ONE HUNDRED SEVENTH CONGRESS

Congress of the United States

House of Representatives

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March 18, 2002

The President
The White House
Washington, DC 20500

Dear Mr. President:

It has come to our attention that the Administration is about to suspend an important regulation that protects children from potentially unsafe and improperly dosed medications. Unless you intervene, FDA intends to announce, as part of a legal settlement, a two-year suspension of the "pediatric rule" on drugs and biologic products. This rule assures that new medications vital for children's health are studied so that essential safety and dosing information is available to clinicians. It also gives FDA authority to require pediatric safety and efficacy testing for existing drugs.

We are writing to urge you to direct FDA to reverse course and preserve this important safety measure.

The Pediatric Rule

In the 1990s, there was growing frustration among pediatricians and parents that the pharmaceutical industry was not conducting needed pediatric studies and that there was frequently insufficient information in drugs' labeling to use them safely in children. Only one in five drugs marketed had any instructions for pediatric use. Among newly approved drugs, only about one in three with potential usefulness in children had any information on the label about use in children.[1] What labeling did exist often excluded the youngest children, who are at the greatest risk of getting the wrong dose. As a result of inadequate pediatric information in the label, children were sometimes under-dosed and sometimes over-dosed, suffered unexpected adverse reactions (including serious injury and death), and frequently did not receive the best available treatment for their conditions.[2]

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[1] 66 *Federal Register* 66633 (Dec. 2, 1998).
[2] 62 *Federal Register* 43901 (Aug. 15, 1997).

The pediatric rule imposed, for the first time, a requirement on manufacturers to conduct pediatric studies on new drugs and required that the information gained from the studies be placed in the drug's label. The pediatric rule was proposed in 1997 and finalized in 1998. At the time the rule was proposed, President Clinton announced at the White House, "The executive action that I take today simply is designed to ensure that parents and pediatricians have the safety information they need." Otherwise, said the President, "the pediatricians' other alternative is to guess -- with potentially grave consequences."[3]

The pediatric rule was intended to generate essential safety and efficacy data on new drugs used by children. It requires manufacturers to study those new drugs that (1) provide a meaningful therapeutic benefit to children over existing treatments or (2) are likely to be used in a substantial number of pediatric patients.

The rule also gave FDA authority to require that manufacturers of already marketed drugs and biological products conduct pediatric studies in certain circumstances. This is very valuable authority, although it is unclear the extent to which it has been exercised by FDA.

Drug Industry Opposition

The drug industry opposed the pediatric rule. In comments submitted to FDA, the Pharmaceutical Research and Manufacturers of America asked the Agency not to publish or implement a final version of the rule. Last year, when we proposed codifying the pediatric rule as part of reauthorization of the FDA Modernization Act of 1997, the drug industry opposed our efforts.

The industry argued that the pediatric rule was unnecessary because of the "pediatric exclusivity provision" of the FDA Modernization Act of 1997. The pediatric exclusivity provision, which was reauthorized last year, gives manufacturers a substantial economic incentive -- 6 months of exclusive marketing without generic competition -- to conduct pediatric studies. It is up to each manufacturer to decide whether to conduct studies, and the exclusivity is granted when the study is submitted to FDA. There is no requirement that the study results be included in the drug's label. Since 1997, many manufacturers have taken advantage of the provision, which has reaped the industry huge profits.[4] The six-month extension for Prozac, for example, resulted in $700 million in profits for Eli Lilly.[5]

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[3]*Prescription Drugs and Children; Clinton Announces Action to Force New Studies, Different Labeling*, Washington Post (Aug. 14, 1997).

[4]It has been estimated that pediatric studies cost manufacturers somewhere between $500,000 and $5,000,000, while 6 months of exclusivity for drugs with large revenues has, in several cases, generated profits of several hundred million dollars.

[5]*Children Test New Medicines Despite Doubts*, New York Times (Feb. 10, 2001).

FDA rejected the drug industry argument, viewing the pediatric rule as complementary to the exclusivity provision -- not redundant to it. At the time the final rule was issued, FDA stated that there was "an important need" for it because the exclusivity provision was likely to leave many drugs and age groups unstudied. FDA based this prediction on the following: (1) the incentive was voluntary and likely to generate studies on the drugs with the largest revenues rather than on drugs of the greatest importance to children; (2) the provision provided no incentive for studies on many pharmaceuticals, such as biologics, antibiotics, and off-patent drugs; and (3) there was no requirement that the data from pediatric studies be included in the drug's label.[6]

Experience has justified these concerns. Under the exclusivity provisions, manufacturers have focused their pediatric studies on the largest selling drugs (because the value of the exclusivity is proportional to the sales of the drugs) rather than on the drugs most needed by children.[7] In 2001, when Congress was considering reauthorization of the pediatric exclusivity provision, FDA told Congress that while the exclusivity provision had been highly successful in producing clinical studies on many drugs, the passage of time had also confirmed the following significant gaps in the effectiveness of the provision:

- Because exclusivity is granted for submitting studies rather than for placing needed information into the drug's label, some manufacturers have delayed putting information from the studies in their drugs' labels, particularly where the information reveals adverse consequences from use of the drug in children. Of the 50 drugs that have received exclusivity, only 29 have pediatric labeling, and labeling for some of the 29 drugs was not added for over a year after exclusivity was granted.[8]

- Some important drugs for children remain unstudied because they are antibiotics, biological products, or off-patent, none of which are eligible for the financial incentive, or because, for some covered drugs, the incentive has not been large enough to prompt studies. The widely used drugs that remain unstudied include the asthma medication albuterol, the antibiotic ampicillin, and the attention deficit disorder medication Ritalin.[9]

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[6]63 Federal Register 66633-4.

[7]*Pediatric Testing Program Extended*, Boston Globe (Dec. 20, 2001). ("[M]any of the most commonly prescribed drugs remain unstudied. These drugs, including the antibiotic ampicillin and the allergy medicine albuterol, are no longer covered by patent so drug companies have no financial incentive to study them.")

[8]Compare labeling changes listed at www.fda.gov/cder/pediatric/labelchange.htm, with drugs granted exclusivity listed at www.fda.gov/cder/pediatric/exgrant.htm.

[9] The Pediatric Exclusivity Provision – January 2001 Report to Congress, Appendix B, www.fda.gov/cder/pediatric/reportcong01.pdf.

- How to use drugs safely in the youngest children, including newborns and infants, is frequently not being studied. In some cases, the ideal time to conduct these studies is after safety has been established in older children. However, once the financial incentive is granted for the studies on older children, drug manufacturers do not follow through with studies on newborns and infants because there is no remaining incentive to conduct subsequent studies. This leaves clinicians who need to treat newborns and infants without critically important data. [10]

These gaps are filled by the pediatric rule. Without the rule, manufacturers of new drugs could limit their pediatric studies to those drugs that will produce the greatest profits rather than those drugs that children need most. Moreover, FDA would not have the authority to require manufacturers of existing drugs to conduct pediatric studies on those drugs.

The Rollback of the Pediatric Rule

After the pediatric rule was issued in December 1998, the Association of American Physicians and Surgeons, the Competitive Enterprise Institute, and Consumer Alert brought suit against FDA, challenging the agency's legal authority to require pharmaceutical companies to conduct pediatric studies. The plaintiffs were represented in the case by Daniel Troy, who subsequently became FDA's Chief Counsel and was, until recently, the highest ranking political appointee at the agency. (Mr. Troy has reportedly recused himself from the case.)

What we have learned is that FDA is now planning to notify the court it will suspend the pediatric rule for two years. During this period, FDA will evaluate whether to revoke the rule permanently. This means that manufacturers seeking approvals for new drugs will no longer be required to conduct studies on pediatric safety and efficacy. It will also strip FDA of its ability to require pediatric testing for existing drugs.

We urge you to direct FDA to reverse course and preserve access to vitally important safety and dosing information for children.

Sincerely,

Henry A. Waxman
Ranking Minority Member
Committee on Government Reform

John D. Dingell
Ranking Minority Member
Committee on Energy and Commerce

Sherrod Brown
Ranking Minority Member
Subcommittee on Health
Committee on Energy and Commerce

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[10]The Pediatric Exclusivity Provision – January 2001 Report to Congress, www.fda.gov/cder/pediatric/reportcong01.pdf; FDA briefings and written responses to Congressional questions following hearing on reauthorization of the pediatric exclusivity provision.