiences in the hopes that they will not have to complete them when the statutory mandates draw to a close.\textsuperscript{211} Legislation must be enacted for a longer period of time—a minimum of ten years, forcing companies to begin testing products in children because it will become unprofitable for these companies to simply wait out the term of the statute.

\textbf{VII. THE REENACTMENT – DOES IT SOLVE THE PROBLEMS?}

The reenactment of BPCA and PREA successfully closes some of the loopholes that allowed pharmaceutical companies to delay compliance. In addition, the enactment of the Pediatric Medical Device Safety and Improvement Act of 2007 attempts to deal with the problem of too few devices designed and appropriately sized for small children. As dis-

\begin{footnotesize}
\begin{enumerate}
\item[206] Groopman, \textit{supra} note 81.
\item[207] \textit{Id}.
\item[208] \textit{Id}.
\item[209] \textit{Id.}(quoting Dr. Charles Coté, a pediatric anesthesiologist).
\item[210] \textit{Id.}(\"[T]he reforms include a 'sunset clause' that will cause them to expire in 2007. (This clause was added as a result of pressure from drug companies and groups that oppose government regulation.\")\).
\item[211] Conger, \textit{supra} note 1; \textit{see also}, Groopman, \textit{supra} note 81 (\"Advocates worry that many drug companies will exploit the clause by agreeing to conduct a trial but allowing the study to languish until 2007, when a different Congress may decline to renew the reforms.\")
\end{enumerate}
\end{footnotesize}
discussed earlier, devices designed for children are particularly important because usually devices need to be sized specifically for children, and simply using a device approved for adults is insufficient. The Act provides incentives to medical device manufacturers to create products for children and sets forth procedures to approve and monitor development.\textsuperscript{212}

Under the Act, any new device applications submitted to the FDA must also describe pediatric subpopulations suffering from the condition targeted by the device and the total number of affected pediatric patients.\textsuperscript{213} In addition, the Act expands the existing humanitarian device exemption ("HDE") which permits a device to be marketed with minimal efficacy data if it also targets a condition affecting fewer than 4,000 persons.\textsuperscript{214} Prior to enactment, a company with an HDE was prohibited from making a profit on the device.\textsuperscript{215} However, this Act creates an incentive for manufacturers to develop devices for pediatric subpopulations by expressly permitting those companies to profit from a device covered by HDE that is intended to treat or diagnose conditions that affect fewer than 4,000 minors. The Act also encourages pediatric medical device research by requiring the FDA to develop a research agenda, in consultation with medical experts, within 180 days of enactment.\textsuperscript{216} In addition, the FDA must issue a request for proposals within ninety days for "demonstration grants" to support activities of nonprofits in promoting and facilitating the development of pediatric medical devices.\textsuperscript{217} The Act authorizes payment of six million dollars annually through 2012 to fund these demonstration grants.\textsuperscript{218} Further, the Act gives the FDA's Pediatric Advisory Committee the ability to recommend improvements to the pediatric device system, and also gives the FDA authority to order manufacturers to conduct surveillance on pediatric devices already in the marketplace.\textsuperscript{219} This important addition will undoubtedly fix a significant problem seen in BPCA 2002 and PREA 2003.

\textsuperscript{213} Id.
\textsuperscript{214} Id.
\textsuperscript{215} Id.
\textsuperscript{216} Id.
\textsuperscript{217} Id.
\textsuperscript{218} Id.
\textsuperscript{219} Id.
BPCA 2002 and PREA 2003 were enacted to make more drugs available to children, because, prior to their enactment, doctors were left to make judgment calls about how to prescribe a particular treatment in pediatric patients. However, realizing that this type of off-label prescribing alone was not enough to successfully treat children and sometimes actually put children at risk of illness or death, Congress offered pharmaceutical companies incentives to test their drugs on children. As a follow up, Congress allowed the FDA to mandate testing of all new pharmaceuticals unless the drug company obtained a waiver because their product was not intended for pediatric audiences. This policy has helped to stimulate growth in the area, generating more drugs that are available for children.

BPCA 2007 and PREA 2007 have been revised to prevent companies from taking advantage of exclusivity provisions in order to maximize profits. However, like their predecessors, these laws are enacted for a relatively short period of time—only five years. On the plus side, companies who want the market exclusivity will ultimately have to comply with the law before their patents expire. However, generally pharmaceutical patents last for twenty years, so plenty of companies not yet facing patent expiration have no incentive to test their products on children unless the law is reenacted for a more substantial period of time—at least ten years. In addition, while pharmaceutical companies have no choice but to comply with BPCA 2007 and PREA 2007, there are significant problems with the way they conduct this mandatory testing.

These statutes require additional provisions. First, these statutes should be law for a period of at least ten years in order to force drug companies to actually begin conducting these trials. Next, there must be a revival of the FACT Act, the Enhancing Drug Safety and Innovation Act or other similar legislation requiring companies to publish research results even if they are not favorable. This way, families making decisions about which treatment to pursue will be able to do so armed with information. In addition, the government should create guidelines regarding appropriate methods for conducting testing in pediatric audiences including proper guidelines for payment incentives. With these measures in place, pediatric testing will be safer and will likely result in better treatments for children in the future.

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