DRAFT 8/7/97 5:00 P.M.

FIRST LADY HILLARY RODHAM CLINTON
STATEMENT AT PEDIATRIC DOSAGE EVENT
THE ROSE GARDEN
AUGUST 13, 1997

JENN AND LISSA,

HERE'S A ROUGH DRAFT. JENN -- I'LL BE IN AFTER 12 TOMORROW.

I would like to welcome you to the White House. We are here to take a major step in protecting the health of America's children. The action the President is taking today will see to it that important medications are tested and made available for children faster and more efficiently than ever before. It will also ensure that parents and doctors have the most complete information possible when it comes to knowing how much medicine they can safely give a child.

I would like to say a special word of thanks to a number of people whose efforts have made this achievement possible. [acknowledgments tk]

I would also like to remember the contributions of someone who isn't here: Elizabeth Glaser.

Elizabeth's struggle to get medication for her young daughter, Ariel, and for other children with AIDS made clear a heartbreaking problem: Too many medical treatments that are saving adult lives are slow in finding their way to children.

In the Glazer's case, Elizabeth contracted HIV from a blood transfusion she was given shortly after giving birth to her daughter. The virus was passed on to Ariel. Yet while Elizabeth was able to take AZT to fight the disease, Ariel was not. Priceless time was lost because doctors were not authorized to administer the treatment to children. Nor did they have any idea of what size dose would be safe and effective for a young child.

The plan the President is announcing today grows out of Elizabeth's efforts to see to it that no child or parent will have to endure this kind of agony. It will guarantee that children get the same access to newly developed drugs as their parents. And it will extend not just to medication for critical illnesses, but also to treatment for chronic conditions, like asthma, and for traumatic ones, like the pain that comes with a sprained ankle or a broken arm.

This plan, in short, answers the two most important questions parents with a sick child have: What medicine works and how much of it do you give. It doesn't get more basic than that.

Today's proposal is part of the President's comprehensive children's health agenda.

Last week, the President signed into law a balanced budget that will help extend health insurance to up to 5 million children -- for everything from regular checkups to antibiotics to major surgery. This $24 billion investment -- paid for in part by a 15-cents-a-pack tax on cigarettes -- is the largest expansion of children's health coverage since the passage of Medicaid in 1965.

Last month, the President announced that 90 percent of our 2-year-olds received their recommended vaccinations, surpassing the goal this administration set in 1993. The President also announced steps that will help us immunize the remaining children who are still missing their recommended vaccinations.

Since he came to office, the President has taken a number of important steps to protect the health of our children: keeping tobacco away from our kids...fighting drugs...signing the Family and Medical Leave Act and the Kassebaum Kennedy legislation into law. This administration has focused on early childhood development and put in place strong regulations to safeguard the food our children eat, the water they drink, the air they breathe. In fact, earlier this summer, the President approved the most stringent air quality regulations in XX years. These regulations alone will allow XX children with asthma to breathe easier.

When it comes to the health of our children, I am proud to say that my husband is as courageous as Harrison Ford and as relentless as the Energizer Bunny. He will not stop.

None of this progress on behalf of children's health would have been possible -- especially the efforts to reform government and make it respond swiftly and efficiently to people's needs -- without the hard work and leadership of the gentleman I now have the pleasure of introducing: the Vice President, Al Gore.

PEDIATRIC LABELING FOR DRUGS

BACKGROUND

Children suffer from most of the same diseases as adults, and by necessity, are treated with many of the same drugs as adults. Manufacturers of drugs are not currently required to study and label their products for use in children, even where they can anticipate that the products will be prescribed for children. Although pediatric studies are conducted for some drug classes and by some manufacturers, the majority of drugs and biological products that pediatricians use have not been tested by their manufacturers in pediatric populations. As a result, product labeling frequently fails to provide directions for safe and effective use in children. The absence of pediatric labeling information poses a serious risk of inappropriate dosing and unexpected adverse effects in children. It also may result in failure to provide children with optimal treatment in cases where physicians are reluctant to prescribe potentially toxic drugs to children before the drugs have undergone pediatric testing.

Despite these risks, pediatricians often have no choice and the use of drugs that have not been adequately labeled is widespread. An FDA survey of drugs prescribed during 1994 identified the ten drugs prescribed most frequently to children without adequate labeling. Together, these ten drugs were prescribed to children more than 5,000,000 times in one year (see Tab 1). The pediatric physician community has therefore urged FDA to take steps to ensure that drug labels provide information on the safe and effective use of the drugs in children.

In recent years, FDA has undertaken several initiatives to encourage the voluntary addition of pediatric use information to drug labels. FDA implemented a "Pediatric Plan" designed to focus attention on, and encourage, voluntary development of pediatric data during drug development. As part of the Plan, FDA staff meets with manufacturers at several stages of drug development and encourages them to conduct pediatric studies of their drugs. FDA has also identified the top ten drugs used in children without adequate labeling instructions, and has written the manufacturers of these drugs requesting that they submit supplemental applications to add pediatric use information to their drug labels. In 1994, FDA issued a new rule that allowed pediatric use information to appear on labels on the basis of substantially less data than required before. The rule also required manufacturers to survey existing data to determine whether there was sufficient information to support pediatric use information on the drug's label.

These voluntary efforts to increase the amount of pediatric use information on labeling have not resulted in significant gains. The response to the 1994 rule has not been encouraging. Moreover, efforts to date have not increased the number of new drugs entering the marketplace with adequate pediatric labeling. As shown in the chart below, a comparison of new molecular entities (NME's) approved in 1991 through 1996 shows no improvement in the percentage approved with adequate pediatric labeling. While approximately 56% of the drugs approved in 1991 with potential use in children had some pediatric labeling, 37% of those approved in 1996 with potential use in children had pediatric labeling. The data also suggest that commitments by manufacturers to conduct pediatric studies after approval frequently do not result in pediatric labeling.

FDA estimates that pediatric studies are needed for approximately 10-15 products per year that would not otherwise have been studied in children. This figure includes an estimated 10-13 new drugs and biological products and two already marketed products.

Status of pediatric labeling/studies for NME's approved in 1991-1996	1991	1992	1993	1994	1995	1996	Total
Total number of NME's approved	30	25	25	22	28	53	183
Those with potential use in children (pediatric studies needed)	16	14	14	15	14	40	113
Label included some pediatric use information or pediatric studies complete at time of approval (as a percent of NME's needing pediatric studies)	9 (56%)	4 (29%)	5[1] (36%)	6[1] (40%)	5 (36%)	15 (37%)	44 (39%)
Post-approval pediatric studies promised or requested	7	10	10[2]	10[2,3]	10[2]	17	64
Pediatric labeling added after approval	1	0	1	0	0	0	2

REGULATORY STRATEGY

The absence of adequate pediatric labeling continues to pose a significant public health issue. New approaches to the problem are needed. Financial incentives may be successful in generating pediatric labeling for some drugs, but there is no assurance that such incentives will work since they would leave it up to the manufacturer's discretion to conduct the studies. In addition, FDA's experience shows that a significant minority of manufacturers conduct needed pediatric testing without financial incentives. Providing exclusive marketing rights to companies that would have conducted pediatric studies without incentives may impose

[1] In one case, pediatric use information provided for one of two approved indications.

[2] In one case, pediatric data requested for second of two approved indications.

[3] In one case, pediatric data requested for additional age groups.

unnecessary costs on prescription drug consumers, and on governmental and third party payers in the form of more expensive drugs.

The adequacy of pediatric labeling can be substantially improved by imposing a limited pediatric study requirement applicable only to the drugs and biological products needed most urgently by children. Pediatric studies would be required for certain innovative new drugs and never-before approved biological products if they (1) provide a meaningful therapeutic advance to children over existing treatments, or (2) are likely to be widely used in pediatric patients. The requirement could be deferred until after approval if, or example, it was appropriate to delay pediatric studies until sufficient data were collected in adults, or if imposition of the requirement would delay the availability of an important new therapy. Where deferral was permitted, a deadline for submission of the studies could be established. The study requirement could be waived altogether if among other things, the product was likely to be unsafe or ineffective in pediatric patients, pediatric studies were impossible or highly impractical, or reasonable efforts to develop a pediatric formulation had failed.

The pediatric study requirement would also, in compelling circumstances, apply to manufacturers of already marketed drugs and biological products to support pediatric use labeling for already approved indications. Appropriate circumstances would be (1) where the marketed product is widely used in children and the absence of pediatric labeling presents significant risks to children, and (2) where the product offers a meaningful therapeutic benefit over existing therapies, but additional dosing or safety information is needed to permit safe and effective use in children.

In the event that a manufacturer failed to carry out a required pediatric study, the drug would not be disapproved or withdrawn, because such an action would deprive adult patients of important therapies. Instead, an order from a Federal court requiring the manufacturer to conduct or fund the needed studies would be sought.

6-3709

President Continues to Fight to Expand Health Care Coverage for Our Nation's Children

oday, the President announced that he is committed to assuring that the balanced budget agreement's children's ealth plan have meaningful benefits and that it include the Senate-passed 20 cent tobacco tax which increases the ıvestment for children's health care from $16 billion to $24 billion. This would represent the largest investment ı children's health since Medicaid passed over thirty years ago. In making this announcement, the President utlined the principles he will use in evaluating children's health coverage emerging from the Budget Agreement:

That coverage is meaningful: from checkups to surgery -- children should get a full range of benefits to ensure that children receive the care they need to grow up strong and healthy. It must also ensure that families are not forced to shoulder excessive costs for their children.

That it supplements not supplants coverage: these funds must be used wisely. This investment should cover children who do not currently have insurance; it should not replace public or private money that already covers children;

- **That it includes revenue from the Senate-passed tobacco tax:** in an overwhelming bipartisan basis, the Senate passed a 20 cent tobacco tax and allocated revenue from this tax for children's health. Including these additional revenues in the children's health initiative will not only further reduce the number of uninsured children, but it will serve as a financial barrier to help prevent our children from starting smoking in the first place.

Today's announcement builds on the President's previous successes in strengthening health care coverage for children.

- **Children and Immunization.** As the President announced today, 90 percent or more of America's toddlers in 1996 received the most critical doses of each of the routinely recommended vaccines -- surpassing the goal set by the President in 1993.

- **Children and Tobacco.** The President issued guidelines to eliminate easy access to tobacco products and to prohibit companies from advertising tobacco to kids. Each day about three thousand children become regular smokers and 1,000 of them will die from a tobacco-related illness. According to former FDA Commissioner David Kessler, the possibility of a comprehensive, public health oriented settlement with the tobacco industry could not have come about without the President's leadership in this area.

- **Children and the Kassebaum-Kennedy Law.** By signing this bill into law last year, the President helped millions of Americans -- and their children -- keep their health care coverage when they change jobs.

- **Children and the Environment.** Earlier this year, the President signed an Executive Order to reduce environmental health and safety risks to children by requiring agencies to strengthen policies and improve research to protect children and ensure that new regulations consider special risks to children.

- **Children and Medicaid.** Throughout his Administration, the President has fought to preserve and strengthen the Medicaid program; its coverage of about 20 million children, makes it the largest single insurer of children. The Administration has partnered with states through Medicaid waivers to expand coverage to hundreds of thousands of children.

Fact Sheet
Proposed Regulation on Pediatric Labeling

August 11, 1997

"This is an important time for America's children. They're growing up in a world that is changing rapidly. They need our help more than any generation before them. As Hillary says, children are not rugged individualists; they depend upon us -- their parents and others in the community who love them -- to give them love and guidance and discipline, to provide for them, and to defend them. That's as it should be. Their future and ours depends upon how well we do our job."

-- President Bill Clinton, Radio Address, June 1, 1996

Today, President Bill Clinton announced the Administration's intent to provide physicians with more information on using new drugs in children and, consequently, improve the health care American children receive. The proposed regulation would require pediatric-use data for any medicine which may offer improved treatment for children over existing therapies. The regulation also requires pediatric data on approved therapies that are used commonly in kids but lack labeling guidance for health care providers.

The proposed plan was published today in the Federal Register and includes the following key points:

- Many new drugs and biological products represent treatments that are, at least at times, the best available treatment for children, but many of them have not been adequately tested in pediatric populations. This regulation would require these sorts of new drugs to submit pediatric data prior to approval.

- For drugs that are already marketed, this regulation also would codify FDA's authority to require, in compelling circumstances, that manufacturers conduct studies to support pediatric-use labeling for the approved indications.

- The proposed rule would allow post-approval submission of pediatric data if FDA had safety concerns about testing the drug on children prior to approval.

- Likewise, the requirement could be waived if (1) FDA found that the product was likely to be unsafe or ineffective in pediatric patients; (2) that pediatric studies were impossible or highly impractical; or (3) that reasonable efforts to develop a pediatric formulation had failed.

- Because this rule has just been proposed, the Administration invites written

comments on the proposal from the public and industry, which may be submitted to the Dockets Management Branch, HFA-305, Food and Drug Administration, 12410 Parklawn Drive, Room 1-23, Rockville, MD 20857, until Nov. XX, 1997.

Improving American Children's Health Care

In 1963, Dr. Harry Shirkey coined the phrase "therapeutic orphans" to describe children. Shirkey was alluding to the plight of children for whom many drugs have not been studied. Pharmaceutical firms have had little incentive to study drugs for use in children because the population--and therefore the financial return--is likely to be small. Moreover, testing drugs in children can be more complicated than in adults.

In 1992, the Food and Drug Administration issued a regulation to encourage drug manufacturers to submit pediatric data voluntarily for review. However, many new drugs are still being approved without information on how they should be used in children.

Today's proposal would require data that can then be put on a drug's label to help pediatricians and other health care providers make treatment decisions based on scientific information aimed at their patient population.

When drug labels do not include pediatric information, health care providers are forced to guess at the appropriate dose or forego possibly the best treatment available. Likewise, without pediatric data, these health care providers have no information on potential side effects that might occur specifically in this patient population.

More information on this proposed rule is available at http://www.fda.gov/cder/regguide.htm.

Executive Office of the President
August 11, 1997

Draft Press Release

FDA PROPOSES TO REQUIRE PEDIATRIC DATA PRIOR TO DRUG AND BIOLOGIC PRODUCT APPROVALS

FDA has proposed a rule to provide physicians with more information on using new drugs in children. Published in today's Federal Register, the proposed rule would require pediatric-use data for any medicine which may offer improved treatment for children over existing therapies.

For drugs that are already marketed, this regulation also would codify FDA's authority to require, in compelling circumstances, that manufacturers conduct studies to support pediatric-use labeling for the approved indications.

Despite FDA efforts in recent years, many prescription drugs commonly prescribed for children have labeling that states the safety and effectiveness in children has not been established. Without adequate information, physicians may be reluctant to prescribe certain drugs for their pediatric patients, or they may prescribe them inappropriately. As a result, children may be exposed to an increased risk of adverse reactions or decreased effectiveness of the drugs, or they may be denied access to valuable therapeutic agents.

Today's proposal would require data that could then be put on a drug's label to help pediatricians and other health care providers make treatment decisions based on scientific information aimed at their patient population.

"Kids deserve the same access to newly developed drugs that their parents get," said Donna E. Shalala, secretary of Health and Human Services. "With this proposal, we will have the power to ensure pediatricians and other health care providers who treat children have the best scientific information available on which to base their medical decisions."

"When drug labels do not include pediatric information, health care providers are forced to play a guessing game and may not properly dose their patients," said Michael A. Friedman, M.D., FDA lead deputy commissioner. "Not only does this mean sick kids sometimes don't get better, but they also have the potential to get worse as a result of unexpected adverse events."

The proposed rule would allow post-approval submission of pediatric data if FDA had safety concerns about testing the drug on children prior to approval.

Likewise, the requirement could be waived if:

- FDA found that the product was likely to be unsafe or ineffective in pediatric patients
- that pediatric studies were impossible or highly impractical
- that reasonable efforts to develop a pediatric formulation had failed.

FDA invites written comments on the proposal from the public and industry, which may be submitted to the Dockets Management Branch, HFA-305, Food and Drug Administration, 12410 Parklawn Drive, Room 1-23, Rockville, MD 20857. The closing date for comments is Date, 1997. All comments received will be reviewed and considered by the agency in developing the final rule.

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PEDIATRIC LABELING Qs and As

1. Why are you doing this now?

Despite efforts in recent years to address this issue, most drugs still lack adequate pediatric labeling.

2. Can't you achieve the same effect through voluntary compliance?

That has been the primary approach taken thus far. However, voluntary efforts have not substantially increased the number of products entering the marketplace with adequate pediatric labeling.

3. Have children been at risk in the past?

The lack of adequate pediatric labeling has resulted in the use of many products that have only been tested for adults, causing an increased risk of inappropriate and unexpected adverse effects. Also, sometimes useful drugs not have been used in children because their effects in kids were uncertain..

4. How many drugs that are commonly used in children lack this data?

FDA estimates that one-half of the drugs approved in the past five years that had potential usefulness in kids had no pediatric labeling at the time of approval.

5. What kinds of drugs are commonly missing this pediatric data?

Drugs such as anti-asthmatics, steroids, drugs to treat gastrointestinal problems, strong pain medications, antidepressants, and antihypertensives commonly lack appropriate pediatric labeling.

6. What do doctors do when they don't have this information?

Many physicians rely on referenced pediatric handbooks for dosing and use information. Others are reluctant to prescribe certain products to children without adequate pediatric labeling on the product.

7. What drugs now have the best pediatric data?

Vaccines and antibiotics are the most adequately labeled drugs for children.

8. Why haven't companies provided this information in the past?

Some companies do provide this information, however, pediatric labeling has not been required until now. Lack of familiarity with pediatric studies, need for a pediatric formulation, and cost

may account for the lack of adequate pediatric information.

9. How much will this cost drug manufacturers?

The costs of pediatric studies will be less than 1% of the total costs of developing a drug. FDA estimates that the total annual industry costs will be less than $20 million per year (for a multi-billion dollar industry).

10. Will drug prices increase as a result of this regulation?

Because the cost of pediatric studies to manufacturers is expected to be small, it is anticipated that there will be little or no price increases to patients

11. Does this regulation cover all drugs?

It covers all drugs that are widely used in, or important to, children.

12. Will this requirement hold up drug approvals?

No, the proposal allows for postapproval submission of pediatric data if concerns about pediatric testing arise prior to approval. Additionally, the requirement may be waived in certain cases.

13. How will these waivers work and won't they make the regulation meaningless?

The waivers are only intended to be used in those cases in which the drug would not be widely used and would not represent a meaningful benefit over existing treatment or where the study(ies) are impossible or highly impractical or pose undue risks to pediatric patients.

14. Why doesn't it cover medical devices? Do we not have this kind of problem with medical device pediatric data?

Once the agency gains experience in requiring pediatric studies for drugs and biologics, it may decide to require them for devices.

15. What kind of improvement can we expect in our childrens' health as a result of this regulation?

We expect safer and more effective medicines for children. The primary benefits expected are the reductions in avoidable adverse drug reactions and under or over treatments that would result from better informing health care practitioners about whether, and in what dosages, a given drug was safe and effective for use in children.

16. When will this regulation go into effect?

There is a 90 day period for comment on the proposed rule after which the agency will evaluate and respond to the comments and publish a final rule. The final rule will take effect 2 years after

issuance for new drugs. For drugs already on the market, 3 months after issuance, the agency in compelling circumstances may request that pediatric studies be initiated.

17. What kind of "legal action" can FDA take to force companies to provide this data on approved drugs?

FDA can go to court and ask the court to require the company to comply with the regulations. If the company does not comply, the court can impose penalties.

18. Would pediatric study participants' lives be at risk without having all the adult data from the start?

Pediatric participants are not enrolled in studies until enough data on the drug have been obtained so that the risk to the pediatric participants is low