PEDIATRIC LABELING EVENT

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Use of Antidepression Medicine - Young Patients Has Soared

..olster Market, Makers Seek F.D.A. Sanction

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By BARBARA STRAUCH

The Long Island girl is nearly 15 years old, and she has been taking Prozac since she was 5.

Before Prozac, she was a mess. She could not be left alone, even for minutes. Strangers terrified her, and she was obsessed by thoughts that her parents were dying or burglars were breaking into her house. Conventional therapy failed, said the girl's mother, who spoke on the condition that she and her daughter not be identified.

But after taking Prozac, the girl was transformed. Today, she is in her school's honors program.

In the decade the girl has taken Prozac — now in its 10th year on the market and the most popular antidepressant ever in the United States — the drug was never approved for children. No antidepressant has ever been formally cleared for children or adolescents.

But that could be about to change. The drug company that makes Prozac, Eli Lilly, recently submitted data on the drug to the Food and Drug Administration in an effort to have it approved for children. The agency has asked for more information.

Companies making similar new antidepressants, most of which regulate mood by adjusting the brain chemical serotonin, are gathering information and conducting pediatric studies in hopes of getting Federal approval for use of their drugs in children.

...Kline Beecham is analyzing ...om two large studies of its ...il, on adolescents. The Bris...s Squibb Company is doing a ...f Serzone and the American ...me Products Corporation is testing Effexor.

F.D.A. approval is, in fact, not necessary. Once the agency approves a drug for sale, doctors can prescribe it to anyone for any purpose. So the new medications have quietly flowed into the children's market. But the agency's approval of an antidepressant for children would be a tremendous marketing lift for the drug.

Continued on Page 24

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drug.

Last year, nearly 600,000 children and adolescents were prescribed Prozac, Paxil or Pfizer's Zoloft, the most common of the new drugs, according to IMS America Ltd., a research concern. Prozac prescriptions for those 13 to 18 years old increased 47 percent last year. Over all, Prozac sales totaled $1.73 billion in the United States in 1996, Eli Lilly said.

But the adult market for the drugs has become saturated. New adult prescriptions for Prozac fell 5 percent last year and 2.7 percent the year before, after increasing 13 percent in 1994. Companies are looking for customers. Formal F.D.A. clearance of antidepressants for children would mean companies could directly market them for use by children.

"It would be a positive," said Barbara Ryan, managing director of Alex. Brown & Sons, who analyzes the pharmaceutical industry. "The companies are looking for expanded markets."

Critics worry, though, that not enough is known about how antidepressants work on the growing brain and that cost-conscious insurance companies will turn too quickly to drugs instead of costly conventional psychotherapy. Others fear that formal approval could encourage excessive prescriptions of the drugs or even accidental overdoses, especially because some companies are already preparing them in mint and orange-flavored liquid versions.

"Depressed kids need all the help we can give them," said Dr. Leon Eisenberg, professor of social medicine at Harvard Medical School. "But even a good drug can be abused; look what happened with Ritalin. The availability of the pill has allowed doctors to disregard the importance of trying to find out what's going on with these kids."

Ritalin is a widely prescribed drug used to treat attention deficit disorders or related problems in childhood, and many children have used it for years. Some critics see this pattern as an abuse of the drug.

Marsha Levy Warren, a Manhattan clinical psychologist, said that she was worried that F.D.A. approval of antidepressants for the young might mean teen-agers would be medicated just for acting like teenagers and that by promoting drugs without counseling, children would get the wrong message.

"If we are giving them medication to stabilize their moods," Ms. Warren said, "they may not be able to handle the ebb and flow of emotion that is part of life."

But for the mother of the Long Island girl, F.D.A. approval would be a long-awaited vindication.

"It's scary enough to give your child medication," said the mother, a social worker, "but to give something that isn't approved is even scarier. There was no research and I was against medication. But now I'm a believer; I look at people with mental problems and say, 'Hey, why don't you take this drug?' "

Her daughter's psychiatrist, Dr. Harold S. Koplewicz, a professor of clinical psychiatry at New York University School of Medicine, has had dozens of children on the new antidepressants. The author of "It's Nobody's Fault" (Times Books, 1996), on brain disorders in children, he acknowledges that depression is difficult to diagnose in children and counseling should be tried first.

But, Dr. Koplewicz said, children's depression remains undertreated and underdiagnosed, and medication can be lifesaving. Far from encouraging drug use, he said, treating depression with medicine can "keep kids from medicating themselves with feel-good drugs" that are illegal. "If a child truly has depression, medication should be considered as part of the treatment," Dr. Koplewicz said. "This is no Prozac party; these drugs only work if you need them."

Dr. Peter Jensen, chief of the child and adolescent disorders research branch of the National Institute of Mental Health, said rates of both adolescent depression and suicide had risen over the last decade, with the teen-age suicide rate now equaling that of adults. "We don't want to leave these kids as therapeutic orphans," Dr. Jensen said. "This is an urgent public health concern."

Even after 10 years of Prozac, however, the psychiatric field remains divided. Counseling is considered crucial, but there are worries that doctors are being pushed to prescribe drugs too quickly for a growing variety of ailments from depression and obsessive-compulsive disorders to even extreme shyness. Already, many complain about pressure from health maintenance organizations in favor of relatively low-cost drugs over counseling and hospital stays.

"But a drug that works coupled with the financial crunch on a health provider could be a problem," Dr. Eisenberg said. "Managed care and psychotropic drugs are a Satanic mix."

Drug companies have been reluctant to try earlier antidepressants on children because of their more severe side effects, like heart irregularity. The few studies that had been done on the early antidepressants and children showed that the drugs were no better than dummy pills. And until about 15 years ago, no one thought children could suffer depression. Now, experts estimate that about four million American children — or 5 percent — suffer depression.

Lately, researchers have begun studying how children respond to the newer drugs, called selective serotonin reuptake inhibitors, or S.S.R.I.'s. Prozac, the first of the new class, was initially criticized for possibly inducing suicide in adults. Those concerns have eased, and researchers say there have not been any documented cases of newer antidepressants pushing children to suicide. Some case studies have suggested that all the S.S.R.I.'s can sometimes cause restlessness and impulsive behavior or even mania. But because they have less effect on the heart, there is much less fear of a lethal overdose.

F.D.A. officials say that so far they have not received reports from doctors that would have raised a red flag about the use of Prozac by children.

Doctors like Donna Moreau, director of the children's anxiety and depression clinic at Columbia Presbyterian Medical Center, see clear results with drugs like Prozac. About 50 percent of severely depressed children get better with six weeks of psychotherapy, Dr. Moreau said. But for the rest, drugs, usually given along with counseling, seem to help, she said, adding, "I'm convinced it's the medication working."

Still, only one major study has shown the drugs are effective on children. Conducted over eight weeks by Dr. Graham Emslie, professor of psychiatry at the University of Texas Southwestern Medical Center in Dallas, the study found that out of 96 children, half got better taking Prozac, compared with one-third taking a dummy drug, similar to results in adult studies.

Within a year, 17 children in the study had relapses and three developed mania, possibly part of their original illness. About half those who suffered relapses were taking the drug and half were not.

"Clinically, we've felt these drugs were helpful, but no one had shown it," Dr. Emslie said. His research is to be published this fall in the journal Archives of General Psychiatry.

But such studies do little to quiet concerns about long-term effects on developing brains. Although most adult drugs have never been specifically tested on children, there is added worry about antidepressants because they are often taken for years. Also, it can be difficult to calculate the correct dosage for children. And with so many new drugs, some children, like some adults, are mixing medications.

"We're flying by the seat of our pants," concedes Dr. Bruce Waslick of the New York State Psychiatric Institute and Ruane Center in Manhattan, who is also studying Prozac and adolescents. "But with severely ill kids, families want us to try something. We can't just say come back in 20 years."

That is, of course, exactly the problem faced by the F.D.A. Dr. Paul Leber, director of the agency's division of neuropharmacology, calls consideration of antidepressants for children a "difficult issue" of such "importance and public interest" that it is likely to be discussed with the agency's outside advisers. Evidence from studies with children is still "weak and inconsistent," Dr. Leber said.

Dr. Thomas Laughren, the agency's head of psychiatric drug products, added: "Children are undergoing physiological changes and may be particularly vulnerable to the effects of drugs. Unfortunately, it's difficult to obtain long-term data to determine if adverse findings are drug related."

The New York Times
Sunday, August 10, 1997

President to Order Drug Makers to Conduct Pediatric Studies

By ROBERT PEAR

WASHINGTON, Aug. 12 — President Clinton will order changes in the testing of prescription drugs to insure that manufacturers specifically examine the drugs' effects on children if the medications are to be used by any significant number of young patients, White House officials said today.

The officials said they decided to require such studies because drug companies were not doing enough pediatric studies on their own.

Mr. Clinton will announce the new policy on Wednesday at the White House, the officials said.

Chris Jennings, a White House aide who coordinates health policy, said: "Medications used for pediatric populations have been woefully and inadequately tested to date. Only 42 percent of drugs that have proved highly useful in pediatric populations have been tested on children."

The order is the latest example of the Clinton Administration's emphasis on protecting children. Mr. Clinton recently persuaded Congress to create a health insurance program for children. Under his direction, Federal agencies are trying to halt the sale of tobacco to minors and to protect children from environmental health hazards, sex and violence on television, and liquor advertising.

Under a rule to be issued on Wednesday by the Food and Drug Administration, Mr. Jennings said, "we will require drug manufacturers to conduct studies to determine the safety and appropriate dosage levels for any prescription drugs used widely by children."

In addition, he said, "we will require appropriate labeling" to reflect the results of those studies.

Alan F. Holmer, president of the Pharmaceutical Research and Manufacturers of America, a trade association for drug companies, said the industry would work with the Government in a cooperative spirit.

"I would expect that there would be some increase in testing of drugs in children as a result of this regulation," he said, "but it's hard to determine the precise magnitude until we have a chance to see the text of the regulation."

Dr. John D. Siegfried, deputy vice president of the association, said it might be difficult for drug makers to recruit children for clinical trials.

"F.D.A. assumes that thousands of children are willing to be tested and that their parents are willing to have them tested," Dr. Siegfried said. "But in reality, there are not a lot of parents who want their kids to be in clinical tests just for the sake of satisfying the Government."

In addition, he said, children of different ages may react differently to the same dose of a particular drug. So the studies will be difficult to design.

Under the proposed regulation, drug companies would not have to evaluate a new drug in children if it was "impossible or highly impractical" to do so.

Explaining why the White House had decided to act now, Mr. Jennings said: "In the last few years, we have requested the pharmaceutical industry to provide this information and to put it on drug labels. Unfortunately, we have had a fairly low success rate in getting the companies to do it voluntarily."

Many drugs used by children, including asthma medications and antibiotics, have not been specifically studied in children or approved for use in children. They are approved for adults and prescribed for children, for uses not specifically recognized on the labels.

Mr. Holmer said drug trials for children must not delay the development, approval and marketing of drugs for adults.

But Donna E. Shalala, the Secretary of Health and Human Services, said: "Children are not simply small adults. Under the new rule, manufacturers of drugs likely to be used by children will be required to complete studies and place information on drug labels to help physicians make scientifically based decisions when prescribing drugs for children."

In addition, Mr. Holmer said, drug companies will have to conduct new studies of some drugs already in wide use among children.

Dr. Robert M. Ward, a professor of pediatrics at the University of Utah and chairman of the American Academy of Pediatrics' committee on drugs, welcomed the President's initiative.

"This is one of the most important advances for pediatric drug therapy in several decades," Dr. Ward said in an interview. "It will improve the information that doctors have available to them when they select and prescribe medications for children."

For example, Dr. Ward said, "Patients with asthma are often treated with steroids taken through an inhaler. These are among the most effective treatments available for asthma. But drug companies have not spent the money or the time to study these drugs in large groups of children and to submit the data to the F.D.A."

Susan DeLaurentis, a co-founder of the Pediatric AIDS Foundation, praised the new rule.

"Drug companies will be required to evaluate the safety and dosing of drugs that will be used in children," she said. "They are not required to do that now. This is a huge change. It's fantastic."

White House Talks Seen Likely on Medicaid Cut

By JAMES DAO

ALBANY, Aug. 12 — Advisers to President Clinton said today that the White House was prepared to open negotiations with the Pataki administration to resolve a dispute that had jeopardized the payment of hundreds of millions of dollars in Federal Medicaid money to the state.

The three-year-old argument came to the forefront on Monday when the President used his new line item veto powers to delete a Federal budget provision intended to preserve rules that have allowed New York State to collect up to $2.6 billion in Federal Medicaid matching funds since 1992. State officials say they are concerned that the veto will lead to a reduction in Federal Medicaid payments to the state by $200 million or more in the coming year.

Because the Medicaid funds in dispute have helped finance health care programs for the poor, Mr. Clinton's veto came under intense attack by state labor leaders, hospital officials and political leaders in both parties today, many of whom said they had already begun lobbying blitzes to persuade the President to reverse his action.

Amid the protests, Chris Jennings, deputy assistant to the President for health policy, said that he would attempt to convene a meeting between budget and health care advisers to the President and aides to Mr. Pataki and Mayor Rudolph W. Giuliani within the next several weeks.

"We will do everything we possibly can to work this out," Mr. Jennings said.

His remarks came as an array of Democratic and Republican officials denounced Mr. Clinton's inaugural use of the line item veto, saying it was inappropriate and vowing to challenge it in court.

At City Hall, Mr. Giuliani, appearing with several Democratic members of Congress, said that if Mr. Clinton did not reverse his action, the city would start a lawsuit challenging the constitutionality of the line item veto. "I think the case is a very strong one," the Republican Mayor said.

In Albany, aides to State Comptroller H. Carl McCall, a Democrat, said that he had spoken today to Clinton Administration officials, including Treasury Secretary Robert E. Rubin, urging them to resolve the dispute quickly and in a way that would not be costly to the state.

"The Comptroller believes the President was wrong to have singled out New York and vetoed this provision," said Steven Greenberg, a spokesman for Mr. McCall.

The New York Times

Clinton Wants Drug-Safety Tests for Children

By Laurie McGinley
Staff Reporter of The Wall Street Journal

In a major change in the nation's drug-approval policy, President Clinton will propose today that new drugs likely to be prescribed for children should first be

PHARMACEUTICALS

tested on kids for safety, dosage and, in some cases, effectiveness.

The policy could pose a quandary for the drug industry, which would face new research costs but can't afford to appear insensitive to children's needs. Alan Holmer, president of the Pharmaceutical Research and Manufacturers of America, the industry's Washington-based trade group, said manufacturers are committed to increasing their pediatric testing but questioned whether a government mandate is needed.

The drug-testing proposal follows an increasing clamor from children's health experts about what they see as a growing problem: Drugs commonly used for kids often don't – and, indeed, aren't required to – undergo pediatric testing. In the case of new AIDS drugs, doctors have been reluctant to prescribe them to children because they don't know how the drugs, which have severe side effects, will work.

Only about 40% of drugs considered highly beneficial for young patients undergo pediatric testing, including medications for such common childhood ailments as asthma, allergic reactions and ear infections, administration officials say. Only about 20% of the drugs on the market have been tested on children.

While pediatricians often prescribe drugs that haven't been studied in children, they frequently lack important information on precisely how much medication to use and how it will affect their patients.

As a result, physicians are sometimes forced to choose between "prescribing drugs without well-founded dosing and safety information or utilizing other potentially less effective therapy," says a copy of a draft Food and Drug Administration rule. In fact, administration officials say, the percentage of drugs tested on children is decreasing, and is largely absent for children under two years of age. In the case of AIDS, only five of the 11 approved drugs have been tested in children.

The administration estimates the plan would cost the drug industry between $13.5 million and $20.9 million a year. Part of that reflects a requirement that manufacturers develop drug formulations, such as liquids, that could be used by children.

Mr. Holmer of the drug makers' group called the administration's cost estimate too low. "It widely misses the mark and fails to reflect the enormous scientific difficulties that are often involved" in conducting pediatric tests and developing formulations for children, he said.

Industry officials say that pediatric trials are particularly challenging because parents are often reluctant to enroll their children. Another problem: The tests may have to be repeated in children of different ages to get enough useful information.

But health groups and administration officials note that drug companies have been conducting safe clinical trials involving children for years. "Safety isn't a concern," says Susan DeLaurentis, co-founder of the Pediatric AIDS Foundation, a Santa Monica, Calif., group that has pushed hard for increased pediatric testing. She notes that both the American Academy of Pediatrics and the federal government have issued guidelines on how to conduct such tests ethically. And other AIDS activists say the regulation virtually ensures that manufacturers developing the next generation of AIDS drugs conduct pediatric testing before seeking FDA approval.

The Clinton administration's plan would require prescription drug makers to submit pediatric data to the FDA when they apply for approval to sell the drugs to adults, or shortly after approval is granted. The rule would cover drugs that are expected to be a significant advance for children and medications likely to be taken by more than 100,000 children a year. The FDA expects 12 of the new drugs it approves each year to trigger the requirements, and it would decide which they were.

While manufacturers that don't comply would face court action and fines, they

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wouldn't be threatened with drug-approval delays or product recalls – enforcement actions the administration rejected as unethical.

For drugs already on the market, manufacturers would be required to submit pediatric information if there were "compelling circumstances" – for example, if the drugs could help children but weren't being used because of a dearth of data. In cases where children and adults are affected similarly by a disease, companies would have to test a drug for safety and dosage but not perform more elaborate effectiveness testing.

Some drug companies are already testing their drugs in children. A Glaxo Wellcome PLC spokeswoman says the company includes pediatric studies for its HIV drugs, among others. Glaxo also tested its drug Ultiva, an analgesic used in anesthesia procedures, in children two and older, and it is now testing the drug in children ranging in age from newborn through 18. Various forms of Glaxo's asthma drug, Ventolin, are approved for children as young as two, she adds.

SmithKline Beecham PLC is testing its antidepressant, Paxil, in young people, a spokesman says. He also notes that the company conducted pediatric trials for its leading antibiotic, Augmentin.

A spokesman for Novartis AG, the company that makes Ritalin, says the drug, to treat attention deficit disorder has pediatric approval but isn't recommended for children under six years of age. He declined to comment on the proposed requirement to test drugs in children because the company hasn't seen the proposal.

The new rule, which is still subject to change, will become effective sometime after the close of a 90-day public-comment period. Manufacturers submitting new drug applications would have between 15 and 21 months to hand in kids' studies, depending on when they filed their FDA application.

–Elyse Tanouye contributed to this article.

Drug 'quantum step' in treating heart disease

By Steve Sternberg
USA TODAY

A new drug for people undergoing coronary angioplasty cuts their risk of death, heart attack and collapsed blood vessels, but it may be too costly for all but the sickest people.

The anti-clotting drug, abciximab, reduced the one-year death rate by 19% and the three-year death rate by 13% overall, researchers say.

The drug worked best in the sickest people: one 12-hour intravenous infusion cut the death rate by 60%.

"We have never seen any drug that has a lasting impact on patients undergoing angioplasty," says lead investigator Eric Topol, of the Cleveland Clinic Foundation.

About 1 million people each year undergo coronary angioplasty in which a balloon is opened inside an artery to clear a blockage. For half, the newly opened arteries collapse by the first anniversary of treatment.

Like aspirin, the new drug prevents blood clots from forming and may also block inflammation within blood vessels, reducing the odds that a newly cleared artery will collapse.

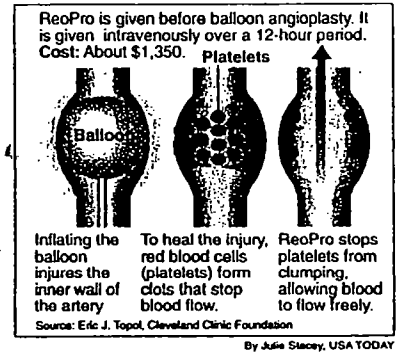
The new drug, says Topol, "takes aspirin a quantum step further."

The drug, which is sold as ReoPro, is in the vanguard of a powerful new class of drugs that prevent clot-forming red blood cells from clumping.

David Fischman of the Jefferson Medical College in Philadelphia says researchers are now also trying to make oral versions of these drugs.

The study is an extension of an earlier one. In the new trial, doctors measured the drug's long-term benefit in 2,001 people; half got abciximab before angioplasty, half a placebo. The findings are in today's *Journal of the American Medical Association*.

The drug, made by Centocor Inc. of Malvern, Pa., costs $1,350. Since it appears to work best in the riskiest patients, Fischman notes in a companion editorial that it may be too costly to use in low-risk patients.



Clinton to seek more tests on drugs given to kids

By Steve Sternberg
USA TODAY

President Clinton today will propose a new regulation requiring drug makers to study adult medicines that are routinely given to children and label them with pediatric doses.

The rule would go into effect next year.

Only 42% of the drugs that have been proven effective in children were tested in children before they were approved for marketing.

As a result, most do not include pediatric doses on the labels, officials say.

"Pediatricians who need this information to make informed judgments about prescribing are left blind about what course of treatment to pursue," says Christopher Jennings, Clinton's health policy adviser.

Guesswork is particularly risky when doctors are prescribing potent medication to small children with such diseases as AIDS, asthma, arthritis and diabetes, he says.

The industry has resisted Food and Drug Administration efforts to generate more information on pediatric doses and include them in labeling.

"We believe that there is a very extensive amount of testing of children ongoing," says Alan Holmer, president of the Washington-based pharmaceutical trade group Pharma. "We question whether a formal government mandate is needed."

He added, however, that the drug manufacturers are anxious to work with the administration to refine the proposed regulation. "We want to try to make sure the regulation that's implemented is one that achieves the goals we all share, better medicines for children."

Companies now seeking FDA approval to market an experimental drug do most of their testing in adults unless the drug is specifically intended for children.

Under the proposed regulation, the FDA would determine if a drug has potential for use in children. If so, it could order the company to develop a plan for appropriate testing.

FDA action would not slow approval of the drug for adults, and it would not take years, officials said. It would, however, involve a few months of tests to determine the proper dose for children. The dose would be added to the drug's label.

"The order is the latest example of the Clinton Administration's emphasis on protecting children. Mr. Clinton recently persuaded Congress to create a health insurance program for children. Under his direction, Federal agencies are trying to halt the sale of tobacco to minors and to protect children from environmental health hazards, sex and violence on television, and liquor advertising."

-Robert Pear,
New York Times
August 13, 1997

One-Pager

President Clinton Continues to Fight to Improve the Health of Our Nation's Children

Children and Prescription Drug Testing. Today's announcement requiring manufacturers to do studies on pediatric populations for new prescription drugs and those currently on the market builds on an impressive array of children's initiatives advocated by President Clinton.

- **Children and Insurance Coverage.** The President fought hard to ensure that the Balanced Budget Act included $24 billion -- the largest investment in children's health care since the passage of Medicaid in 1965 -- to provide meaningful health care coverage to as many as five million of our nation's uninsured children. He also fought to include revenue from a 20 cent tobacco tax which will not only further reduce the number of uninsured children, but it will also serve as a financial barrier to help prevent our children from starting to smoke in the first place.

- **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 Insurance Reform.** By signing the Kassebaum-Kennedy bill into law last year, the President helped millions of American children keep their health care coverage when their parents lose or change jobs.

Children and Juvenile Diabetes. The President fought to include $150 million ($30 million annually for five years) for research to help find the cure for diabetes. Americans with this disease often suffer severe consequences, such as blindness and kidney disease, even when they receive the best treatment and care. The HHS Secretary will have discretion to target the new funds toward the best scientific opportunities. This represents the largest single new investment in Juvenile Diabetes.

- **Children and Immunization.** As the President recently announced, over 90 percent 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 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.

Two-Pager

PRESIDENT CLINTON ANNOUNCES NEW MEASURES TO INCREASE AVAILABILITY OF INFORMATION ON SAFE USE OF MEDICATIONS USED TO TREAT CHILDREN

August 13, 1997

Today, President Clinton unveiled a new FDA regulation that will protect children by requiring manufacturers to study the safety and appropriate dosage levels of drugs for pediatric populations. The regulation also requires proper labeling of drugs for use in children. Even though many drugs affect children differently than adults, most drugs have not been tested on pediatric populations. Under this rule, manufacturers of prescription drugs likely to be used by children will be required to complete studies and place information on drug labels to help pediatricians and other health care providers make scientifically-based treatment decisions when prescribing drugs to children.

WHY THIS REGULATION IS NEEDED

Most drugs -- even those commonly used in children -- have not been widely tested on pediatric populations. According to the American Academy of Pediatrics, only a small fraction of drugs and biological products marketed in the United States have had clinical trials performed in pediatric patients. Despite evidence that drugs affect children differently than adults, 80 percent of all drugs marketed in the United States have been labeled for use by infants, children, and adolescents. Forty-two percent of drugs that are widely used in pediatric populations have been tested on children.

- Many drugs commonly given to children under the age of six including Prozac, Zoloft, Ritalin, and drugs for asthma, allergic reactions, and ear infections are inadequately tested and labeled for use in children. These drugs, taken together, are given to over five million children each year.

- Less than half of the drugs used in the treatment of HIV infections carry any safety or effectiveness information for children. Of those that do, the data is often incomplete.

- Safety and effectiveness information is especially sparse for the over seven million children under the age of two.

- The percentage of drugs being tested on children decreased by over one-third between 1996 and 1991.

Drugs are likely to have a different impact on children than on adults. The appropriate use and dosage levels of medication for children and adults is usually different because of disparities in organs, the immune system, and metabolism.

Children who take prescription drugs that have not been tested on pediatric populations are at serious risk for unexpected adverse reactions. Evidence suggests that prescribing drugs that have not been adequately tested on children can be extremely dangerous. One example of the possible harm is the case of "gray baby syndrome" where a number of babies died from chloramphenicol, an antibiotic that their immature livers were unable to accept. Other children had withdrawal symptoms from prolonged administration of fentanyl, a pain killer used as an adjunct to anesthesia in infants and small children. Still others have suffered seizures and cardiac arrest from bupivacaine, a local anaesthetic not adequately tested in pediatric populations.

Some physicians are reluctant to prescribe much needed therapies to children because they have not been tested on pediatric populations. Physicians report that they have denied children important new drugs because, in the absence of adequate testing and labeling, they would have to guess at an appropriate dosage, and they do not want to take that risk. As a result, too many children do not receive the treatment they need and deserve.

SUMMARY OF THE RULE

Pediatric Studies for New Drugs. Under this proposed rule, manufacturers of new drugs would have to do studies on pediatric populations under two circumstances: when the product represents a meaningful therapeutic benefit over existing treatments; or when the product is expected to be widely used on pediatric patients. The FDA anticipates that about twelve new drugs each year would meet this requirement. Manufacturers could receive waivers from the requirement to do a pediatric study under any one of the following circumstances:

(1) The product does not represent meaningful benefits over existing treatments and is not likely to be used on a substantial number of pediatric patients as a whole; or

(2) Necessary studies are impossible or highly impractical-- i.e., the number of patients is too small or geographically diverse; or

(3) There is evidence strongly suggesting that the product would be unsafe or ineffective in pediatric populations.

Pediatric Studies For Existing Drugs. For drugs that are already on the market, the new FDA regulation requires additional testing on the pediatric population only if there is a "compelling need for more information." The criteria used is:

(1) If the product is widely used in pediatric populations and the absence of adequate labeling could pose significant risks to pediatric populations; or

(2) If the product is indicated for very significant or life threatening illness, but additional dosing or safety information is needed to permit its safe and effective use in pediatric patients.

Event Memo

THE WHITE HOUSE

WASHINGTON

August 12, 1997

PEDIATRIC DOSAGE AND LABELING ANNOUNCEMENT

DATE:	August 13, 1997
LOCATION:	Rose Garden
BRIEFING TIME:	1:15 pm - 1:35 pm
EVENT TIME:	1:45-2:15 pm
FROM:	Bruce Reed

I. PURPOSE

To demonstrate your commitment to children's health issues by announcing a new FDA regulation to improve the safety of pediatric drugs.

II. BACKGROUND

You will be unveiling a new FDA regulation that will require drug manufacturers to study the effects of drugs on children. The regulation will apply both to certain new prescription drugs and to certain drugs currently on the market. Under this regulation, drug manufacturers will be required to complete clinical studies and place information on drug labels to help physicians make informed decisions when prescribing drugs to children.

Although children have distinct needs with regard to doses and potential side-effects of medications, most drugs have not been tested on pediatric populations. Currently, only 42 percent of drugs are tested on children. As a result, physicians are reluctant to prescribe many drugs to children because they do not want to risk giving an inappropriate dosage.

There are at least ten drugs used by millions of children that do not have adequate labeling. These include Prozac, Zoloft, Ritalin, and drugs for asthma, allergies, and ear infections. In addition, less than half of the drugs used in the treatment of HIV are being studied on children. The Pediatrics AIDS Foundation has lead the fight for this new regulation on behalf of the 10,000 to 12,000 children with HIV.

Representatives from the Pediatric AIDS Foundation, the National Association of Children's Hospitals, the American Academy of Pediatrics, and other children's health organizations will be in attendance.

III. PARTICIPANTS

Briefing Participants
Secretary Shalala
Bruce Reed
Chis Jennings
Jennifer Klein
Maria Echaveste

Events Participants
Vice President
First Lady
Secretary Shalala
Parent of child with asthma

Meet and Greet Participants (Prior to Event)
Bill Schultz, Deputy Commissioner of the FDA, and family.
Mike Freedman, Acting FDA Commissioner, and family.
Dr. Joseph A. Zanga, Vice President, American Academy of Pediatrics
Susan DeLaurentis, Co-Founder, Pediatrics AIDS Foundation
Francesca DeLaurentis, daughter
Lawrence McAndrews, President and CEO, National Association of Children's Hospitals

IV. PRESS PLAN

Open Press.

V. SEQUENCE OF EVENTS

- You will be announced onto the stage accompanied by stage participants.
- The First Lady makes welcoming remarks and introduces Secretary Shalala.
- Secretary Shalala makes remarks and introduces the Vice President.
- The Vice President makes remarks and introduces parent of child with asthma.
- Parent makes remarks and introduces you.
- You will make remarks and then depart.

VI. REMARKS

Remarks Provided by Lowell Weiss in Speechwriting.

Quotes

SUPPORTERS OF THE PRESIDENT'S INITIATIVE ON PEDIATRIC LABELING

PROVIDERS

American Academy of Pediatrics
American Academy of Family Physicians
American Medical Association
National Association of Children's Hospitals
National Association of Pediatric Nurse Associates and Practitioners, Inc.
American College of Physicians

CONSUMERS

American Foundation for AIDS Research
American Lung Association
American Thoracic Society
Pediatric AIDS Foundation
Juvenile Diabetes Foundation International
National Organization for Rare Disorders
Center for Medical Consumers
National Medical Association

PHARMACY

National Association of Chain Drug Stores

OTHER VALIDATORS

C. Everett Koop, M.D., Sc.D.
Senator Barbara Boxer

QUOTES SUPPORTING THE PRESIDENT'S ANNOUNCEMENT ON PEDIATRIC LABELING

"I am writing to applaud the efforts of you and your Administration on children's pharmaceuticals. After long years of working with inadequate data, the nation's physicians, pharmacists, and parents will finally have solid information about the safety and dosing of medicines for children...I know how desperate families can become when their sons and daughters are sick...The policy you are proposing would create a new and better choice: drugs that have been studied for pediatric use. You should be congratulated on taking this step."

-- C. Everett Koop, M.D., Sc.D.

"The American Academy of Pediatrics enthusiastically applauds President Clinton's efforts to ensure that children will no longer be "therapeutic orphans." The availability of medication approved for infants, children and adolescents just took a much needed step today, and the President is to be commended."

"Currently, only 20 percent of all drugs marketed in the United States have been labeled for use by infants, children and adolescents. As a result, pediatricians must prescribe drugs based on information from limited medical studies, rather than more comprehensive clinical trials in children."

"For children, we label the food they eat and the television shows they watch. However, when it comes to prescribing children's medicine, information about how much and how often to give it to them is sorely lacking."

"The impact of these proposed regulations, properly implemented, cannot be understated. Pediatricians and other health care professionals will now be armed with more precise information that takes into account various ages and stages of child development so that the best drug, at the right dose, can be prescribed."

-- American Academy of Pediatrics

"On behalf of the 85,000 members of the American Academy of Family Physicians, I would like to commend you for your initiative to improve labeling of drugs prescribed for children. Your proposed regulation will help ensure that our nation's children receive safe and effective medications."

"We are highly supportive of an initiative that will provide family physicians with additional information to use as we prescribe drugs for children. America's family physicians stand ready to assist you in implementing an initiative that will be of enormous benefit to our youngest patients."

-- American Academy of Family Physicians

"Product labeling information that would provide all health professionals with readily accessible information about proper dosage for the use of adult medications by children would further assist pharmacists and other providers in determining the appropriate use of these medications for children. We strongly support efforts that would increase the amount of useful information available to health care providers in treating and counseling patients."

-- National Association of Chain Drug Stores

"The American Medical Association today celebrates President Clinton's proposal to make more information on using drugs to treat children available to physicians. We applaud President Clinton for this initiative, and for all his hard work in the area of children's health."

"Currently only about 20% of all prescription drugs marketed in the U.S. are labeled specifically for use by children. As a result, many physicians prescribe drugs for children based on limited research, and without comprehensive information based on clinical trials with children. We hope today's move will dramatically increase the amount of information available, allowing physicians to more confidently treat children using a wider range of prescription medications."

-- American Medical Association

"The Administration has taken an important first step towards ensuring that American children receive the very best pharmaceutical care in the world. The generic industry applauds the White House for its strong public support of this initiative."

-- Generic Pharmaceutical Industry Association

"For too long the routine course has been that drugs will be tested only for adult use and that parents, pediatricians, and pharmacists will be left without solid data on which to base decisions regarding treatments for a sick child. I am pleased that these regulations will finally address this deficiency."

-- Senator Barbara Boxer

"Today's announcement will change history. From now on, children will not be automatically left out. From now on, it will be rule that drugs are tested for children, unless there's a good reason not to. Once again you have demonstrated that this is an Administration that truly cares about children."

-- Pediatric AIDS Foundation

"The National Association of Children's Hospitals (N.A.C.H.), representing more than 100 children's hospitals across the country, strongly commends the Clinton Adminstration's recognition of a serious failing of the health care market place -- the absence of adequate market incentive or requirements for testing and labeling of pharmaceutical products for use by children."

"Three weeks ago, in a hearing before the Senate Public Health and Safety Subcommittee, a number of the nations' leading pediatric researchers cited the serious lack of pharmaceutical products tested for children' use as one of the most important challenges facing the pediatric health care community in its efforts to convince the nation of the need for increased investment in research devoted to children's illnesses and conditions."

"As parents and pediatric providers understand all too well, children are not miniature adults. Their health care needs are not appropriately met by providing either adult-sized treatments or even miniature versions of them. All too often, our children's care givers must rely only on their personal judgement in deciding which drugs and which dosages are best suited for their patients."

-- National Association of Children's Hospitals

"The Juvenile Diabetes Foundation International (JDFI) applauds President Clinton's leadership in attempting to improve the health care of all children, particularly those who suffer from diabetes. This announcement demonstrates an important understanding that children are not simply small adults, and therefore may require additional measures to ensure that they receive the best possible treatments currently available."

-- Juvenile Diabetes Foundation International

"A physician's clinical decisions must be based on scientific evidence, and the Administration's action will take us another step towards evidence-based medical practice."

-- American College of Physicians

"Your new FDA regulation requiring pediatric data on new drugs is long overdue and essential to the well being of ill children throughout the nation. It is vitally important that henceforth manufacturers will be required to include children in clinical trials, and that data from pediatric studies will be included on pharmaceutical labeling."

"Mr. President, on behalf of the millions of American children who are afflicted by rare disorders, most of which are genetic, we are truly grateful for your leadership and concern for improving the lives of America's children."

-- National Organization for Rare Disorders, Inc.

"Prescription drugs are used to treat all segments of the population, yet the clinical trial experience on which their approval is based often excludes the very young and the very old. once a drug is marketed, however, it is widely prescribed even though the thresholds for safety and effectiveness may differ among age groups. It is time to stop putting children unnecessarily in harm's way by improving the information required on drug labeling pertaining to pediatric use."

-- Center for Medical Consumers

"We greatly appreciate the Administration's effort to ensure that pharmaceuticals are adequately tested in children and that such studies are used to support better labeling for pediatric drugs. Giving health care providers adequate and appropriate information about usage is crucial in ensuring the health and safety of our nation's children."

-- National Association of Pediatric Nurse Associates & Practitioners, Inc.

"Because of limitation in testing of many drugs in pediatric populations and labeling for pediatric use of specific drugs, children can be considered an underserved population for certain drug therapies. The proposed regulation requiring pediatric-use data on new drugs, with provisions pertaining to existing drugs, has the potential for improving available treatments and increasing the effectiveness and safety of treatments for this vulnerable population."

-- National Medical Association

C. EVERETT KOOP, M.D.

August 12, 1997

Honorable William J. Clinton
The President
The White House
1600 Pennsylvania Avenue
Washington, DC

Dear Mr. President:

I am writing to applaud the efforts of you and your Administration on children's pharmaceuticals. After long years of working with inadequate data, the nation's physicians, pharmacists, and parents will finally have solid information about the safety and dosing of medicines for children. I am very pleased that you have moved to require that drugs be tested for pediatric patients unless there's a good reason not to do so. This is a common-sense and workable policy that will do a lot of good.

Throughout my medical career of working with children one-by-one and my public health career of working with the children of America, I know how desperate families can become when their sons and daughters are sick. The current drug approval system usually leaves them with only two choices: Give the children drugs that have not been tested for safety or withhold a treatment that works in adults. It is an unsatisfactory choice.

Instead, the policy you are proposing would create a new and better choice: drugs that have been studied for pediatric use. It is the right policy to choose. We should ensure that children benefit from biomedical research and medical progress as much as adults do. You should be congratulated on taking this step.

Sincerely yours,

C. Everett Koop, M.D., Sc.D.

6707 DEMOCRACY BOULEVARD, SUITE 107, BETHESDA, MD 20817-1129 (301) 493-6603 FAX (301) 493-8160

BARBARA BOXER
CALIFORNIA

COMMITTEES:
APPROPRIATIONS
BANKING, HOUSING, AND URBAN AFFAIRS
BUDGET
ENVIRONMENT AND PUBLIC WORKS

United States Senate
HART SENATE OFFICE BUILDING
SUITE 112
WASHINGTON, DC 20510-0505
(202) 224-3553
senator@boxer.senate.gov
http://www.senate.gov/~boxer

August 11, 1997

The President
The White House
Washington, DC 20500

Dear Mr. President:

I write in support of your Administration's proposed regulations on children's pharmaceuticals. These new regulations have the potential to do much to improve child health in America. Your actions to raise the visibility of them will also educate parents across the nation regarding important health issues involved in giving prescription drugs to children.

For too long the routine course has been that drugs will be tested only for adult use and that parents, pediatricians, and pharmacists will be left without solid data on which to base decisions regarding treatments for a sick child. I am informed that 80 percent of drugs on the market have never been tested for safety in children, even drugs that are routinely prescribed for them. I am pleased that these regulations will finally address this deficiency.

When the FDA regulations become final, I am informed that the new presumption will instead be that drugs will be tested for children's use unless there is a reason not to. This is clearly the appropriate way to proceed.

I am particularly touched that much of this action has been undertaken in the spirit of Elizabeth Glaser, for whom I had the highest regard. From the first moment that I met her, to the time she testified before Congress at my invitation, to the last days of her life, Elizabeth worked tirelessly to get drugs and drug research for children. She was near desperation when she first discovered that the drug that she herself was taking was not available to treat her daughter, Ariel. She and the Pediatric AIDS Foundation, which she co-founded, set themselves a goal of ensuring that this does not happen again--for children with AIDS or for children with any serious disease.

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SUITE 240
SAN FRANCISCO, CA 94111
(415) 403-0100

☐ 2250 EAST IMPERIAL HIGHWAY
SUITE 545
EL SEGUNDO, CA 90245
(310) 414-8700

☐ 501 CAPITOL MALL
SUITE 1544
SACRAMENTO, CA 95814
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☐ 2500 TULARE STREET
SUITE 130
FRESNO, CA 93721
(209) 497-5109

☐ 525 B STREET
SUITE 980
SAN DIEGO, CA 92101
(619) 239-3884

☐ 290 NORTH E STREET
SUITE 210
SAN BERNARDINO, CA 92401
(909) 889-8525

I know I speak for the Foundation--and, I am somehow sure, for Elizabeth--when I thank you for your actions, congratulate you on the new proposals, and express every hope and wish that the broadest possible number of children will benefit.

Sincerely,

Barbara Boxer
United States Senator

BB/jo

F7

Q: → BOLD

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

A

OFFICE OF POLICY

REGULATIONS POLICY AND MANAGEMENT STAFF

5600 FISHERS LANE
HF-26, ROOM 12A-17
ROCKVILLE, MD 2085

FAX: 301-443-2946
PHONE: 301-443-3480

DATE: August 12, 1997

TO: Sarah Bianchi
FAX: 202-456-5557
PHONE:

FROM: Diane Sullivan-Ford

Number of Pages (including cover): 3

RE:Pediaric Labeling proposed rule - fact sheet revisions (again) and revised Qs and As.

Any questions, call me at 301-827-0870

nerican
ademy of
diatrics
hirteenth Street, N.W.
400 North
ington 20005

August 13, 1997
1:45 p.m. (EST)

Contact: Marjorie Tharp
Gem Benoza
202/347-8600
800/336-5475

PRESS STATEMENT on
CHILDREN AND DRUG LABELING
(This statement can be attributed to Joseph R. Zanga, M.D., AAP Vice President)

The American Academy of Pediatrics enthusiastically applauds President Clinton's efforts to ensure that children will no longer be "therapeutic orphans." Thanks to the proposed Food and Drug Administration (FDA) regulations, drug manufacturers will routinely conduct pediatric studies of most new and specific classes of drugs already in the market. The availability of medication approved for infants, children and adolescents just took a much needed step today, and the President is to be commended.

Several members of Congress, including former Sen. Nancy Kassebaum (R-Kan.), have long recognized the need to actively pursue this goal. We believe the proposed regulations will complement AAP-backed legislation introduced in the 105th Congress. The Better Pharmaceuticals for Children Act, sponsored by Sens. Christopher Dodd (D-Conn.) and Mike DeWine (R-Ohio), and Reps. Jim Greenwood (R-Pa.) and Henry Waxman (D-Calif.), will solidify the establishment of a drug development system that meets the unique needs of children.

Proper drug studies must be done to ensure that children receive optimal treatment. The wrong drug, or even too much or too little of the right drug, does no good and may do harm. Currently, only 20 percent of all drugs marketed in the United States have been labeled for use by infants, children and adolescents. As a result, pediatricians must prescribe drugs based on information from limited medical studies, rather than more comprehensive clinical trials in children. Adults have had the benefits of testing and labeling for over half a century. For children, we label the food they eat and the television shows they watch. However, when it comes to prescribing children's medicine, information about how much and how often to give it to them is sorely lacking. For example, asthma is the leading cause of hospitalization of children in the United States, and commonly affects children younger than age 5. Despite that, there is only one asthma drug labeled for use in children under the age of 6.

The impact of these proposed regulations, properly implemented, cannot be understated. Pediatricians and other health care professionals will now be armed with more precise information that takes into account various ages and stages of child development so that the best drug, at the right dose, can be prescribed.

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The American Academy of Pediatrics is an organization of 53,000 primary care pediatricians, pediatric medical subspecialists, and pediatric surgical specialists dedicated to the health, safety, and well-being of infants, children, adolescents and young adults.

P e d i a t r i c A I D S F o u n d a t i o n

P n with AIDS

August ..., 1997

Honorable William J. Clinton
The President
The White House
1600 Pennsylvania Avenue
Washington, D.C.

Dear Mr. President,

I want to thank you for announcing today a proposed Food and Drug Administration regulation requiring drug manufacturers to perform pediatric studies for new drugs that will be used by children. Thank you for raising this issue to the highest visibility and for taking this step to ensure that children are no longer left behind in the progress of biomedical research.

The Pediatric AIDS Foundation was established to get drugs and research for children with HIV. We have been active on this issue because children with HIV couldn't get the same drugs as their parents. My best friend and fellow co-founder, Elizabeth Glaser, was shocked to find that the drugs that were available to her were not available to her daughter, Ariel.

A decade later, that is still too often the case. Last year, there was great news for adults with AIDS--protease inhibitors offered new hope. But the hope wasn't available to kids for almost a full year later. Only this spring, two of these drugs were finally approved for older children. One was a drug that did its adult trials long before its pediatric trials--the usual story for most AIDS drugs. The other, however, was the drug manufactured by Agouron, a company that did the right thing by developing their drug for children at the same time as for adults.

But still none of these new protease inhibitors have been approved for infants and newborns. This is especially tragic since recent studies show that the most promising time to control and potentially reverse the effects of HIV could be in a newly infected newborn.

Children should not be an afterthought. Progress in research should include both adults and children. And while we have been primarily involved in AIDS, we recognize that this problem affects children with many other illnesses. So the solution should not be disease-specific. It should be for all diseases. It should be children-specific.

Today's announcement will change history. From now on, children will not be automatically left out. From now on, it will be the rule that drugs are tested for children, unless there's a good reason not to.

For that, I am grateful to you. Once again you have demonstrated that this is an Administration that truly cares about children.

Sincerely yours,

Susan DeLaurentis

Susan DeLaurentis
Co-founder

CO-FOUNDERS: Susan DeLaurentis/Elizabeth Glaser/Susie Zeegen
1311 Colorado Avenue, Santa Monica, California 90404

ciation of
Children's Hospitals

LAWRENCE A. McANDREWS, FACHE
President & Chief Executive Officer

N · A · C · H

Statement

Lawrence A. McAndrews

CHILDREN'S HOSPITALS URGE FEDERAL ACTION TO STIMULATE MANUFACTURERS' TESTING OF PHARMACEUTICAL PRODUCTS FOR CHILDREN'S USE

August 13, 1997

The National Association of Children's Hospitals (N.A.C.H.), representing more than 100 children's hospitals across the country, strongly commends the Clinton administration's recognition of a serious failing of the health care market place -- the absence of adequate market incentives or requirements for testing and labeling of pharmaceutical products for use by children.

The proposal for public comment of new regulations mandating testing of pharmaceuticals for pediatric use by the Food and Drug Administration (FDA) reflects the strong, ongoing personal commitment of President Clinton and the First Lady to public policy that helps every family meet its children's needs for health, education, safety, and security. Certainly a serious concern for any parent whose child requires medication is the realization that only about 20 percent of all of the drugs marketed in the United States have been tested and labeled specifically for use by children.

Three weeks ago, in a hearing before the Senate Public Health and Safety Subcommittee, a number of the nation's leading pediatric researchers cited the serious lack of pharmaceutical products tested for children's use as one of the most important challenges facing the pediatric health care community in its efforts to convince the nation of the need for increased investment in research devoted to children's illnesses and conditions.

These researchers included academic leaders from Children's Hospital in Boston and Le Bonheur Children's Medical Center in Memphis. They recognize that the market's failure would not be a problem if children's health care needs were identical to those of adults. But that, of course, is not the case. As both parents and pediatric providers understand all too well, children are not miniature adults. Their health care needs are not appropriately met by providing either adult-sized treatments or even miniature versions of them.

401 Wythe Sreet. Alexandria VA 22314
(703) 684-1355 Fax (703) 684-1589

All too often, our children's care givers must rely only on their personal judgment in deciding which drugs and which dosages are best suited for their patients. Because they devote such a large share of their services to children with complex conditions requiring specialized care, children's hospitals are very aware of the limited extent of testing and labeling of pharmaceuticals for children.

N.A.C.H. believes the Administration's new initiative to develop the most appropriate ways to stimulate product testing through regulation can complement the important legislation proposed by Senators Christopher Dodd (D-CT) and Mike DeWine (R-OH) plus Representative Jim Greenwood (R-PA) and Henry Waxman (D-CA) to create market incentives for manufacturers to undertake pediatric studies of new and FDA-approved pharmaceuticals. Their legislation, which has strong bipartisan support, continues the effort begun in 1991 by former Senator Nancy Kassebaum (R-KS) to persuade the Congress of the need to address the lack of pharmaceutical testing for children.

Because they represent only about 30 percent of the nation's population, less than 15 percent of health care spending, and the poorest segment of the population, children do not command the attention of the health care market for investment in research and development (R&D). This is true not just for R&D for children's health care in particular, but for all R&D related to children.

According to the National Science and Technology Council's April 1997 prepublication report on "A National Research Initiative for America's Children for the 21st Century,"

> "...(T)he share of total national R&D toward children is less than 1.2 percent. Unlike other areas of research, the Federal Government bears almost total responsibility for children. For example, the private sector provides over 50 percent of health and energy R&D funding and over 90 percent of transportation R&D. In contrast, the Federal Government provides approximately 90 percent of children's R&D."

Clearly, strengthening the federal investment in research devoted to children remains critical. But children's needs will not be fully met if the federal government alone shoulders the responsibility for pediatric research and development. Through a balanced commitment to market incentives and regulation, the federal government can stimulate manufacturers' investment in product testing to meet children's unique health care needs more fully.

Just last week, Congressional and White House commitment to bipartisanship in budget policy helped to launch the most important new federal commitment to strengthening children's health insurance coverage in a generation. We are confident that the same spirit of bipartisanship can lead to effective federal policy combining appropriate incentives and regulations to ensure the necessary testing of pharmaceutical products for pediatric use, which both children and their parents deserve.

Juvenile Diabetes Foundation International
The Diabetes Research Foundation

Government Relations

August 12, 1997

Contact: Eric Schutt (202) 371-2760

Statement Provided by the Juvenile Diabetes Foundation International (JDFI)
Regarding Proposed Regulation on Pediatric Labeling:

The Juvenile Diabetes Foundation International (JDFI) applauds President Clinton's leadership in attempting to improve the health care of all children, particularly those who suffer from diabetes.. This announcement demonstrates an important understanding that children are not simply small adults, and therefore may require additional measures to ensure that they receive the best possible treatments currently available.

1400 I Street N.W. · Suite 500 · Washington, D.C. 20005 · 202-371-9746 · Fax: 202-371-2760

"A physician's clinical decision's must be based on scientific evidence, and the Administration's action will take us another step towards evidence-based medical practice." American College of Physicians.

American Medical Association
Physicians dedicated to the health of America

Statement

FOR IMMEDIATE RELEASE

July 13, 1997

AMA CELEBRATES PEDIATRIC LABELING PROPOSAL

Stresses need for clinical research and dosage information specifically for children

Statement attributable to: Yank D. Coble, MD
Trustee, American Medical Association

"The American Medical Association today celebrates President Clinton's proposal to make more information on using drugs to treat children available to physicians. We applaud President Clinton for this initiative, and for all his hard work in the area of children's health.

"Currently only about 20% of all prescription drugs marketed in the U.S. are labeled specifically for use by children. As a result, many physicians prescribe drugs for children based on limited research, and without comprehensive information based on clinical trials with children. We hope today's move will dramatically increase the amount of information available, allowing physicians to more confidently treat children using a wider range of prescription medications.

"Although the FDA previously encouraged drug manufacturers to submit pediatric data on new drugs, today's proposal would *require* that data be put on a drug's label so physicians can make treatment decisions based on scientific information aimed specifically at their youngest patients.

"The AMA has also supported the Better Pharmaceuticals for Children Act, sponsored by Sens. Christopher Dodd and Mike DeWine and Reps. Jim Greenwood and Henry Waxman. This bill, introduced in the 105th Congress, would provide incentives to drug manufacturers who conduct pediatric studies and provide pediatric dosage formulations.

"We look forward to working with the President and Congress on future efforts to insure that America's children have the best health care possible."

#

For more information, please contact:

Brenda L. Craine
AMA Washington
202/789-7447

1101 Vermont Avenue, NW
Washington, DC 20005
202 789-7400

National Organization for Rare Disorders, Inc.®

NORD • 100 Rt. 37, P.O. Box 8923 • New Fairfield, CT 06812-8923
(203) 746-6518 • FAX: (203) 746-6481 • TDD: (203) 746-6927
http://www.nord-rdb.com/~orphan • e-mail: orphan@nord-rdb.com

...out of the darkness, into the light...

August 12, 1997

President Bill Clinton
The White House
1600 Pennsylvania Ave.
Washington, DC
Attention: Barbara Wooley

Via FAX: 202-456-6218

Dear President Clinton:

The National Organization for Rare Disorders (NORD), representing an estimated 20 million Americans with more than 5,000 rare "orphan diseases," applauds your important initiative to ensure that pediatric information is included on pharmaceutical labeling. As you are keenly aware, until now most prescription drugs have not been tested on children, and appropriate dosage information for pediatricians is absent from product labeling.

Your new FDA regulation requiring pediatric data on new drugs is long overdue and essential to the well being of ill children throughout the nation. It is vitally important that henceforth manufacturers will be required to include children in clinical trials, and that data from pediatric studies will be included on pharmaceutical labeling. The inclusion of an enforcement mechanism is vital to the success of the new regulation, ensuring that all manufacturers will obey the new rule.

Mr. President, on behalf of the millions of American children who are afflicted by rare disorders, most of which are genetic, we are truly grateful for your leadership and concern for improving the lives of America's children.

Very truly yours,

Abbey S. Meyers [signature]

Abbey S. Meyers
President

American Academy of Family Physicians
The doctors who specialize in you

2021 Massachusetts Avenue, N.W.
Washington, DC
20036-1011

(202) 232-9033
Fax (202) 232-9044

E-mail:
capitol@aafp.org
http://www.aafp.org

August 8, 1997

The Honorable William J. Clinton
The White House
Washington, DC 20500

Dear President Clinton:

On behalf of the 85,000 members of the American Academy of Family Physicians, I would like to commend you for your initiative to improve labeling of drugs prescribed for children. Your proposed regulation will help ensure that our nation's children receive safe and effective medications.

Family physicians in the United States see millions of children each year. For example, in 1993, more than 37 million office visits to family doctors included patients under the age of 17, which means that 25% of children's visits to a doctor were to a family physician. Consequently, we are highly supportive of an initiative that will provide family physicians with additional information to use as we prescribe drugs for children.

Again, thank you for initiating this important proposal. America's family physicians stand ready to assist you in implementing an initiative that will be of enormous benefit to our youngest patients.

Sincerely,

Douglas E. Henley, MD
Chair, Board of Directors

CENTER FOR MEDICAL CONSUMERS
237 THOMPSON STREET NEW YORK, N.Y. 10012-1090
(212) 674 7105 • FAX (212) 674 7100

August 12, 1997

President Bill Clinton
The White House
Washington, D.C.

Dear President Clinton:

I am writing to express my support for the FDA's proposed requirement that drug manufacturers provide more labeling information about the safety and efficacy of their products for use in pediatric populations.

Prescription drugs are used to treat all segments of the population, yet the clinical trial experience on which their approval is based often excludes the very young and the very old. Once a drug is marketed, however, it is widely prescribed even though the thresholds for safety and effectiveness may differ among age groups.

It is time to stop putting children unnecessarily in harm's way by improving the information required on drug labeling pertaining to pediatric use.

Sincerely,

Arthur Aaron Levin, MPH
Director

National Association of Pediatric
Nurse Associates & Practitioners, Inc.

August 12, 1997

President William Jefferson Clinton
1600 Pennsylvania Avenue, N.W.
Washington, D.C. 20500

Dear President Clinton:

On behalf of the 5,300 members of the National Association of Pediatric Nurse Associates and Practitioners and the children they serve, I commend you for your leadership in addressing pediatric pharmaceutical research and labeling.

As providers of health care for children, we understand the great importance of pharmaceutical research that recognizes children are not "little adults" -- their metabolism, response rates, and tolerance levels are different from adults.

We greatly appreciate the Administration's effort to ensure that pharmaceuticals are adequately tested in children and that such studies are used to support better labeling for pediatric drugs. Giving health care providers adequate and appropriate information about usage is crucial in ensuring the health and safety of our nation's children.

Thank you again for keeping our children's interests at the forefront of national health policy. We look forward to assisting the Administration in development of these new regulations.

Sincerely,

Patricia Franklin

Patricia Franklin, MSN, RN, CPNP
President

1101 Kings Highway, North, Suite 206 / Cherry Hill, New Jersey 08034-1912 / 609-667-1773 / FAX 609-667-7187
E-mail: 74224,51@Compuserve.Com Internet: www.napnap.org

NACDS

National Association of Chain Drug Stores

August 11, 1997

The President
The White House
Washington DC. 20500

Dear Mr. President:

On behalf of the members of the National Association of Chain Drug Stores, we are writing to support the intent of a new proposed regulation to be issued by the Food and Drug Administration that would provide pharmacists and other health care providers with additional information on prescription drugs that can be used in treating child illnesses.

The National Association of Chain Drug Stores (NACDS) membership consists of more than 130 retail chain community pharmacy companies. Collectively, chain community pharmacy comprises the largest component of pharmacy practice with over 86,000 pharmacists. These pharmacists are responsible for filling approximately 60% of the more than 2.6 billion prescriptions dispensed annually in the United States.

Pharmacists are considered one of the most accessible and trusted health care professionals, and frequently the only health professional available in many small towns and rural areas. On a daily basis, community retail pharmacists counsel patients on proper use of their medications and answer questions about prescription drugs prescribed for them or their family members.

Product labeling information that would provide all health professionals with readily accessible information about proper dosage for the use of adult medications by children would further assist pharmacists and other providers in determining the appropriate use of these medications for children. We strongly support efforts that would increase the amount of useful information available to health care providers in treating and counseling patients.

Sincerely,

Ronald L. Ziegler
President and Chief Executive Officer

National Medical Association

1012 Tenth Street, Northwest
Washington, D.C. 20001-4492
(202) 347-1895 FAX (202) 842-3293

SENT VIA FACSIMILE TO 202/456-6218

August 12, 1997

The White House
Office of Public Liaison
Attention: Ms. Barbara Wooley
122 Old Executive Office Building
Washington, D.C. 20502

Re: Proposed Regulation on Pediatric Labeling

Dear Ms. Wooley:

Throughout its 102 year history, the National Medical Association has been a leading voice to eliminate disparities in health, particularly among the poor, minorities, and underserved populations. Because of limitations in testing of many drugs in pediatric populations and labeling for pediatric use of specific drugs, children can be considered an underserved population for certain drug therapies. The proposed regulation requiring pediatric-use data on new drugs, with provisions pertaining to existing drugs, has the potential for improving available treatments and increasing the effectiveness and safety of treatments for this vulnerable population.

Sincerely,

Nathaniel H. Murdock

Nathaniel H. Murdock, M.D.
President

Date: August 12, 1997

RE: The proposed FDA regulation to provide health care professionals with more information regarding pediatric doses drugs.

While your intentions may be noble, the proposed regulation will further confuse the public by allowing health professionals and, in turn, parents to assume that the FDA has required a careful well-controlled study before making recommendations for drug doses intended for infants and children.

Any regulation, intended to protect the safety and well-being of infants and children, by providing health care professionals with more information regarding pediatric doses of a drug, must include a requirement that the drug manufacturer disclose whether or not those dosages have been determined by well-controlled, randomized trials and approved by the FDA. The information should also discuss whether or not a follow up has been carried out to determine the long-term effects of the drug on child development.

Respectively submitted,

Doris Haire

Doris Haire, President

AmFAR

August 8, 1997

The President
The White House
Washington, DC

Dear Mr. President:

The American Foundation for AIDS Research (AmFAR) endorses your support of the proposed rule by the Food and Drug Administration to require safety and dosing studies for new drugs that will be used in children. It is a clear statement that this nation is concerned about the health of its children. This decision will be an additional milestone in FDA progress, increasing the certainty that all individuals will benefit from the best of our therapeutic discoveries. Life-saving treatment must be available to men, women and children simultaneously. No one should be denied treatment because of age. No parent should be concerned about the safety of a drug for their child.

For years we have watched as life-saving drugs were approved for adults but not for children. Nowhere has this been more dramatic and visible that in the HIV/AIDS epidemic. Currently, there are 11 drugs approved for adults to treat HIV and only 5 for children. Parents have pleaded for these new drugs for their children as they have watched their own health or that of their adult friends improve while their children worsened.

We at AmFAR have strongly supported FDA rules that have accelerated the availability of promising treatments for patients with HIV infection and other diseases. We have seen new treatments return people to healthy and productive lives. We also strongly support equal access for all individuals to these therapies. Your decision to support this new FDA rule has the potential to bring closure to an inequity in health care by bringing life-saving treatments to this and future generations of our children.

Sincerely,

Mathilde Krim, Ph.D.
Founding Co-Chair and
Chairman of the Board

Arthur J. Ammann, M.D.
President

Fran Du Melle
Director
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John R. Garrison
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Marilyn Hansen
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AMERICAN THORACIC SOCIETY

AMERICAN LUNG ASSOCIATION®

August 12, 1997

William J. Clinton
1600 Pennsylvania Avenue, NW
Washington, DC 20500

Mr. President:

On behalf of the American Lung Association and its medical section, the American Thoracic Society, we want to congratulate you for the Food and Drug Administration's (FDA) proposed rule on Pediatric Drug Labeling requirements. The proposed rule you have announced today will help the FDA, health care providers, the pharmaceutical industry and patients reach a needed consensus on labeling and information requirements for pediatric prescription drugs.

The pharmaceutical industry has improved the lives of millions of American children by developing new drugs to treat the array of pediatric diseases. However, some of the prescription drugs were initially developed with adults in mind and are used to treat children as almost an after-thought. Drugs are often used to treat children without understanding the unique health and dosing needs of a child. Our nation's children are not after-thoughts.

Today the goal should be for health care providers, pharmaceutical companies and patients to work together to collect and distribute information on the pediatric application of prescription drugs. Mr. President, I applaud your announcement today as being a first step in reaching that goal.

Sincerely,

Donald I. Clark
President,
The American Lung Association

Talmadge E. King
President,
The American Thoracic Society

Q + A's

Q + A's

PEDIATRIC LABELING Qs and As

Q: WHY ARE YOU DOING THIS REGULATION NOW?

A: Despite efforts to increase the number of studies on pediatric populations, still too many children take prescription drugs that have not been tested on children. Over 80 percent of drugs manufactured in the United States have not been tested on children and over 50 percent of drugs that are known to be widely tested in children have not been tested.

As a result, some physicians are reluctant to prescribe much-needed therapies to children. Physicians report that they have denied children important new drugs because, in the absence of adequate testing and labeling, they would have to guess at an appropriate dosage, and they do not want to take that risk.

In some cases, guessing can be extremely dangerous. One example of the possible harm is the case of "gray baby syndrome" where a number of babies died from chloramphenicol, an antibiotic that their immature livers were unable to accept. Other children have had withdrawal symptoms from prolonged administration of fentanyl, a pain killer used as an adjunct to anesthesia in infants and small children. Still others have suffered seizures and cardiac arrest from bupivacaine, a local anaesthetic not adequately tested in pediatric populations.

Q: CAN'T YOU ACHIEVE THE SAME EFFECT THROUGH VOLUNTARY COMPLIANCE?

A: FDA has already implemented reforms to encourage voluntary compliance. However, as 80 percent of drugs manufactured in the United States and over 50 percent of drugs widely used in children still do not have a adequate pediatric labeling, FDA has concluded that this new rule is necessary to ensure that children get the protection they need.

Q: GIVEN THAT THE DRAFT FDA REFORM LEGISLATION, PENDING IN CONGRESS, CONTAINS FINANCIAL INCENTIVES TO ENCOURAGE VOLUNTARY COMPLIANCE, WHY IS THIS RULE NECESSARY?

A: The Congressional approach, while thoughtful and worthy of serious consideration, would not assure that most or all of prescription drugs used by children are tested and labeled appropriately. We believe that the Dodd/Dewine legislation has the potential to complement the regulation the President is unveiling today, but it is not a replacement for it.

Q: DO YOU SUPPORT THE DODD LEGISLATION AS CURRENTLY DRAFTED AS A COMPONENT OF THIS EFFORT?

A: We are reviewing this legislation to determine if it can be designed to compliment and bolster our efforts today. We believe that it has great potential to compliment the legislation but we are not prepared to accept it as currently drafted before we consider all of the ramifications of overlaying the important regulation the President is announcing today.

Q: HAVE CHILDREN BEEN AT RISK IN THE PAST?

A: Yes. In some cases physicians do not prescribe drugs because they determine that it is simply not worth taking the risk of prescribing drugs that have not been tested in children.

In other cases, physicians choose to prescribe treatment, because it is the only means to cure a child's nagging illness or even a life threatening disease. Those physicians are left to make their best guess at the appropriate doses -- rather than rely on the through studies and information that the rest of us take for granted.

In some cases, however, guessing can be devastating. One example of the potential for harm is the case of "gray baby syndrome" where a number of babies died from chloramphenicol, an antibiotic that their immature livers were unable to accept. Other children had withdrawal symptoms from prolonged administration of fentanyl, a pain killer used as an adjunct to anesthesia in infants and small children. Still others have suffered seizures and cardiac arrest from bupivacaine, a local anaesthetic not adequately tested in pediatric populations.

Q: HOW MANY PRODUCTS WILL BE AFFECTED BY THE RULE?

A: FDA anticipates that this will impact about 12 new drugs each year. The agency will also review drugs already on the market to determine which ones should have pediatric studies. FDA will work as quickly as possible to ensure that in a few years the drugs most important to children will have directions for use in kids on their labels.

Q: WHAT KINDS OF DRUGS ARE COMMONLY MISSING THIS PEDIATRIC DATA?

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

Q: WHAT DO DOCTORS DO WHEN THEY DON'T HAVE THIS INFORMATION?

A: In some cases they choose not to prescribe the drugs at all. In other cases, they take their best guess -- without the assistance of information that we rely on for adult medications. Sometime, however, guessing can have dangerous consequences, such as seizures, heart problems, or even death.

Q: WHEN CAN PARENTS EXPECT THAT INFORMATION TO SUPPORT SAFE AND EFFECTIVE USE OF PRODUCTS IN CHILDREN WILL BECOME AVAILABLE?

A: We believe that, in some cases, the information already exists and the drug companies merely need to analyze and compile it. In these cases, the information can be made available on the labeling of the products fairly quickly. In other cases, studies need to be conducted. Under the requirements of FDA's 1994 regulation, where the effects of the product and the disease for which it is indicated are sufficiently similar in both adults and children, these studies can be done within one year.

Q: HOW MUCH WILL THIS COST DRUG MANUFACTURERS?

A: FDA estimates that the costs of pediatric studies will be less than 1% of the total costs of developing a drug.

Q: WILL DRUG PRICES INCREASE AS A RESULT OF THIS REGULATION?

A: 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.

Q: WILL THIS REQUIREMENT HOLD UP DRUG APPROVALS?

A: Clearly we will provide every incentive to complete the study before the drug is approved. However, the rule explicitly ensures that a drug's entrance into the market is not held up even if all studies on pediatric populations have not yet begun. We will rely on other legal and financial remedies to ensure that companies comply as soon as possible.

Q: WHEN WILL THIS REGULATION GO INTO EFFECT?

A: 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 3 months after issuance. At that time, for drugs already on the market, FDA, in compelling circumstances, may request that pediatric studies be initiated. Manufacturers of new drug and biologic products, under review at the agency, will have 2 years to comply with the pediatric study requirement. Manufacturers of new products, not yet submitted for review, will have 18 months to comply with the requirement. Drugs already on the marketplace will have 3 months to comply.

Q: WHAT IS THE ENFORCEMENT MECHANISM FDA WILL TAKE TO FORCE COMPANIES TO PROVIDE THIS DATA ON APPROVED DRUGS?

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

CHINA PNTR ECONOMIC POLICY WORKING GROUP

March 31, 2000.
Office of Gene Sperling

AGENDA

I. Levin Follow Up

- Approach/Timing
- Human Rights Commission
- China Safeguard Mechanism
- Admin. Counterproposal on Congressional Review of China's Implementation of WTO Commitments
- Initial Reaction on Levin Section 301 Proposals
- Outline of List of Administration Trade/Labor Actions

II. Approach on Labor-Related Concerns -- Elements of Response

President's Speech

Draft 8/12/97 8pm

PRESIDENT WILLIAM J. CLINTON
REMARKS ON PEDIATRIC-DOSE LABELING
THE WHITE HOUSE
AUGUST 13, 1997

Acknowledgments: V.P. Gore, the First Lady; Rep. Jim Greenwood; Dr. David Kessler, who was instrumental in preparing this rule; Dr. Michael Friedman, Acting Commissioner of the FDA; Reagan Ralph, who introduces you.

Little Samuel's story is not unique. According to the American Academy of Pediatrics, more than 50% of medicines that have proved helpful for children have not been adequately tested for children's use. That is simply unacceptable. Today, I will take executive action to ensure that parents and pediatricians will have the safety information they need.

Doctors have long known that children react differently from adults to prescription drugs. In many cases, children must have vastly scaled down doses. In some cases, their bodies have not developed enough to take any quantity of a medicine that has been proven safe for adults.

We are aware of these dangers, and yet we still do not have good information about dications for some of the most common childhood illnesses -- like asthma, allergic reactions, ..id ear infections. We also don't know enough about medications to treat life-threatening diseases. Less than half of the drugs used to treat the estimated 12,000 children with HIV infection have been tested for use in children. Information is particularly sparse for children under two.

Without clear guidance, pediatricians sometimes decide not to prescribe for children drugs used successfully by adults. That means children are sometimes deprived of what might be the very best treatment available.

The pediatrician's other alternative is to guess. But guessing -- even educated guessing -- can have grave consequences. Some time ago, doctors gave infants small doses of a crucial antibiotic commonly used by adults. It turned out that the infants were unable to clear the drug from their bodies and large amounts built up in their livers. Because needed dosage studies had not been done, 23 infants died.

The rule I am announcing today will put an end to the guesswork. The new rule I am announcing today will require the manufacturers of all medicines needed by children to study the drugs' effects in young people. The results will then be displayed on drug labels to help pediatricians and other health-care professionals make good decisions about how to treat their ..oung patients. I am pleased to report that groups representing patients, physicians, nurses,

pharmacists, and drug manufacturers have all indicated their willingness to help implement this new rule.

I want to applaud Senators Dodd and DeWine and Congressmen Greenwood and Waxman, who have introduced legislation that would provide additional incentives for drug manufacturers to perform the needed dosage studies in children. Their approach is compatible with the rule we are introducing today. I look forward to working with them on this issue as the Congress continues our efforts to pass comprehensive FDA reform this fall.

Through the common-sense initiative I have announced today, we will take one more significant step toward assuring quality health care for our children. Last week, I signed a balanced budget agreement with the largest new commitment to health care since Medicaid was enacted, more than three decades ago. Under this law, as many as 5 million uninsured children will get health care coverage.

Now we are working to ensure that the treatments we give our children are safe and that cutting-edge medicines are available to children just as soon as they are available to adults. We owe this much to parents like Reagan Ralph and Elizabeth Glaser, whom the First Lady just spoke of a few minutes ago. We owe this to every parent and every child. As the First Lady says, children are not rugged individualists; they depend upon us to give them love, guidance, discipline, and the benefit of good medical care. Their future and ours depends on how well we do our job.

Speeches

VP

Pediatric Labeling Event
The Rose Garden
Wednesday, August 13, 1997

Thank you, Secretary Shalala. In a few moments, President Clinton will announce new steps he is taking to help parents and pediatricians care for our children -- to have the information they need to provide the very best care available. But today's announcement represents a commitment that is much broader, and much deeper, for this administration.

As President Clinton has said so often, the toughest job in the world -- the most important job in the world -- isn't being President; it's being a parent. Providing the love, support, and caring that strengthen future generations. Passing on our values, and our ideals. And any parent knows that the greatest responsibility of all is caring for a child when he or she is sick.

Government can't do those jobs -- nor should it try. But government can make it a whole lot easier for parents to succeed, and raise the kinds of healthy, strong children that make us all proud. That's our purpose here today -- and that's what President Clinton has been fighting to achieve these past four and a half years.

The First Lady has very eloquently described our achievements in expanding health care for children and families. But this administration's commitment to children's health goes far beyond the doctor's office. That's why this President has enacted the toughest-ever measures to cut off children's access to tobacco -- and a crackdown on cigarette ads aimed at our children. If it weren't for this President, Joe Camel would still be puffing away.

President Clinton dramatically expanded meat inspections, so parents can be sure the food they serve their children is safe. Our tough new air quality standards will make sure that the air our children breathe is clean and safe -- especially for those children who have respiratory difficulties. Thanks to those new regulations, children like **insert new name when we get it** Frances Doyle, a four-year-old with asthma, can breathe a lot easier.

But as Frances's father Johnthan will tell you in just a few moments, there are a lot of parents who want to do the right thing for their children -- especially when it comes to prescription medicines -- but they just don't have the right information. Two out of three drugs that Frances has to take for her asthma do not have adequate pediatric information. That means Frances's parents often have to guess -- even though Frances's mother, Kristen, is a nurse. When it comes to our children's health, guessing isn't good enough. And I'm pleased to introduce Johnthan Doyle, who will tell us more about what this problem means to his family...

Shalala

Mr. President, Mr. Vice President, Mrs. Clinton, Mrs. [parent], other distinguished guests:

Today we announce another dose of good medicine for our children's health -- and another victory for good government.

As our kids get ready to head back to school, their parents are worrying about whether they'll have the right books, the right classes, and, even the right clothes.

But, when a child gets sick there's one thing parents should never have to worry about -- and that's whether their children will have the right medicines -- safe medicines. And, that's why we're here.

Over the last four years, we have fought hard to make sure that all citizens have access to promising new drugs that are safe, effective, and arrive on time.

The results? More cancer drugs are reaching people who need them -- when they need them.

Drug approval times have been slashed in half -- and are now as fast or even faster than every other nation.

Miles of red tape have been cut. Piles of regulations have been thrown away.

And we're working with the Congress to reach consensus on balanced FDA reform.

But, even as we work to make the FDA more efficient, there is one thing we must never do: We must never lose sight of -- or compromise -- its fundamental mission:

... To promote the public health, to maintain the public trust, and to improve the lives of all Americans -- especially children.

Every once in awhile, we have an extraordinary opportunity to do that.

When an FDA doctor named Francis Kelsey was faced with a decision about approving Thalidomide more than 30 years ago, she knew she had an opportunity to prevent birth defects in countless children.

And she did it.

When this Administration was faced with a decision about whether to regulate tobacco use by children, we knew we had the opportunity to save an entire generation from a deadly addiction. And we did it.

And now, once again, we see too many children placed in harm's way.

Too many children with asthma, depression, and other ailments and not enough information about what medicines and what dosages will help them.

Too many pediatricians forced to play a high-stakes guessing game about whether to forgo an effective treatment or risk prescribing one that could hurt -- not heal -- a child.

Now, once again, as a government and as a nation, we have an opportunity -- and a responsibility -- to act.

We have an opportunity to place our most exciting scientific discoveries firmly within the grasp of every American child. And today we are.

Now, I'm very pleased to introduce a leader who has dedicated his entire life to keeping our earth in the balance, to ensuring that our science and technology are on the cutting-edge, and to always putting our public health first.

Through his words and deeds, he has created a vision for good government that can protect our health today and meet our challenges tomorrow. It is my great honor to ntroduce Vice President Al Gore.

Reagin Ralph

Mr. President, Mrs. Clinton, Vice President Gore, Secretary Shalala, and other guests:

Sam, my husband and I are very honored to be here today. This is a day I'll never forget and, quite frankly, one Sam may never remember. But the occasion is one that marks a tremendous advance for children and one that will yield benefits for millions of children for decades to come.

Mr. President, thank you for the strength and commitment you have demonstrated by issuing these regulations today--I thank you as a parent and a citizen.

Just 21 months ago I became a mother for the first time. It came with all the joy and chaos that parenthood brings. I barraged my pediatrician with all the first time questions: Should he sleep on his side or his back? How do I cut those tiny little fingernails? and WHEN will he sleep through the night???

When Sam was just four months old he had his first asthma attack. I was petrified. I was still working on the diaper rash questions and now he needed medication so his little lungs could sustain him. Before his first birthday he had been in the emergency room several times.

Sam's pediatrician prescribed a couple drugs to try and control his asthma--albuterol and Intal. So far, they seem to be working for Sam, he hasn't been hospitalized for about seven months.

It wasn't until recently that I learned that those drugs have not had extensive clinical trials in children Sam's age. If Sam were older, those drugs would have labeling but for his age, my pediatrician had to rely on limited medical studies, rather than comprehensive clinical trials.

I must thank Dr. Jeralyn Bernier, Sam's pediatrician. She has been with us every step of the way during Sam's illness. She was able to determine how much medication to give Sam but she should have been able to rely on a proper pediatric label to make that determination.

Mr. President, asthma drugs are only one example of the medications that need proper labeling for children. Scores of other drugs need to have pediatric clinical trials done--drugs for pediatric AIDS, heart conditions, infections, and allergies just to site a few.

These regulations being announced today will help Dr. Bernier and thousands of other pediatricians and health care professionals make medical decisions with the precise information they need so that the best drug and the correct dose can be prescribed and my son and millions of other children can get the high quality treatment they need and deserve.

Now it is my honor to introduce to you the President of the United States, William Jefferson Clinton.

Background Report

PROPOSAL TO ADDRESS THE LACK OF PEDIATRIC LABELING FOR DRUGS

BACKGROUND

Children suffer from most of the same diseases as adults, and, by necessity, are treated with most of the same drugs as adults. The majority of new drugs and biological products, however, have not been tested in pediatric populations. As a result, product labeling frequently fails to provide directions for safe and effective use in children, despite widespread use. An FDA survey of drugs prescribed during 1994 identified the 10 drugs prescribed most frequently to children without adequate labeling. Together, these 10 drugs were prescribed more than 5,000,000 times. Because of differences in size and ability to metabolize drugs, children require different doses than adults and may be subject to different adverse reactions. The absence of pediatric labeling information thus poses a serious risk of inappropriate dosing and unexpected adverse effects in children. It may also result in failure to provide children with optimal treatment in cases where physicians are reluctant to prescribe potentially toxic drugs to children before they have undergone pediatric testing. For example, a survey by the Pediatric AIDS Foundation found that fewer than 10% of children with AIDS were receiving protease inhibitors, the newest and most promising AIDS drugs.

In recent years, FDA has undertaken several initiatives to encourage the voluntary addition of pediatric use information to drug labels. FDA has implemented a "Pediatric Plan" designed to focus attention on and encourage voluntary development of pediatric data during drug development. FDA has also identified the top 10 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 label on the basis of substantially less data than before, and that required manufacturers to survey existing data to determine whether there was sufficient information to support pediatric use information in the drug's label.

These voluntary efforts to increase the amount of pediatric use information in labeling have not resulted in significant gains, particularly with respect to new drugs entering the marketplace. A comparison of drugs approved in 1991 and 1996 showed that approximately 47% of the drugs approved in 1991 with potential use in children had pediatric labeling, while 37% of those approved in 1996 with potential use in children had pediatric labeling.

Year	total NMEs approved	potential use in children	pediatric labeling at approval	post-approval study promised	pediatric labeling later submitted
1991	26	15	7	7	1
1996	53	40	15	17	?

PROPOSAL

FDA is considering proposing new regulations to address the lack of pediatric use information by requiring, for the first time, that applications for certain new drug and biological products contain pediatric data. The purpose of the proposed rule would be to ensure that important new drugs and biological products carry adequate pediatric labeling at the time of, or soon after, approval. The pediatric study requirement would be limited to a small group of new drugs and biologics: new molecular entities (the most innovative drugs) and biological products that (1) would provide a significant therapeutic advantage to children suffering from the disease or (2) would be expected to be used in substantial proportion of children. Pediatric studies could be deferred until after approval if FDA found that it was appropriate to delay pediatric studies until sufficient data were collected in adults. The requirement could also be waived altogether under certain circumstances.

The proposed rule might also codify FDA's authority to require in compelling circumstances that manufacturers of already marketed drugs and biological products conduct studies to support pediatric use labeling. The circumstances in which FDA might require pediatric studies of a marketed drug would be: (1) where the drug is widely used in children and the lack of adequate labeling poses significant risks to children, or (2) where the drug offers a significant therapeutic advantage to children but additional information is needed to permit safe and effective use.

The absence of workable penalties has historically hampered FDA's ability to require pediatric studies. It is inappropriate from a public health standpoint to prevent the marketing of a drug that offers a clinical benefit to adults simply because the manufacturer has failed to study the drug in another subgroup of the population. FDA is therefore considering a different type of penalty for failure to conduct a pediatric study. FDA would take manufacturer to court and obtain an injunction requiring the

study to be completed. Violation of the injunction would be punishable by contempt or fines.

8/12/97 7:30 P.M.

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

Good afternoon and welcome to the White House. We are here to take another major step in our comprehensive effort to protect the health of America's children. The action the President is announcing today will see to it that important medications are tested and made available to children more effectively 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 organizations whose work has made this achievement possible: the Pediatric AIDS Foundation, the National Association of Children's Hospitals, and the American Academy of Pediatrics.

I would also like to remember the contributions of someone who isn't here: Elizabeth Glaser -- one of the founders of the Pediatric AIDS Foundation.

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 Glaser's case, Elizabeth contracted HIV from a blood transfusion she received shortly after giving birth to her daughter. The virus was passed to Ariel. Yet while Elizabeth was able to take AZT to fight the disease, Ariel was not. As one doctor told Elizabeth, "We don't even know what dose to give her. We can't just experiment. This is a toxic drug. It could kill her."

The plan the President is announcing today will 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. It will ensure that doctors know exactly what medicine works for children and how much of it to give. It will extend not just to medications for critical illnesses, but also to treatments widely used in children for conditions like asthma, allergies, ear infections, and pain.

In short, this reform will give parents and doctors the peace of mind that comes from knowing that if a drug is out there, and if it can help a child, then we will be able to use it.

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.

In the last five and a half years, my husband has taken a series of important steps to safeguard the health of our children: from protecting and defending Medicaid...to signing cutting-edge legislation like the Family and Medical Leave and Kennedy Kassebaum Acts...to shielding our young people from tobacco and drugs...to seeing to it that our children get the immunizations they need.

The President could not have done this alone. He has had a lot of help from a lot of people committed to his goal of better health for all our children. I have the great pleasure of introducing one of those people to you now -- the Secretary of Health and Human Services, Donna Shalala.