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PROTECTIONS FOR FOSTER CHILDREN ENROLLED IN CLINICAL TRIALS

HEARING

BEFORE THE

SUBCOMMITTEE ON HUMAN RESOURCES

OF THE

COMMITTEE ON WAYS AND MEANS
U.S. HOUSE OF REPRESENTATIVES

ONE HUNDRED NINTH CONGRESS

FIRST SESSION

MAY 18, 2005

Serial No. 109–8

Printed for the use of the Committee on Ways and Means

U.S. GOVERNMENT PRINTING OFFICE

36–660 WASHINGTON : 2007

For sale by the Superintendent of Documents, U.S. Government Printing Office
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PROTECTIONS FOR FOSTER CHILDREN ENROLLED IN CLINICAL TRIALS

WEDNESDAY, MAY 18, 2005

U.S. HOUSE OF REPRESENTATIVES,
COMMITTEE ON WAYS AND MEANS,
SUBCOMMITTEE ON HUMAN RESOURCES,
Washington, DC.

The Subcommittee met, pursuant to notice, at 2:09 p.m., in room B–318, Rayburn House Office Building, Hon. Wally Herger (Chairman of the Subcommittee) presiding.

[The advisory announcing the hearing follows:]

ADVISORY

FROM THE COMMITTEE ON WAYS AND MEANS

SUBCOMMITTEE ON HUMAN RESOURCES

FOR IMMEDIATE RELEASE
May 11, 2005
No. HR–2

CONTACT: (202) 225–1025

Herger Announces Hearing on Protections for Foster Children Enrolled in Clinical Trials

Congressman Wally Herger (R–CA), Chairman, Subcommittee on Human Resources of the Committee on Ways and Means, today announced that the Subcommittee will hold a hearing on protections for foster children enrolled in clinical trials. **The hearing will take place on Wednesday, May 18, 2005, in room B–318 Rayburn House Office Building, beginning at 2:00 p.m.**

In view of the limited time available to hear witnesses, oral testimony at this hearing will be from invited witnesses only. Invited witnesses will include experts familiar with issues related to the enrollment of foster children in clinical trials. However, any individual or organization not scheduled for an oral appearance may submit a written statement for consideration by the Subcommittee for inclusion in the printed record of the hearing.

BACKGROUND:

Recent media reports raised concerns regarding protections in place prior to the enrollment of foster children in clinical drug trials. These included allegations that in some cases foster children may have been enrolled in studies without the benefit of certain protections, such as the appointment of an independent advocate for the child. At the same time, individuals familiar with these studies contend that the enrollment of foster children enhanced their health by offering the best medical treatment available and that independent advocates were not necessary in all cases.

For children who may not safely remain with their families, foster care is a temporary setting in which foster parents, social workers, and court personnel work to protect the child's best interests in lieu of their biological parents. Federal policy has been enacted, most recently with the Adoption and Safe Families Act of 1997 (P.L. 105–89), to ensure that the safety of foster children is paramount in any decision made on the child's behalf. This hearing will examine (1) policy issues surrounding the enrollment of foster children in clinical trials, and (2) whether adequate protections are in place to ensure the safety and well-being of foster children in such trials.

In announcing the hearing, Chairman Wally Herger said: "This hearing will explore issues surrounding the placement of foster children in clinical drug trials, including under what conditions participation is permitted. We are concerned about recent allegations involving the enrollment of foster children in such trials. This hearing will help us assess whether there is any substance to these allegations and if so, what response is appropriate."

FOCUS OF THE HEARING:

The focus of the hearing is on protections for foster children enrolled in clinical trials.

DETAILS FOR SUBMISSION OF WRITTEN COMMENTS:

Please Note: Any person(s) and/or organization(s) wishing to submit for the hearing record must follow the appropriate link on the hearing page of the Committee website and complete the informational forms. From the Committee homepage,

http://waysandmeans.house.gov, select "*109th Congress*" from the menu entitled, "*Hearing Archives*" (*http://waysandmeans.house.gov/Hearings.asp?congress=17*). Select the hearing for which you would like to submit, and click on the link entitled, "*Click here to provide a submission for the record*." Once you have followed the online instructions, completing all informational forms and clicking "submit" on the final page, an email will be sent to the address which you supply confirming your interest in providing a submission for the record. You ***MUST REPLY*** to the email and ***ATTACH*** your submission as a Word or WordPerfect document, in compliance with the formatting requirements listed below, by close of business Wednesday, June 1, 2005. **Finally**, please note that due to the change in House mail policy, the U.S. Capitol Police will refuse sealed-package deliveries to all House Office Buildings. For questions, or if you encounter technical problems, please call (202) 225–1721.

FORMATTING REQUIREMENTS:

The Committee relies on electronic submissions for printing the official hearing record. As always, submissions will be included in the record according to the discretion of the Committee. The Committee will not alter the content of your submission, but we reserve the right to format it according to our guidelines. Any submission provided to the Committee by a witness, any supplementary materials submitted for the printed record, and any written comments in response to a request for written comments must conform to the guidelines listed below. Any submission or supplementary item not in compliance with these guidelines will not be printed, but will be maintained in the Committee files for review and use by the Committee.

1. All submissions and supplementary materials must be provided in Word or WordPerfect format and MUST NOT exceed a total of 10 pages, including attachments. Witnesses and submitters are advised that the Committee relies on electronic submissions for printing the official hearing record.

2. Copies of whole documents submitted as exhibit material will not be accepted for printing. Instead, exhibit material should be referenced and quoted or paraphrased. All exhibit material not meeting these specifications will be maintained in the Committee files for review and use by the Committee.

3. All submissions must include a list of all clients, persons, and/or organizations on whose behalf the witness appears. A supplemental sheet must accompany each submission listing the name, company, address, telephone and fax numbers of each witness.

Note: All Committee advisories and news releases are available on the World Wide Web at *http://waysandmeans.house.gov*.

The Committee seeks to make its facilities accessible to persons with disabilities. If you are in need of special accommodations, please call 202–225–1721 or 202–226–3411 TTD/TTY in advance of the event (four business days notice is requested). Questions with regard to special accommodation needs in general (including availability of Committee materials in alternative formats) may be directed to the Committee as noted above.

Chairman HERGER. Good afternoon, and welcome to today's hearing. To begin the hearing today, I would like to make note that we have a new Member on the Subcommittee, Mr. Devin Nunes of California. Welcome, Devin. We look forward to working with you on the many important issues within the Subcommittee's jurisdiction.

At today's hearing, the Subcommittee will examine an extraordinarily sensitive topic, the enrollment of children in foster care in clinical drug trials involving experimental but potentially lifesaving drugs. Children in foster care have been separated from their biological parents and placed in a temporary setting which can last for years or, in some cases, their entire childhood. Many of these children have special medical needs, including life-threatening illnesses like Acquired Immunodeficiency Syndrome (AIDS). Thousands of foster children in the late 1980s and early 1990s were af-

flicted by AIDS. Treatments for children had not yet been found or tested. For some of these children, clinical trials were seen as a promising and possibly only way to save, lengthen or improve these young lives. When biological parents could not be found or were incapacitated due to addiction or illness, social workers, court personnel and others involved in the children's care had to make life-and-death decisions about whether foster children should be placed in clinical trials. Those trials involved both hope and risk. Concerns have been raised about the right balance between hope and risk, and who gets to make that critical decision.

Recent news stories report that States have a variety of policies for when children in foster care may or may not participate in clinical trials. Even though there are Federal guidelines, there is no consistent policy across States. These reports also suggest that, in some cases, protections were either not enforced or were inadequate. These are serious allegations. That is why it is important that we closely examine the facts. It seems to me there are three main questions involved in today's hearings. First, should children in foster care be involved in clinical trials? Second, if foster children are permitted to participate in clinical trials, what are the protections now in place to ensure their safety? Third, are those protections adequate? Some States have adopted the policy that children in foster care simply cannot participate in clinical trials, as we will hear described shortly. Other States permit participation, but only based on the decision of a judge or following the naming of an independent advocate to monitor the foster child's best interest. Still other States rely on the foster care system and its caseworkers, medical experts and foster parents to make these decisions. In some cases, these decisions are made after trying to consult the child's biological parents.

As I mentioned earlier, our purpose today is to understand these various measures, all of which are designed to protect children in foster care to determine whether those protections are adequate and appropriate. In other words, how do we balance risk and hope? Given the lack of available information on this topic, I have asked the U.S. Department of Health and Human Services (HHS) to survey the 50 States about the specific policies and protections they have in place regarding the enrollment of foster children in clinical trials. I look forward to the results of that survey.

We welcome all our witnesses today to explore these issues. I note there are no Democrat or Republican witnesses here today. I appreciate the cooperation of Mr. McDermott and his staff in selecting the witnesses appearing before us. Joining us are experts on topics ranging from Federal protections for children enrolled in clinical studies to individuals familiar with State policies regarding foster child enrollment. I would also note that we have written background information and written testimony from a variety of sources who could not join us today, including the child protection agencies of New York City and the State of Illinois. The official record of this hearing will remain open for 2 weeks should others wish to offer their input for this Subcommittee's consideration.

We look forward to today's testimony and our witnesses' help in answering our many questions and helping us decide how best to proceed. Without objection, each Member will have the opportunity

to submit a written statement and have it included in the record at this point. Mr. McDermott, would you care to make a statement?

[The prepared statement of Chairman Herger follows:]

Opening Statement of The Honorable Wally Herger, Chairman, and a Representative in Congress from the State of California

Today the Subcommittee will examine an extraordinarily sensitive topic—the enrollment of children in foster care in clinical drug trials involving experimental, but potentially life-saving drugs.

Children in foster care have been separated from their biological parents and placed in a temporary setting which can last for years or, in some cases, their entire childhood. Many of these children have special medical needs, including life-threatening illnesses like AIDS.

AIDS afflicted thousands of foster children in the late 1980s and early 1990s Treatments for children had not yet been found or tested. For some of these children, clinical trials were seen as a promising, and possibly only, way to save, lengthen or improve these young lives.

When biological parents could not be found or were incapacitated due to addiction or illness, social workers, court personnel and others involved in the children's care had to make life and death decisions about whether foster children should be placed in clinical trials.

Those trials involved both hope and risk. Concerns have been raised about the right balance between hope and risk, and who gets to make that critical decision.

Recent news stories report that states have a variety of policies for when children in foster care may or may not participate in clinical trials. Even though there are federal guidelines, there is no consistent policy across States.

These reports also suggest that in some cases, protections were either not enforced or were inadequate. These are serious allegations. That is why it is important that we closely examine the facts.

It seems to me there are three main questions involved in today's hearing:

- First, should children in foster care be involved in clinical trials?
- Second, if foster children are permitted to participate in clinical trials, what are the protections now in place to ensure their safety?
- And third, are those protections adequate?

Some states have adopted the policy that children in foster care simply cannot participate in clinical trials, as we will hear described shortly.

Others states permit participation, but only based on the decision of a judge, or following the naming of an independent advocate to monitor the foster child's best interests.

Still other states rely on the foster care system and its caseworkers, medical experts, and foster parents to make decisions about whether foster children may be included in clinical trials, in some cases after trying to consult the child's biological parents.

As I mentioned earlier, our purpose today is to understand these various measures, all of which are designed to protect children in foster care, to determine whether those protections are adequate and appropriate.

In other words, how do we balance risk and hope.

Given the lack of available information on this topic, I have asked the Department of Health and Human Services to survey states about the specific policies and protections they have in place regarding the enrollment of foster children in clinical trials. I look forward to the results of that survey.

We welcome all our witnesses today to explore these issues. Joining us are experts on topics ranging from federal protections for children enrolled in clinical studies to state policies regarding foster child enrollment.

I would also note that we have received background information and written testimony from a variety of sources who could not join us today, including the child protection agencies of New York City and the State of Illinois.

And the official record of this hearing will remain open for two weeks should others wish to offer their input for the Subcommittee's consideration.

We look forward to today's testimony, and our witnesses' help in answering our many questions and helping us decide how best to proceed.

Mr. MCDERMOTT. Surely. Thank you, Mr. Chairman. First of all, I want to thank the Chairman for having this hearing. I think it is an important issue and one that requires us to be thoughtful. Sometimes issues like this can be sort of explosive, but I think this is an issue to be thoughtful about because I am sure many were shocked when they read the recent press accounts of foster kids being involved in clinical trials without adequate protection. As a physician, I know the role medicine plays in saving and improving lives every day. I have been involved in the AIDS epidemic beginning when I was with the State Department in 1987, so I have seen the evolution of the Department. Many of these cases we are talking about here were late eighties cases, early nineties cases. I think we have to put things in perspective of the real crash feeling there was in those days about getting some treatment and figuring out what we could do for a variety of people in this situation.

However, we learned through top-notch investigative reporting by the AP that children in the child welfare system had participated in scientific experiments used to determine the effectiveness of AIDS medication, and that participating, in my view, is not necessarily bad. I want to say that right up front, because trials are scientific paths to new and more effective treatments. I think what is true, however, is we must be assured that the system defends the best interests of the children involved in these studies. They are alone. They have been taken away from their parents. They are without an advocate. They are vulnerable, and they could be taken advantage of by the system if it fails them.

Over the last 18 months, this Subcommittee has heard hearings about a number of issues affecting kids in the Federal, State child welfare programs, and this issue is like many of them: It is has the potential for being explosive. The child welfare program in the richest, most powerful country in the world is and has been often an abysmal failure. Now, we don't need proof of more of that. We can give you all kinds of examples of it. We know about kids losing their lives in the child welfare system. Practically every State legislature every year deals with one case or another, and everybody wrings their hands, and the problems go on. The kids are sometimes locked up. Sometimes starved under the supervision of the agencies. We know the children have been used without proper supervision for drug testing.

Now, the question the public has to ask us and I think we have to ask ourselves on this Subcommittee is, how do we give that proper supervision? When are we going to reform the child welfare system so that we protect these vulnerable kids and provide them with the opportunity to succeed? They have enough strikes against them going in because they are in the foster system, and the question really is, what can we do not to make it worse for them but to make it better?

We have a group of distinguished witnesses here today, and I for one expect them to give us ideas about how we can improve the system for children. The Subcommittee put out a press release announcing today's hearing. Now, press releases are one part of the political process, but our challenge and really what the public should demand of us is a bipartisan Subcommittee action. I really think, Mr. Chairman, we need to act to improve the welfare of chil-

dren that do not have a stable and safe family. We really need reform on a variety of things, but it takes courage and leadership and new resources, but it needs to be done. It is not an easy job. I dealt with these issues when I was in the State legislature, and they are no less contentious now up here than they were down there. Our Nation's children need us. They need what we put together in a child welfare program that lifts them up rather than puts them down or lets them down. I for one am grateful for you for having this hearing, and I hope that we can come out of it with some things that we can then put into law and actually do something. We have talked a lot and listened a lot, but it is time for us to do something. Thank you, Mr. Chairman.

Chairman HERGER. Thank you, Mr. McDermott. Before we move on to our testimony, I want to remind our witnesses to limit their oral statement to 5 minutes. However, without objection, all the written testimony will be made a part of the permanent record. To start our hearing this afternoon, we will hear from the Honorable Donald Young, M.D., who is the acting principal deputy assistant secretary for planning and evaluation at HHS. Dr. Young, please proceed with your testimony.

STATEMENT OF DONALD YOUNG, M.D., ACTING PRINCIPAL DEPUTY ASSISTANT SECRETARY FOR PLANNING AND EVALUATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. YOUNG. Mr. Chairman, distinguished Members of the Subcommittee, thank you for inviting me here today to discuss Federal protections for foster children enrolled in clinical trials. I am Dr. Donald Young, deputy assistant secretary for planning and evaluation in HHS. The President and Secretary Leavitt have as a first principle the protection of the most vulnerable in our population. Foster children are certainly vulnerable, and failing to protect them will not be tolerated.

Dramatic advances in prevention and treatment of disease have been achieved through research. A crucial part of these medical advances involves participation of human subjects, including children, in clinical trials. The Department of Health and Human Services is deeply committed to ensuring the protection of the rights and welfare of every individual who participates in clinical research. This afternoon, I will discuss the evolution of the Human Immunodeficiency Virus (HIV)/AIDS, the management of the disease, pediatric AIDS and foster care, and the Federal protections in place to ensure the safety of human subjects, including children, and children who are wards.

In 1990, as many as 2,000 babies were born infected with HIV. Now that number has been reduced to a bit more than 200 a year in the United States.. HIV has evolved from a disease that kills to a disease that is chronic and manageable. Clinical research including research in children is necessary to make advances in medicine. Clinical research involves risks, however, and it is the responsibility of the medical research community to ensure that all trial participants fully understand both the potential benefits and the potential risks of their participation.

It is estimated that, through 1989, between 16 and 22 percent of pediatric AIDS patients were children in foster care. Many of these children were placed in foster care because the caretaker parent had died or become incapacitated by AIDS, or because of neglect, abuse, or abandonment associated with parental drug abuse. The fact that fewer than 2 percent of foster children diagnosed as HIV-positive in 1989 were participating in clinical trials was viewed as evidence that the foster care system had failed to completely and effectively cope with the influx of HIV-infected children.

At the time, most State laws allowed only for standard medical treatment for children in foster care; because there were no standard treatments for HIV-infected children, this limitation represented a critical barrier to medical care for children with HIV. Federal regulations are in place to provide protections for human subjects, including children and foster children, involved in HHS conducted, supported or regulated research. Ultimately, however, it is the State and in some cases county foster care agencies that decide who provides permission for these children to be enrolled in clinical trials. Institutional review boards (IRB)—working with researchers establish within Federal guidelines what procedures should be followed to acquire consent in specific study protocols. The HHS and Food and Drug Administration (FDA) regulations also contain a number of other requirements relating to IRB membership and procedures, criteria for IRB approval of research, suspension or termination of IRB approval research and general requirements for informed consent.

The regulations permit IRBs to approve three categories of research or clinical investigation involving children as research subjects. A fourth category requires an additional level of review. First, research or clinical investigations not involving greater than minimal risk to the children: There, the IRB must determine that the research or clinical investigation presents no greater than minimal risk to the children. Second, research or clinical investigation involving greater than minimal risk but preserving the prospect of direct benefit to the individual child subjects: Here, the IRB must determine the risk is justified by the anticipated benefits to the subjects, the relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by alternative available approaches.

In each of the next two categories, HHS and FDA regulations include a provision that provides additional protections for children who are wards of the State or any other agency, institution, or entity. First, research or clinical investigations involving greater than minimal risk and no prospect for direct benefit to the individual child subjects but likely to yield generalizeable knowledge about the subject's disorder or condition: The IRB must determine the risk of the research or clinical investigation represents a minor increase over minimal risk; the intervention or procedure presents experiences to the child subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations; the intervention or procedure is likely to yield generalizeable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition. Second,

research or clinical investigation that the IRB believes does not meet the above categories of the HHS or FDA regulations but finds that the research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children requires a specific level of HHS review beyond that provided by the IRB.

In all cases, the IRB must ensure that adequate provisions have been made for soliciting permission of parents or legal guardians and the assent of the children to the extent required by HHS and FDA regulations. Before children who are wards of the State or any other agency, institution or entity can be included in either of the last two categories of research or clinical investigations, the research must meet the following conditions: The research must either be related to the children's status as wards or conducted in schools, camps, hospitals, institutions or similar settings in which the majority of children involved as subjects are not wards. The IRB must require appointment of an advocate for each child who is a ward in addition to any other individual acting on behalf of the child as guardian.

The Office of Human Research Protections (OHRP) and FDA have implemented oversight activities both to respond to complaints and to monitor compliance with Federal regulations. OHRP's compliance oversight activities can be divided into three major categories. First, for-cause oversight investigations; second, not-for-cause compliance oversight surveillance evaluations; and, third, review and analysis of institutional reports of noncompliance, unanticipated problems involving risks to subjects, or suspensions or terminations of IRB approval of research.

FDA regulation and oversight for clinical research extend not only to IRBs and institutions but to clinical investigators, research sponsors, contract research organizations, laboratory facilities conducting preclinical research and bioequivalence firms. As you know, Mr. Chairman, of recent press reports there is an ongoing investigation, and I will not be able to answer any questions related to the investigation.

In conclusion, we continue to address challenges posed by the threat of HIV/AIDS and are committed to basic and clinical research to strengthen the Nation's ability to cope with this infectious disease. The protection of human subjects, including children, in clinical trials has been and will remain a top priority for HHS. HHS is firmly committed to the protection of the rights and welfare of every individual who participates in human research, consistent with sound ethical standards and regulatory requirements. I will be happy to answer any questions.

[The prepared statement of Dr. Young follows:]

Statement of The Honorable Donald Young, M.D., Principal Deputy Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services

Mr. Chairman and Distinguished Members of the Subcommittee, thank you for inviting me here today to discuss federal protections of foster children enrolled in clinical trials. I am Dr. Donald Young, the Deputy Assistant Secretary for Planning in Evaluation in the U.S. Department of Health and Human Services. The President and Secretary Leavitt have as a first principle the protection of the most vulnerable in our population. Foster children are certainly vulnerable and failing to protect them will not be tolerated. Dramatic advances in prevention and treatment of dis-

ease have been achieved through research. A crucial part of this research involves the participation of human subjects, including children, in clinical trials. Clinical trials of drugs are necessary in children to determine their safety and efficacy in this age group of patients; studies in adults may not adequately predict drug properties in children. Federal policy has sought to preserve the benefits of this research, while at the same time protecting against possible abuse or harm to research subjects. The Department of Health and Human Services is deeply committed to ensure the protection of the rights and welfare of every individual who participates in clinical research.

To provide a better understanding of the issue, I will discuss with you the evolution of HIV/AIDS and the management of the disease, pediatric AIDS and foster care, and the federal protections in place to ensure the safety of human subjects, including children and children who are wards, in research.

Evolution in the Management of HIV/AIDS

Since the world first became aware of AIDS in 1981, the disease has spread around the globe. Today, approximately 39.4 million people worldwide are living with HIV/AIDS. Approximately 2.2 million children are now living with HIV/AIDS. During the past year, approximately 640,000 new HIV infections and 510,000 deaths occurred in children.

Despite these sobering statistics, dramatic advances have been made in the management of HIV infection since HIV was first discovered over two decades ago. In 1990, as many as 2000 babies were born infected with HIV; now that number has been reduced to a bit more than 200 a year in the U.S. From 1985 to 1999, AIDS cases in U.S. children decreased 81%. From 1998 to 2002, the estimated number of children dying from AIDS decreased 68%.

Much has been accomplished since the early days of the HIV/AIDS epidemic, including significant advances in treatment and prevention. HIV has evolved from a disease that kills to a disease that is chronic and manageable. Research has been pivotal to understanding HIV/AIDS and managing the disease. In the United States and other western countries, potent combinations of anti-HIV drugs have dramatically reduced the numbers of new AIDS cases and deaths due to HIV/AIDS. Today, there are over 20 antiretroviral medications that are approved by the Food and Drug Administration (FDA). As another example of the success of research, a pivotal National Institutes of Health (NIH)-supported study conducted in Uganda demonstrated that a single dose of the drug nevirapine given to an HIV-infected woman at the onset of labor, combined with a single dose for the infant just after birth, was 50 percent more effective in preventing transmission to the baby than was a short course of the drug AZT. Research is now underway to determine if the use of nevirapine or other drugs can prevent transmission through breastfeeding, a major mode of mother-to-infant transmission. Other HIV prevention strategies include development of effective chemical and physical barrier methods, research on the use of these methods among different populations, and a study of how antiretroviral therapy might prevent transmission by reducing how much virus a patient sheds in their genital track or in breast milk. However, the early clinical trials of these therapies were conducted only in adults. Pediatric formulations of these treatments were not approved for young children with HIV/AIDS because sufficient studies had not been conducted in children.

Importance of Clinical Research

Clinical research, including research in children is necessary to make advances in medicine. Clinical research involves risks, however, and it is the responsibility of the medical research community to ensure that all trial participants fully understand both the potential benefits and the potential risks of their participation.

As I will describe in more detail below, federal regulations provide specific protections for children and additional protections for wards of the state participating in some forms of clinical trials. Ultimately, however, it is the state, and in some cases county foster care agencies that decide how informed consent is provided for these children. Institutional Review Boards (IRBs) working with researchers, establish, within federal guidelines, what procedures should be followed to acquire consent in specific study protocols.

HHS continues to believe strongly that clinical trials to test new treatments in children are essential and that the framework established by the existing regulation offers adequate protection for individuals participating in trials. We also recognize, however, the importance of continued vigilance to ensure the regulations are adhered to by investigators and the IRBs that oversee their activities.

Pediatric AIDS and Foster Care—An Historical Perspective

Nearly three-quarters of the 3,000 pediatric AIDS cases recorded by the Centers for Disease Control and Prevention by 1991 were in children with at least one parent who was an intravenous drug user. Many of these children were placed in foster care because the caretaker parent had died or become incapacitated by AIDS, or because of neglect, abuse or abandonment associated with parental drug abuse. This was also the period during which "boarder babies" regularly made the headlines—children abandoned in hospitals who were ready to leave but for whom appropriate foster care placements were unavailable. It is estimated that through 1989, that between 16 and 22 percent of pediatric AIDS patients were children in foster care. This significant overlap between risk factors for HIV and the need for foster care meant that pediatric AIDS became a particular concern for child welfare agencies in large cities, where most pediatric AIDS cases were concentrated.

As pediatric AIDS became more prevalent, little was known about the effectiveness or proper dosages in children of drug therapies that were yielding good results in adults. But these treatments seemed to hold the promise of longer and higher quality life for many children who otherwise seemed doomed. State child welfare agencies were strongly urged to reduce barriers to foster children's participation in such trials. The fact that fewer than 2% of foster children diagnosed as HIV positive in 1989 were participating in clinical trials was viewed as evidence that "the foster care system has failed to competently and effectively cope with the influx of HIV-infected children" (McNutt, 1994).

A study published in 1990 found that only seven states had implemented formal policies regarding the participation of foster children in clinical trials, and five states had "mechanisms" through which it was possible to enroll such children in trials. Although the state had legal custody of the children, the permission of biological parents was required in four of the twelve states that had either "policies" or "mechanisms" (Martin and Sacks, 1990). The same research study found that 16 percent of 432 children enrolled in pediatric AIDS trials at the time were in foster care (a total of 69 children), and that nearly three times that many foster children were known to be eligible for those trials but could not be enrolled because a parent or guardian's permission could not be obtained.

In the Omnibus Budget Reconciliation Act of 1987, (P.L. 100–203, section 9138), Congress required the Secretary of HHS to provide information about children with AIDS who had been placed in foster care. The report prepared in response to this congressional mandate found that, in 1989, the states were aware of 804 current and 979 cumulative cases of HIV positive children in foster care nationally, most of them concentrated in just a few states. By that year only 6 states had seen at least 50 cumulative cases of HIV among children in foster care, and 20 states had never cared for a foster child with HIV. At the time, most state laws allowed only for "standard medical treatment" for children in foster care. But because there were no standard treatments for HIV-infected children, this limitation represented a critical barrier to medical care for children with HIV. The report recommended that "State and local child welfare agencies should create systems to manage the participation of children in foster care in special medical treatment and experimental trials" (HHS/ASPE, 1989, p. 60).

Efforts in the early 1990s to increase the enrollment of foster children in clinical trials affected state policies that in many cases continue to the present. Today, child welfare agencies continue to differ in their policies regarding whether or under what circumstances children in foster care may be enrolled in clinical trials. Information gathered from several state foster care agencies suggests that authority to provide permission for other than standard medical treatment typically lies either with the judge supervising the foster care case, with a senior official within the foster care agency, or with a guardian ad litem. Some states continue to preclude the enrollment of foster children in experimental trials altogether, or will provide permission on behalf of the child only if the biological parents also give permission for the child's participation. Under the federal foster care program, health care decisions on behalf of individual foster children are left to states that are acting as parents with respect to children in their custody and that are responsible for assuring the health care needs of foster children are met. With respect to enrolling children in particular clinical trials, the procedures established for each study by the IRB and researcher, working within the federal human subjects regulations described below, would guide children's participation.

Protection of Human Subjects Regulations

Federal Regulations are in place to provide protections for human subjects involved in HHS conducted, supported, or regulated research. Regulations exist to pro-

tect human subjects, including children and foster children, who participate in research.

The HHS and FDA Protection of Human Subject Regulations are codified at 45 CFR part 46, and 21 CFR part 50 and 56, respectively. The regulations in subpart A of 45 CFR part 46 include basic protections for human subjects involved in both biomedical and behavioral research.

In 1991, 14 other Federal departments and agencies joined HHS in adopting a uniform set of regulations that are identical to subpart A of 45 CFR part 46. This uniform set of regulations is known as the Federal Policy for the Protection of Human Subjects, also referred to as the Common Rule. FDA's Protection of Human Subjects regulations at 21 CFR parts 50 and 56 are similar to those in the Common Rule.

The HHS protection of human subject regulations are based in large part on the *Belmont Report* written in 1978 by the Congressionally created National Commission for the Protection of Human Subjects of Biomedical Behavioral Research. The Belmont Report identifies three fundamental ethical principles for all human subjects research—respect for persons, beneficence, and justice.

The HHS regulations at 45 CFR part 46 apply to all non-exempt research involving human subjects that is conducted or supported by HHS. These regulations include provisions for IRB review, informed consent, and assurances of compliance. For example, through an assurance of compliance that is approved by the Department's Office for Human Research Protections (OHRP), an institution pledges to conduct its HHS-funded or supported research in accordance with the human subjects protections of 45 CFR part 46. An institution also may voluntarily extend its assurance to apply to all human subjects research it conducts regardless of funding source.

In addition to assurances of compliance required by the HHS regulations at 45 CFR part 46, the HHS and FDA regulations also contain a number of other requirements for institutions engaged in HHS-conducted, -supported, or FDA regulated research involving humans, including requirements relating to, for example, IRB membership and procedures, criteria for IRB approval of research, suspension or termination of IRB approval of research; and general requirements for informed consent.

Additional Protections for Children Involved in Research

Children have long been recognized as a special and vulnerable population, and are accorded special protections in many areas, including research. In 1983, HHS adopted additional protections for children involved as subjects in research at 45 CFR part 46, subpart D, and in April 2001, FDA adopted similar requirements for children under an Interim Final Rule, 21 CFR part 50, subpart D, Additional Safeguards for Children in Clinical Investigations.

When a proposed research study involves children and is supported or conducted by HHS funding, the research institution's IRB must take into consideration the special regulatory requirements that provide additional protections for the children who would be involved in research. If the proposed research involves FDA-regulated products, then FDA's parallel regulations would apply.

Both the HHS' and FDA's Subpart D regulations permit IRBs to approve three categories of research or clinical investigations involving children as research subjects:

45 CFR 46.404 and 21 CFR 50.51—Research or clinical investigations not involving greater than minimal risk to the children. To approve a research study or clinical investigation in this category, the IRB must make the following determination:

- the research or clinical investigation presents no greater than minimal risk to the children.

45 CFR 46.405 and 21 CFR 50.52—Research or clinical investigations involving greater than minimal risk but presenting the prospect of direct benefit to the individual child subjects. To approve a research study or clinical investigation in this category, the IRB must make the following determinations:

- the risk is justified by the anticipated benefits to the subjects;
- the relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by available alternative approaches.

45 CFR 46.406 and 21 CFR 50.53—Research or clinical investigations involving greater than minimal risk and no prospect of direct benefit to the individual child subjects, but likely to yield generalizable knowledge about the subject's disorder or

condition. In order to approve a research study or clinical investigation in this category, the IRB must make the following determinations:

- the risk of the research or clinical investigation represents a minor increase over minimal risk;
- the intervention or procedure presents experiences to the child subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations;
- the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition.

A fourth category of research or clinical investigation requires a special level of HHS review beyond that provided by the IRB:

45 CFR 46.407 and 21 CFR 50.54—Research or clinical investigation that the IRB believes does not meet the above categories of the HHS or FDA regulations, but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children. The research or clinical investigation may proceed only if the following conditions are met:

- the IRB finds and documents that the research or clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
- the HHS Secretary and/or FDA Commissioner, after consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following an opportunity for public review and comment, determines either:
    - that the research in fact satisfies one or more of the above categories of the HHS or FDA regulations (i.e., 45 CFR 46.404, 46.405, or 46.406 under the HHS regulations, and 21 CFR 50.51, 50.52, or 50.53 under the FDA regulations) or;
    - that the following conditions are met:
    - the research or clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
    - the research or clinical investigation will be conducted in accordance with sound ethical principles.

In all cases noted above (i.e., 45 CFR 46.404, 46.405, 46.406, and 46.407), the IRB must ensure that adequate provisions have been made for soliciting permission of parents or legal guardians and the assent of the children, to the extent required by HHS and FDA regulations.

Additional Protections for Children Who are Wards

The HHS and FDA regulations also include a provision in subpart D that provides additional protections for children who are wards of the State or any other agency, institution, or entity. These special protections for wards apply to two categories of research or clinical investigations: (1) research or clinical investigations that involve greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research or clinical investigation (research/clinical investigations approved under 45 CFR 46.406 or 21 CFR 50.53); or (2) research or clinical investigations determined by the IRB not to meet the conditions of the HHS regulations at 45 CFR 46.404, 46.405, or 46.406, or FDA's regulations at 21 CFR 50.51, 50.52, or 50.53, but found to present a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children (research/clinical investigation approved under 45 CFR 46.407 or 21 CFR 50.54).

Before children who are wards of the State or any other agency, institution, or entity can be included in either of the two categories of research or clinical investigations described above, the research must meet the following conditions:

- the research must be either related to the children's status as wards; or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards;
- and the IRB must require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis.

One individual may serve as advocate for more than one child, and must be an individual who has the background and experience to act in, and agrees to act in,

the best interests of the child for the duration of the child's participation in the research. The advocate should represent the individual child subject's interests throughout the child's participation in the research. The HHS and FDA regulations further require that the advocate not be associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

HHS Compliance Oversight Activities

Due to the nature of the research that is subject to the HHS and FDA regulations, each entity has developed its own system to respond to complaints and monitor compliance with its regulations. These activities are complementary, and the results are shared between OHRP (implementing the HHS regulations) and FDA.

OHRP

OHRP's compliance oversight activities can be divided into three major categories: (1) for-cause compliance oversight investigations; (2) not-for-cause compliance oversight surveillance evaluations; and (3) review and analysis of institutional reports of noncompliance, unanticipated problems involving risks to subjects, or suspensions or terminations of IRB approval of research.

For-Cause Compliance Oversight Investigations

OHRP initiates for-cause compliance oversight investigations in response to substantive written allegations or indications of noncompliance with the HHS regulations for the protection of human subjects. Until recently, nearly all of OHRP's compliance oversight activities involved for-cause compliance oversight investigations.

Institutions engaged in human subject research that is conducted or supported by HHS must provide written Assurances of Compliance to HHS describing the means that they will employ to comply with the HHS Regulations. OHRP approves these Assurances on behalf of the HHS Secretary. An Assurance approved by OHRP commits the institution(s) and its personnel to full compliance with the HHS regulations. In carrying out its oversight responsibility, OHRP evaluates all substantive written allegations or indications of noncompliance with the HHS regulations derived from any source.

OHRP holds accountable and depends upon institutional officials, committees, research investigators, and other agents of the institution to assure conformity with the institution's Assurance and, thus, with the regulations. Only through the partnership established by the Assurance can the shared responsibility to protect the rights and welfare of human subjects be discharged in accordance with Section 491 of the Public Health Service Act.

Sequence of Events for an OHRP For-Cause Compliance Oversight Investigation

The typical sequence of events to be followed in an OHRP compliance oversight evaluation is as follows:

1. OHRP discovers or receives a substantive written allegation or indication of noncompliance with the HHS Regulations (45 CFR Part 46).
2. OHRP determines that it has jurisdiction in the matter on the basis of HHS support and/or an applicable Assurance of Compliance.
3. Upon confirmation that it has jurisdiction, OHRP initiates a compliance oversight investigation by writing to appropriate institutional officials to advise them of OHRP's investigation and to request that the institution investigate the matter and report back to OHRP by a specified date. Activities expected of the institution are explained in writing initially and at appropriate times during the course of the evaluation. Except in rare circumstances when sound ethics dictates the need to act immediately, OHRP takes no action against any institution without first affording the institution an opportunity to offer information which might refute indications of noncompliance or to develop satisfactory corrective actions if the allegations or indications of noncompliance are substantiated.
4. OHRP evaluates the institution's report and any other pertinent information to which it has access. OHRP may (a) request that the institution submit additional information in writing; (b) conduct telephone interviews with institutional officials, committee members, and/or research investigators; or (c) conduct an on-site evaluation of protections under the applicable Assurance of Compliance.
5. OHRP issues in writing a determination for each evaluation to appropriate institutional officials. The determination letter to the institution summarizes (i) findings of noncompliance with the HHS Regulations, if any; and/or (ii) the corrective actions proposed and/or implemented by the institution that appro-

priately address the findings of noncompliance. In such circumstances, any complainant(s) are ordinarily informed in writing of OHRP's determination upon completion of its investigation.

6. An OHRP determination letteris made accessible on the OHRP website http://www.hhs.gov/ohrp) once the document has been requested under FOIA, or ten working days after the document is issued to the institution, whichever occurs first.
7. An institution may request review by the Director of OHRP of determinations and findings resulting from a compliance oversight evaluation.

Possible Outcomes of an OHRP For-Cause Compliance Oversight Investigation

Corrective actions based on compliance oversight investigations are intended to remedy identified noncompliance with the HHS regulations and to prevent reoccurrence. Because each case is different, OHRP tailors its corrective actions to foster the best interests of human research subjects, and to the extent possible, the institution, the research community, and HHS. Most compliance oversight evaluations and resultant corrective actions are resolved at the OHRP level. In some instances, however, OHRP recommends actions to be taken by other HHS officials.

OHRP's compliance oversight evaluations may result in one or more of the following outcomes:

1. OHRP may determine that protections under an institution's Assurance of Compliance are in compliance with the HHS Regulations.
2. OHRP may determine that protections under an institution's Assurance of Compliance are in compliance with the HHS Regulations but that recommended improvements to those protections have been identified.
3. OHRP may determine that protections under an institution's Assurance of Compliance are not in compliance with the HHS Regulations and require that an institution develop and implement corrective actions.
4. OHRP may restrict its approval of an institution's Assurance of Compliance. Affected research projects continue to be supported by HHS only if the terms of the restriction are being satisfied. Examples of such restrictions include, but are not limited to:
   a. suspending the Assurance's applicability relative to some or all research projects until specified protections and corrective actions have been implemented;
   b. requiring prior OHRP review of some or all research projects to be conducted under the Assurance;
   c. requiring that some or all committee members and institutional officials, as well as investigators conducting research under the Assurance, receive appropriate human subject education; and
   d. requiring special reporting to OHRP.
5. OHRP may withdraw its approval of an institution's Assurance of Compliance. The institution's research projects cannot be supported by any HHS component until an appropriate Assurance is approved by OHRP.
6. OHRP may recommend to appropriate HHS officials that:
   a. an institution or an investigator be temporarily suspended or permanently removed from participation in specific projects, and/or
   b. peer review groups be notified of an institution's or an investigator's past noncompliance prior to review of new projects.
7. OHRP may recommend to HHS that institutions or investigators be declared ineligible to participate in HHS-supported research, known as Debarment. Note that a suspension of eligibility for Federal funding may precede a Debarment. If OHRP makes this recommendation, the Debarment process will be initiated in accordance with the procedures specified at 45 CFR Part 76. Any Debarment is Government-wide, and not just applicable to HHS funding.

Not-for-cause Compliance Oversight Surveillance Evaluations

In 2001 OHRP initiated a not-for-cause compliance oversight surveillance program. Under this program, OHRP selects institutions without any active for-cause compliance oversight investigations and conducts an assessment of their human subject protection programs. OHRP initiates a not-for-cause compliance oversight evaluation by writing to appropriate institutional officials at a selected institution to advise them of OHRP's evaluation and to request that the institution provide OHRP by a specified date with IRB records and other documents relevant to the institution's program for the protection of human subjects. In most cases, OHRP conducts a site visit following review of the requested documents. OHRP issues a determination in writing for each evaluation to appropriate institutional officials.

The determination letter to the institution summarizes: (i) findings of noncompliance with the HHS regulations, if any; and/or (ii) the corrective actions proposed and/or implemented by the institution that appropriately address the findings of noncompliance. The possible outcomes of a not-for-cause compliance oversight evaluation are the same as for a for-cause investigation.

FDA

FDA's compliance oversight activities dovetail with some of OHRP's activities described above. FDA has developed a Good Clinical Practice Program, which has prominently displayed the process for filing complaints with the Agency. This is available on FDA's website at: http://www.fda.gov/oc/gcp/complaints.html. Generally, complaints are investigated and handled by the particular Center within FDA (e.g., involving Drug Evaluation and Research; Devices; Biologics, etc.) responsible for the study, which would also be the most knowledgeable about the issues involved in the complaint.

FDA's Bioresearch Monitoring Program

FDA developed its Bioresearch Monitoring Program (BIMO Program) to ensure the protection of the rights, safety, and welfare of human research subjects and the quality and integrity of data submitted to the agency. The BIMO Program encompasses all FDA product areas: drugs, biological products, medical devices, radiological products, foods, and veterinary products. Among other things, the BIMO Program involves site visits to clinical investigators, sponsors, monitors, contract research organizations, IRBs, nonclinical (animal) laboratories, and bioequivalence analytical laboratories. FDA uses Compliance Policy Guide Manuals (CPGM) to instruct its field personnel on the conduct of inspectional and investigational activities. These are available at: http://www.fda.gov/oc/gcp/compliance.html.

FDA conducts IRB inspections to determine if IRBs are operating in compliance with current FDA regulations and if the IRBs are following their own written procedures. The FDA regulations pertinent to IRBs include 21 CFR Part 50 (Protection of Human Subjects), Part 56 (Institutional Review Boards), Part 312 (Investigational New Drug Application), and Part 812 (Investigational Device Exemptions).

FDA inspections of IRBs generally fall into one of two categories:

- Surveillance inspections—periodic, scheduled inspections to review the overall operations and procedures of the IRB; and
- Directed inspections—unscheduled inspections focused on the IRB's review of a specific clinical trial or trials. Directed inspections may result from a complaint, clinical investigator misconduct, or safety issues pertaining to a trial or site.

During an inspection at the site of a clinical investigator, FDA personnel typically verify:

- who performed various aspects of the protocol (e.g., who verified inclusion and exclusion criteria, who obtained informed consent, who collected adverse event data);
- the degree of delegation of authority (e.g., how the clinical investigator supervised the conduct of the study);
- where specific aspects of the study were performed;
- the accuracy of the data submitted;
- how accountability for the investigational product was maintained;
- how the monitor communicated with the clinical investigator; and
- how the monitor evaluated the study's progress.

FDA personnel also audit the study data by comparing the data filed with the Agency or the sponsor with all available records that support the data. These records may come from the doctor's office, hospital, nursing home, laboratories, and other sources. FDA may also examine patient records that predate the study to find out whether: the medical condition under study was in fact diagnosed; the study eligibility criteria were met; and the patient received a possibly-interfering medication before the study began. FDA personnel may also review records covering a reasonable period after completion of the study to determine if there was proper follow-up as outlined in the protocol, and if the clinical investigator reported all signs and symptoms reasonably attributable to the product's use.

After headquarters review, one of the following types of letters is typically sent from the Center to the IRB or clinical investigator depending upon the type of inspection:

1. A letter that generally states that FDA observed no significant deviations from the regulations. This letter does not require any response. Note that a letter may not always be sent when FDA observes no significant deviations.

2. An *informational or untitled letter* that identifies deviations from regulations and good clinical practices. This letter may request a response from the recipient. If FDA requests a response, the letter will describe what is necessary and identify a contact person for questions.
3. A *Warning Letter* that identifies serious deviations from regulations needing prompt correction and a formal written response to FDA. The letter will identify an Agency contact person for questions. For investigator inspections, FDA may inform both the reviewing IRB and the study sponsor of the deficiencies and advise the sponsor if the clinical investigator's procedural deficiencies suggest ineffective monitoring by the sponsor.

In addition to issuing these letters, FDA may take regulatory actions for serious deviations from the regulations. FDA may disqualify the IRB, institution, or clinical investigator. A disqualified clinical investigator is ineligible to receive investigational products. FDA may also place lesser administrative sanctions on the IRB.

Under the BIMO program, FDA conducts approximately 1000 inspections annually of all of thevarious parties that conduct or oversee clinical research studies (i.e., clinical investigators, sponsors, monitors, contract research organizations, and IRBs). Of these inspections, about two-thirds are clinical investigator inspections, approximately 250–300 are inspections of IRBs (mostly drawn from FDA's inventory of about 1600 IRBs identified as responsible for reviewing FDA-regulated research), and the remainder are sponsor or monitor/contractresearch organization inspections. For clinical investigations of drugs alone, FDA conducted approximately 75 inspections of studies involving pediatric subjects from 2001 to 2004.

Review and Analysis of Institutional Reports

The HHS and FDA regulations require that IRBs follow written procedures to ensure the prompt reporting to the IRB, appropriate institutional officials, and the pertinent agency head (OHRP Director for research conducted under an OHRP-approved assurance or FDA Commissioner for research involving FDA-regulated products) of the following incidents:

1. any unanticipated problems involving risks to subjects or others;
2. any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and
3. any suspension or termination of IRB approval.

(See 45 CFR 46.103(b)(4)(iii) for HHS-conducted or-supported research and 21 CFR 56.108(b) for FDA-regulated research.)

When reviewing a report of an unanticipated problem, OHRP or FDA assesses mostclosely the adequacy of the actions taken by the institution to address the problem. Likewise, when reviewing reports of non-compliance or suspension or termination of IRB approval, OHRP or FDA assesses most closely the adequacy of the corrective actions taken by the institution. In particular, an assessment is made whether or not the corrective actions will help ensure that the incident will not happen again, either with the investigator or protocol in question, or with any other investigator or protocol. When appropriate, corrective actions are applied institution-wide.

Conclusion

We continue to address challenges posed by the threat of HIV/AIDS and are committed to basic and clinical research to strengthen the nation's ability to cope with this infectious disease. The protection of human subjects, including children, in clinical trials has been and will remain a top priority for HHS. HHS is firmly committed to the protection of the rights and welfare of every individual who participates in human research consistent with sound ethical standards and regulatory requirements.

Chairman HERGER. Thank you, Dr. Young. The gentleman from California, Mr. Nunes, to inquire.

Mr. NUNES. Thank you, Mr. Chairman, and thank you for welcoming me to the Subcommittee. Welcome, Dr. Young. In relation to some of the news reports that have been out there recently, do we know whether any children in foster care today are participating in clinical trials? If so, do you know how many?

Dr. YOUNG. I do not have that information. We know that across the National Institutes of Health (NIH) there are a number of clinical trials ongoing and children participating, but I do not have numbers of children in foster care that might be in that group.

Mr. NUNES. Okay. Could that be something that you could find out? Could you submit that to the Subcommittee if you do?

Dr. YOUNG. If we can find it through our survey information, I will.

Mr. NUNES. Okay. Another question. Your testimony says that the State child welfare agencies were strongly urged to reduce barriers to foster children's participation in such trials. In the early days of the AIDS crisis, what were those barriers, and who strongly urged State officials to reduce those barriers?

Dr. YOUNG. I think that the desire to reduce those came from across the community. In those years, as I said in my testimony, there was no treatment unless you were involved in a clinical trial. This was an emerging disease, and treatments were just emerging at that time, so there was wide support. The barriers included the State laws and requirements that I mentioned in my testimony that said only standard care could be given to individuals in foster care. That prevented them from being enrolled, and the feeling was that the children in foster care should have the same opportunity to make a decision, an election or to have their wards do it for them, to participate if they wanted to participate and get the value and advantage of that trial.

Mr. NUNES. Thank you, Doctor. Thank you, Mr. Chairman.

Chairman HERGER. Thank you. The gentleman from Washington, Mr. McDermott, to inquire.

Mr. MCDERMOTT. Thank you, Dr. Young. Good testimony and I would like to ask you a couple questions about the structuring of the clinical trials. Is there anything in the NIH requirements that require a State to have in place an advocacy requirement? Or can any physician who wants to do a trial in whatever State send in an application and operate within the laws of that State and be considered acceptable to NIH? In other words, does NIH have a set of standards that require that the State must fit?

Dr. YOUNG. The Office of Human Protection is the Federal agency, has a baseline set of requirements that must be adhered to and that the IRB must follow. That deals with, as I said in my testimony, the last two categories, those clinical trials where there is more than a minimal risk involved. Under those circumstances, then, an advocate needs to be appointed for children in foster care to make the decision and ensure that the child is protected and fully informed.

Mr. MCDERMOTT. The question then comes down to these—it is always words. In your testimony, you said you may say that protection is not required if the research has minimal risk—minimal being the operative word—or if it has the prospect of direct benefit. Those again being the operative words. Who makes those decisions as to what is minimal, what is direct benefit to the child? How is that determined?

Dr. YOUNG. The Institutional Review Board has the responsibility to approve all research protocols that are put forward by in-

vestigators. Most of those institutional review boards are under a hospital, academic medical center or other place that also has the responsibility to ensure that there is IRB compliance to that. There is a set of Federal rules. There are then the requirements that the IRB must consider in making a decision whether to approve the research as well as any additional requirements that come from the institution. Beyond that, there are a number of States that have also passed laws that may—putting stronger requirements in place.

Mr. MCDERMOTT. Could it be possible today to have a child brought into a clinical trial in a State where there was no requirement for advocacy for something—these AIDS drugs when we were looking back at them in 1987 and 1988 and 1989, there was no children's research being done. What this was about is really the first children's research. How did anybody decide it was minimal risk or that it was a direct benefit to the kids? How did they come up—without an advocate—it would seem to me like you would want to automatically have an advocate in something as new as that.

Dr. YOUNG. Yes. There are two parts to your question. One is the advocate and the situations more than minimal risk that there must be an advocate. That is not to say, however, in all situations there isn't the State agency or a ward that is making decisions. Somebody has to consent to it, and it has to be an informed consent. It is only when the risk is more than minimal and the conditions that I described in my testimony that, in addition to that, you need a special advocate for the patient. Now, the second part of that are the rules and requirements for research to make sure that it is conducted properly. You need an advocate, but you need a research protocol that is laid out that protects the individuals in that trial, whether they are foster children, adults or children not in foster care.

Mr. MCDERMOTT. The reason I ask those questions, I can envision a situation in which a child care worker who is dealing with AIDS cases coming out of a city hospital or whatever may have 30, 40 kids or 60 kids, and to expect the child care worker to be on top of the case, it seems to me, sets the ground for kids slipping through the cracks as they do in a variety of different ways in the system. I wonder if you—, if you don't have minimum requirements for how many—or maximum requirements for how many kids a worker is responsible for, to expect he or she to cover 60 kids, all of whom are in AIDS treatment programs all over the city or whatever, it seems like you would want to have somebody for each kid to look after or at least—you can see my problem.

Dr. YOUNG. I do, and let me try to explain it one more time. There is an advocate appointed for the children in foster care. That advocate is different under the requirements. That advocate is different than the State agency. That advocate could be part of the PRB. It could be somebody who is particularly interested in kids. Each advocate might have one, two or three kids. This is not the caseworker who is the advocate under those situations. The advocate is somebody in addition to the State foster care agency.

Mr. MCDERMOTT. So, this is a volunteer who comes in and gets involved in the advocacy program in the local State agency and has

three kids with maybe no background whatsoever in the specific issues.

Dr. YOUNG. No. There are requirements also regarding the advocacy that are part of the PRB requirements, that the advocate have the knowledge and be familiar with the condition. It is not anyone off the street can come in and be an advocate.

Mr. MCDERMOTT. I wasn't implying that they were just off the street. This is a specific, very difficult decision to put a kid into a treatment case., the reason I am sensitive about this is, we have a cancer center in Seattle. I have seen what happens when you are using advanced treatments in cancer and then people later say, well, I didn't know the risks. There is a whole lot of responding backward and forwards about what people knew. In this case, you have a kid who doesn't have a clue what is going on. He is being brought or she is being brought, put into the system, and I am wondering how you know, how you can guarantee that that kid has somebody who really understands what is going on?

Dr. YOUNG. I understand your question. That is the issue of what is informed consent, and how much knowledge must you have to achieve informed consent? That question is directly relevant to all research, and particularly to research on kids, and then foster kids add an additional level and layer. So, there is a responsibility to attempt to communicate as clearly as one can, but as you know, in lay terms, it is sometimes difficult to communicate fully and yet keep a message simple that people can understand. That is a challenge for this kind of research. It is a challenge for cancer research in children, any kind of research that has substantial risks but substantial rewards.

Chairman HERGER. The gentleman's time has expired. The gentleman from Colorado, Mr. Beauprez, to inquire.

Mr. BEAUPREZ. I thank the Chairman, and I thank Dr. Young as well for his testimony and for being here with us today. I think the gentleman from Washington has probably already begun going down a path that is of most concern to the Subcommittee. Let me stay in that track for a minute. Doctor, as I first heard about this issue, I guess one of the knee-jerk reactions would be, well, let us just not submit foster children to clinical trials. That is not really where we want to go. Is it? I am guessing that the numbers—they are staggering numbers, frankly, that you shared with us of 16 to 22 percent of children now with HIV back in 1990 were foster care children. We would actually want them to have access to some of the state-of-the-art treatment. I am assuming that that is correct?

Dr. YOUNG. Yes, sir, I agree with you. They should have the opportunity to make their—their guardians should have the opportunity to make the decision if they wish to participate. If they choose not to, that is fine. To exclude them from even having the opportunity to make that decision I don't believe is correct.

Mr. BEAUPREZ. Unfortunately, sometimes, it is that very population that disproportionately is burdened with some of the diseases we would like to get a handle on.

Dr. YOUNG. That was particularly true back in the late eighties for HIV/AIDS when clinical research, clinical trials was the only opportunity, the only hope for treatment.

Mr. BEAUPREZ. The question becomes who then best make this decision or assist the child in making this decision and that is what I want to probe a little bit more with you. I contacted some of our folks back in Colorado who wrestle with this, and the idea of the child advocate seemed to make perfect sense to me: Let us get someone out there who has maybe even met some standard across some threshold on the per chance that we have got a foster parent—because we hear about these tragic cases where the foster parent was not the best choice for the child's well-being, and we all are traumatized by that, as the child who at least is traumatized. What I found out is that, in the opinion at least of the medical professionals back in my State, many, many, many times it is the foster parent on their way to becoming the adoptive parent because, apparently, we have a very high percentage of exactly that that happens, that may well be the person with the child's best interest at heart. It crosses my mind that we would not want to categorically preclude foster parents from the process, either. Would that be a fair assessment?

Dr. YOUNG. Yes, I think that is a fair assessment. We are balancing a lot of different factors here. There is also the biologic parent and what role they should have. Some States allow both or even require both be appointed. Those kinds of decisions in many cases are best made locally by the people who know the State, know the procedures, know what is going on there. There is room for Colorado to make modifications in keeping with the broad set of Federal basic requirements.

Mr. BEAUPREZ. Which gets me to, I guess, the next question I would raise of you. I understand that we have got Federal guidelines, but as you testified just moments ago to us, really it is up to State and local and many cases city and/or county officials to not only apply the rules, but in some cases, I suppose, adjust the rules. They have some local flexibility. Is there more than ought to be done at the Federal level to protect certainly the interests of the child? I will emphasize again, the interest of the child can go both ways. We certainly don't want them to get put into a clinical trial situation that we would all think was inappropriate, too great a risk, but we also don't want to somehow subjectively preclude them from having the opportunity to have access to the latest state-of-the-art medical techniques. What should we be doing at the Federal level?

Dr. YOUNG. I think your points are good ones. I think one of the things the Department will be doing very closely is, following this hearing, following what you are learning and hearing from the witnesses. We are not aware of any changes that we believe need to be made. If they are identified, we will be very happy to consider them and make a decision as how best to proceed. We share with you the concern about the adequate protection of foster children. At the same time, the opportunity to let them participate and get the advantage of clinical research, if that is theirs and their guardian's decision.

Mr. BEAUPREZ. If there is a second left, can you comment on the difference between assent and consent.

Dr. YOUNG. Consent means that you have the legal authority to agree to participate, in this case in research. A minor, generally

under 18, legally cannot consent by law, but the minor can assent. There are requirements that the subjects need to assent to. That is to say, yes, I am willing to do this. That doesn't carry the legal weight of consent, but it says that the minor has agreed to participate. One is a legal concept; one is a concept of agreeing.

Mr. BEAUPREZ. Thank you. Thank you, Mr. Chairman.

Chairman HERGER. Thank you. The gentleman from California, Mr. Becerra, to inquire.

Mr. BECERRA. Thank you, Mr. Chairman. Dr. Young, thank you for being with us and thank you for your testimony. Let me ask a preliminary question, because I am not real familiar with how this all works. How much knowledge does HHS have, first of all, with regard to the number of foster care children who participate in these different studies?

Dr. YOUNG. We do not have good detailed information on that to answer that question.

Mr. BECERRA. Let me back up even further then. We know there is value in some of the research and the clinical trials that occur, and we know that, oftentimes, we want to be able to help children because they have so many years of life ahead of them if we are able to do some good work and help them medically. At what point do we believe that our responsibility by using taxpayer dollars to help fund some of this research or these trials extends to ensuring that we know who those who are conducting the trials or the research are when they approach these children, especially foster children, are trying to protect their rights?

Dr. YOUNG. That is where the Department's compliance activities come into place. As I said, we will follow up where we hear reports. We will do random surveys periodically. We will talk to the State agencies, but that then becomes an issue of Federal checking, investigation, if you would, of compliance to identify problems and to correct those problems.

Mr. BECERRA. Now, how large is your Office of Human Research Protection?

Dr. YOUNG. I am sorry. I will have to submit that for the record. I do not know that.

Mr. BECERRA. Any idea? How many folks do you have to investigate?

Dr. YOUNG. I am not in the Office of Human Protection and Research. I am in HHS assistant secretary for planning and evaluation. I just don't have that information.

Mr. BECERRA. Do you have anybody here with you who might be able to answer that question?

Dr. YOUNG. I don't believe so.

Mr. BECERRA. Well, give me your sense from what you know of how much—how much in resources do we have to try to provide some surveillance, some oversight to ensure that, in the first instance, those who are using Federal tax dollars to conduct their research or these clinical trials are at least trying to follow Federal law? Certainly, there must be State law that is implicated because the State has custody of these foster care children. Do you have any sense of what kind of resources we spend?

Dr. YOUNG. I am sorry, sir, I just don't. As I say, that is not an issue that I looked at in preparation for this hearing.

Mr. BECERRA. Mr. Chairman, perhaps what we could do is ask Dr. Young to see if HHS could get back to us with some information.

Dr. YOUNG. I would be happy to.

Mr. BECERRA. To get a better sense, because I suspect one of the problems we have is you all just don't have the resources to try to be more vigilant about how these clinical trials or this research is being conducted. So, the first thing is, we have to get a handle on whether or not folks are following through and at least abiding by their commitments when they obtain Federal funding to follow Federal law. I suspect that the State probably would respond the same way and all the different States would respond the same way, saying they probably don't have enough money to probably do some oversight over their wards, the children that are within their custody through the foster care system. Let me ask. In terms of the type of oversight that you might think would be helpful—because we can't have someone overseeing every clinical trial or every bit of research that we fund. Is there some guidance you can give us on what we should be looking to see HHS do when it comes to protecting the interest of that child as we try to promote their well-being?

Dr. YOUNG. First, let me remind you again that the first level of oversight is at the local institution, and there is substantial oversight at that level; that these research protocols are on patients who have physicians taking care of them, who may or may not be involved in the research, who provide oversight. The Institutional Review Board will provide oversight.

Mr. BECERRA. Dr. Young, how do we ensure that that first instance of oversight is occurring? We are giving Federal tax dollars. Most of the research will be done locally in a particular State. States have obligation to take care of these wards, the wards of the State or kids who are in foster care. How do we ensure that, when we release those Federal dollars, that in fact, at that local level, that oversight will occur? While locally there is more control and responsibility for the child, I think all of us would still believe that we should not relinquish whatever rights we have to ensure that that child is taken care of or handled properly.

Dr. YOUNG. I absolutely agree with you. There is the level that is local at the physician, the physician caring for the patient. There is the Institutional Review Board. There is the institution, that may be a hospital, in which the Institutional Review Board is housed. There are the State agencies on foster care, and then there is the Federal rules on compliance and on investigations that flow from that compliance. We will get back to you with the information you asked in terms of the size of the agency budget, and so forth.

Mr. BECERRA. Mr. Chairman, may I ask one last question, quick question?

Chairman HERGER. The gentleman's time has expired.

Mr. BECERRA. Fifteen seconds.

Chairman HERGER. One other quick question.

Mr. BECERRA. Just a quick comment. Then maybe what we can do is, if you can tell us if there are any consequences for those who we have found to not be following Federal regulations or even State law in the—as they use these Federal tax dollars to do their re-

search or trials, clinical trials, to see how we can try to get to those who aren't following through with their own responsibility.

Dr. YOUNG. A very quick answer. Yes, there are ways to do that. The FDA regulations in fact lay out, specifically, sanctions that can be brought toward those who do not follow the rules.

Mr. BECERRA. Thank you. Thank you, Mr. Chairman.

Chairman HERGER. Thank you. The gentleman from Michigan, Mr. Camp, to inquire.

Mr. CAMP. Well, thank you, Mr. Chairman. I want to follow up on that compliance line of questioning that Congressman Becerra brought up. I realize you can't talk about ongoing HHS investigations, but can you tell us about any previous findings of noncompliance with HHS regulations involving children in foster care and their participation in clinical trials?

Dr. YOUNG. I cannot. I simply don't have that information as to the past history of any investigations and the outcome of those.

Mr. CAMP. What happens if an institution is found to be out of compliance in such cases? Are you aware of that?

Dr. YOUNG. Yes. Individuals cannot be allowed to participate in research if the findings are egregious enough from the research side. Or the Institutional Review Board will be asked to restructure and to change its membership to get a better mix of membership that is more appropriate to dealing with the problems so that there are a number of ways that there can be changes made if there are deficiencies going on. The ultimate is, of course, not funding the research.

Mr. CAMP. Has that actually happened? Have institutions been suspended from receiving Federal funding or declared ineligible to participate?

Dr. YOUNG. As I said a moment ago, I simply don't know the answer to that question.

Mr. CAMP. All right, so we don't know what institutions. For what reasons?

Dr. YOUNG. There may be some information on that that I simply don't have.

Mr. CAMP. All right, to Congressman Nunes, I believe your response was that you don't have any knowledge of the number of children in foster care in clinical trials.

Dr. YOUNG. That is correct.

Mr. CAMP. Are you making attempts to find that out? Is there a process in place to determine that? Or is that not something you are pursuing?

Dr. YOUNG. The Chairman mentioned the survey that is ongoing, and I will have to look in more detail to see what the content of that survey will be.

Mr. CAMP. All right. Do we have any idea of whether there are any States that require independent advocates for children to be—any foster children who might be participating in the clinical trials?

Dr. YOUNG. The anecdotal reports, including those in the press, suggested that there are some States. I do not have any primary knowledge on that question one way or the other.

Mr. CAMP. Federal regulations require advocates under certain circumstances, do you know how many persons have served as advocates for children in clinical trials? Do you know of any number.

Dr. YOUNG. I do not have information on that.

Mr. CAMP. I guess what I am trying to get at is, how do we know about the nature of the trials, the relative risk and benefit for children without that information?

Dr. YOUNG. We are depending primarily, again, at the local level, on the Institutional Review Boards, the institutions, and the oversight that is provided there. We in turn then at the Federal level will do the investigations as currently being reported in the press and the compliance activities. There is a lot of reliance on what is happening locally, the medical and research community at the local level.

Mr. CAMP. The Institutional Review Boards are charged with determining how and under what conditions children may participate in those trials. To what extent does that information get back to HHS?

Dr. YOUNG. We don't routinely collect information from the IRBs. We have the broad set of rules, and we will check compliance overall, but we will not collect information.

Mr. CAMP. All right. Thank you, Mr. Chairman.

Chairman HERGER. Thank you. Dr. Young, there were several questions that Mr. Camp inquired of and I believe another Member. So, would you mind responding in writing to the Subcommittee on that? Our record will be open for 2 weeks.

Dr. YOUNG. Yes.

Chairman HERGER. Thank you. The gentleman from California, Mr. Stark, to inquire.

Mr. STARK. Dr. Young, I am sorry I missed your testimony, but we did have a chance to review it. I want to go back to this, as I just heard in the few minutes that you have been responding to questions, that you feel that having an independent advocate for each foster child is taken care of locally, but in the Federal regulations, the rules state, for example, that in experiments involving prisoners, the IRB has to include a prisoner advocate to protect the rights of prisoners. Why shouldn't children get that same protection?

Dr. YOUNG. The same rules apply to children as to——

Mr. STARK. No.

Dr. YOUNG. Well, just a moment. As to prisoners, there, the rules are that, where there is a frequent IRB interaction, if there is one prison study and a lot of others that are not, the IRB does not have to. They are encouraged to have people who understand and know the situation, whether it is children or prisoners, but they do not have to have a prisoner if there is a single research protocol that has gone forward through the IRB.

Mr. STARK. Well, I am not at all sure that you and the inspector of the GAO agree, but let us come back. I am going to stick with my assertion from the CRS that the Federal regulations in fact do require that the IRB has to include a prisoner advocate if there is in fact a prisoner involved in the study. Now, we can find that out subsequently, and I am sure that your knowledge of the law is superior to mine. Based on that, why in the world wouldn't it be—

what would be wrong with requiring an advocate for a child, for a foster care child in these experiments?

Dr. YOUNG. The current rules do require an advocate. Now, I am making a distinction between the IRB's composition and the advocate. The advocate requirement is above and beyond the IRB, and the advocate requirement is there when there is more than minimal risk——

Mr. STARK. Okay.

Dr. YOUNG. When there is more than minimal risk and where the value of it is not commensurate with that. There needs to be——

Mr. STARK. Who decides whether there is more than minimal risk?

Dr. YOUNG. The IRB.

Mr. STARK. You don't think it would be necessary on the IRB to have a child's advocate?

Dr. YOUNG. If the IRB is involved in looking at a substantial number of research protocols, for example, in a pediatric hospital, then, yes, I think that is a very reasonable requirement.

Mr. STARK. What about any program in which a foster child is involved? Why shouldn't the IRB include an advocate for that child?

Dr. YOUNG. If there is a—let me make sure I understand your question. If there is a research protocol going through that is no more than minimal risk, then the IRB will look at it. That IRB does not need to have a pediatrician on the IRB, and there is no requirement separate from that for an advocate. I think that gives adequate protection.

Mr. STARK. Dr. McDermott, would you yield to me? Do you think that is adequate protection?

Mr. MCDERMOTT. I don't know. Let me think about it.

Mr. STARK. Okay. I am talking to a pediatrician in his former life.

Mr. MCDERMOTT. Psychiatrist.

Mr. STARK. Well, pediatric psychiatrist, as I recall, and it just troubles me that my suspicion is that we have more concern about prisoners and more protections than we do for kids. We have seen so many examples of minimal risk in drug testing, for instance. We have got to bring the pharmaceutical industry to heel. They have been testing things, you know, giving drugs to kids without involving them in tests. My feeling is that children, and particularly children in foster care who perhaps have a higher—we have an adverse selection there. I would guess that it is fair to suggest, Mr. Chairman, that children in foster care children tend to be poorer and perhaps have had poorer health care for whatever reason as a population and would be more apt to show up in many of these studies. I am worried that the tendency is to say, well, it is okay to let the local people take care of that, because I am not sure that all local jurisdictions would be—for instance, here in Washington, D.C., and I conclude, they can't find half the kids in foster care. How would you like to have a foster care child from the District of Columbia when its present foster care system is in a State of upheaval and say, Gee, they will take care of it? I don't think I believe that. I would rather you doing it. I trust you.

Chairman HERGER. The gentleman's time has expired. Dr. Young, what do Federal regulations require in terms of the naming of independent advocates for foster children in clinical trials?

Dr. YOUNG. If the clinical trial involves more than minimal risk and if the value of the clinical trial is not commensurate with that for the individual patient, then the advocate must be appointed to make the decision for the child in foster care.

Chairman HERGER. Is there evidence to suggest that children with advocates who participated in these trials had better outcomes, they live longer, had better health, are still alive today than those without advocates?

Dr. YOUNG. I don't believe there is any information on that subject. I would not see why there would be any particular difference related to the variable of an advocate only. The advocate is there for a decisionmaking of yes or no. It is the ethical structure of the clinical trial that determines whether it is appropriate, number one, for the individual to even be eligible for the trial. So, I don't know information of that, but I would not expect that that would be a variable.

Chairman HERGER. Well, I thank you very much, Dr. Young, for your testimony. With that, I would like to invite our next panel to have seats at the table. On this panel we will be hearing from Dr. Alan Fleischman, senior advisor at the New York Academy of Medicine; Ms. Roberta Harris, Deputy Secretary of the Wisconsin Department of Health and Family Services; Dr. Marjorie Speers, executive director of the Association of Accreditation of Human Research Protection Programs; and Dr. Moira Szilagyi, on behalf of the American Academy of Pediatrics. Dr. Fleischman.

STATEMENT OF ALAN FLEISCHMAN, M.D., SENIOR ADVISOR, THE NEW YORK ACADEMY OF MEDICINE, NEW YORK, NEW YORK

Dr. FLEISCHMAN. Mr. Chairman, Subcommittee Members, thank you for inviting me. My name is Alan Fleischman. I am a physician, pediatrician and medical ethicist. My professional background and expertise is in the written testimony, but I speak today as and individual. Clinical research with therapeutic intent involving children in foster care is an ethical imperative and can, and was, performed in an appropriate manner fully consistent with good ethical practice and compliant with Federal regulations that govern research. In order to understand the issue of enrollment, I will share with you some of the data that Dr. Young did as well about the late eighties and early nineties in HIV care and treatment of children.

Twenty-five percent of babies born to women who were HIV-infected developed HIV, AIDS was universally fatal in children, and 25 percent of infected children died by age 5. Many of the young children with HIV were boarder-babies, were in foster care because they had become orphans due to the death of their mothers or because their mothers were impaired. Great strides were being made at that time with new drugs developed for the treatment of HIV and AIDS and its complications, but initial trials were only in adults. These new treatments were not available for children, and

there weren't any pediatric formulations of the drugs available to the doctors caring for such children.

The National Institutes of Health developed clinical research trials, and that is our first step of safety for the children in order to study the effectiveness of the various new treatments in children. Some of the drugs had potential for side effects. They were serious drugs. They were against a serious virus, but those possible risks were far outweighed, as doctors would know, by the potential therapeutic benefits. In New York City, the agency responsible for supervision of foster children developed mechanisms that made enrollment of foster children in clinical trials possible, because it would have been unjust not to offer these children the very best prospect of life-saving treatments. The first protection was that individual medical institutions conducted the trials only after Institutional Review Board prospective review and approval.

The consent of biologic mothers or legal guardians was obtained when possible. An agency permission on an individual basis was required before the child could be enrolled in the trial, and foster parents were involved in these discussions because of their need to administer treatments and bring children back for follow-up visits to the hospital in order to be successful in the trials. The appointment of advocates for the children, while a laudable procedural approach, was not required. We did choose that approach in the Bronx, but we were not required to do that by the Federal regulations.

Today, pediatric AIDS treatment in the United States is different, because of clinical trials there are effective treatments to prevent children from becoming infected in utero, and there are effective treatments to prevent children from—there are effective standard treatments for the smaller number of children who are now infected. AIDS in children has become a chronic disease with less than 1 percent mortality each year for children treated in AIDS centers in the United States. Children in foster care who are infected with AIDS today are getting standard treatments and are rarely participating in clinical trials because it is no longer a matter of life and death. There may be a time in the future, perhaps with the emergence of a new dreaded disease, when we will once again be faced with the critical need to enroll foster children in clinical trials in order to provide needed life-saving treatments. Our past experience with HIV and AIDS and the present Federal regulatory structure on research allows us to do that, if we need to.

In conclusion, those of us involved in the treatment of children infected with HIV knew that a large percentage of our patients were poor, minority children, and many of those children were in foster care. We demanded the very best treatment for these vulnerable children. The only way to provide it, in fact, to provide treatment in HIV care to any child with AIDS, at that time was through clinical trials. We enrolled children in treatment trials and gathered information on the effects of the new drugs on children while we attempted to save and enhance lives of our patients. It would have been unethical to have behaved in any other way. Thank you.

[The prepared statement of Dr. Fleischman follows:]

Statement of Alan Fleischman, M.D., Senior Advisor, New York Academy of Medicine; Ethics Advisor, National Children's Study at the National Institute of Child Health and Human Development; Clinical Professor of Pediatrics and Clinical Professor of Epidemiology and Population Health, Albert Einstein College of Medicine in New York

Mr. Chairman and Committee members, thank you for inviting me to share my views with the Committee on the issue of **Protection of Foster Children Enrolled in Clinical Trials**. My name is Alan Fleischman; I am a physician, pediatrician and medical ethicist. I am Senior Advisor at The New York Academy of Medicine and Ethics Advisor to the National Children's Study at the National Institute of Child Health and Human Development, as well as Clinical Professor of Pediatrics and Clinical Professor of Epidemiology and Population Health at the Albert Einstein College of Medicine in New York. ***I speak today as an individual, the opinions I will express represent my own and do not represent the views or opinions of any organization or institution with which I am or have been affiliated.***

In the late 1980s and the early 1990s I was Professor of Pediatrics and Professor of Epidemiology and Social Medicine at the Albert Einstein College of Medicine in New York and served as Director of the Division of Neonatology at the Montefiore Medical Center, that included responsibility for the newborn services at the voluntary hospital, Montefiore, and two public hospitals operated by the New York City Health and Hospital Corporation, Jacobi Medical Center and North Central Bronx Hospital. I was also a member of the two Institutional Review Boards for research involving human subjects that was responsible for approval of all research involving humans conducted at each of these hospitals.

I was a member of the American Academy of Pediatrics National Bioethics Committee from 1983–1989, and a member of the American Academy of Pediatrics AIDS Committee from 1993–1999. In New York State, I was a member of the Department of Health, AIDS Advisory Council Work Group on Ethical Issues in Access to Treatment. In addition, I was asked, in 2001, by the Secretary of the U.S. Department of Health and Human Services (DHHS) to serve as a member of the National Human Research Protections Advisory Committee to the Office for Human Research Protections and to chair the review of the federal regulations that govern research involving children. I have also served as an expert advisor to the Institute of Medicine's Committee on Ethical Conduct of Clinical Research Involving Children.

I am currently a member of the New York State Governor's Task Force on Life and the Law, the New York City Mayor's Commission on Women's Issues, the DHHS Secretary's Advisory Committee on Human Research Protections' Subcommittee on Research Involving Children, and the Institute of Medicine Committee on Ethical Issues in Housing-Related Health Hazard Research Involving Children Youth, and Families.

I am here today to express my strong belief that clinical research with therapeutic intent involving children in foster care is an ethical imperative and can be performed in an appropriate manner fully consistent with good ethical practice and compliant with federal regulations that govern research.

In order to understand the issue of the enrollment of foster children in AIDS clinical trials, you need to have a picture of AIDS care for children in the late 1980s and the early 1990's:

—25% of babies born to women who were HIV infected developed HIV through viral transmission in utero;
—AIDS was a universally fatal disease in children, with 25% of infected children dying by 5 years old;
—many of the young children with HIV were "boarder-babies" who stayed in hospitals or were placed in foster care because they had become orphans due to the death of their mothers from AIDS, or because their mothers were too ill or impaired to care for them;
—great strides were being made with new drugs developed for the treatment of HIV and AIDS and its complications, but initial trials of these drugs included only adults; multiple drug therapy was shown to save lives, and reverse some of the major life-threatening illnesses associated with AIDS, but these new treatments were not available to children;
—in fact, pediatric formulations of these drugs were not available to physicians caring for young children with HIV and AIDS;
—the National Institutes of Health developed clinical research trials in order to study the effectiveness of various new treatments in children; Some of the drugs had the potential for side effects, but those possible risks were viewed by doctors to be far out weighed by the potential therapeutic benefit of the new drugs against AIDS, then a uniformly and often rapidly fatal disease.

A large percent of the children with HIV and AIDS in the late 1980s and the early 1990s in New York City and other parts of the country were poor, minority children, and many of these children required foster care. It would have been unconscionable and unjust, not to offer these children the very best prospect of life saving and life-enhancing treatment. Enrollment in clinical trials was the only way to accomplish that goal. If the agencies responsible for supervising the care of foster children in the early 1990s refused to allow children to be enrolled in treatment trials, I and many other clinicians would have demanded action in the interests of those children.

In New York, the Administration for Children's Services, the agency responsible for supervision of foster children, developed mechanisms that made enrollment of foster children in clinical trials possible. Local Institutional Review Boards for research involving human subjects, like ours in the Bronx, approved the NIH treatment trials for use in all children infected with HIV and helped investigators and the Administration for Children's Services to develop mechanisms to allow enrollment of children in foster care.

The consent of biologic mothers was obtained when possible, agency permission on an individual basis was obtained, and foster parents were involved in these discussions because of their need to administer treatments and bring children back for followup visits to the hospital.

Let me also comment on the federal regulations that govern research involving children with a specific emphasis on the section on "wards" in the regulations (§ 45CFR46.409). I took the opportunity last week to clarify the regulations with a senior member of the Office for Human Research Protections at the U.S. Department of Health and Human Services and I believe that my views of the regulations are consistent with his.

Clinical trials that include treatment with the prospect of direct benefit to the individual child are governed by section § 45CFR46.405 of the federal regulations. This section requires the permission of the parent or legal guardian in order to enroll any child in a study. It does not require the creation of an advocate for each child that is a ward or in foster care. This approach is based on a clinical treatment model. Only if the proposed research does NOT provide the prospect of direct benefit for the individual child AND has a level of risk greater than minimal is the creation of an advocate required by the regulations (§ 45CFR46.409).

Let me add that virtually all of the research projects involving foster children in New York City were treatment trials with therapeutic intent. The individual institutions conducting the trials had an Institutional Review Board that had to prospectively approve the studies and may or may not have created special advocates or processes for enrolling foster children. We did in the Bronx, but it was not mandated by the regulations. What was required was the permission of the biologic parent or of the guardian, either the legal guardian or the agency fulfilling that responsibility for the child.

Today, Pediatric AIDS treatment in the U.S. is different. Because of clinical trials conducted in the 1990s, there are effective treatments to prevent children from becoming infected in utero and standard treatments for the small number of children who are infected. AIDS in children has become a chronic disease with less than 1% mortality each year for children treated in AIDS centers in the U.S. Children in foster care infected with HIV are getting standard treatment and are rarely participating in clinical trials because it is no longer a matter of life and death. But there may be a time in the future, perhaps with the emergence of a new dreaded disease, when we will once again be faced with the critical need to enroll foster children in clinical trials in order to provide needed life saving treatments. The present federal regulations allow us to do that, if we had to.

In conclusion, those of us involved in the treatment of children infected with HIV in the late 1980s and 1990s knew that a large percentage of our patients were poor, minority children and many of those children were in foster care. We demanded the very best treatment for these vulnerable children. The only way to provide the best treatment to any child with HIV at that time was through clinical trials—the drugs were just not available any other way. We enrolled children in treatment trials and gathered information on the effects of the new drugs on children, while we attempted to save and enhance the lives of our patients. It would have been unethical to have behaved in any other way; if we denied those new treatments to children in foster care we would stand today open to severe criticism for having allowed our most vulnerable children to have suffered or even die rather than offer them the best chance of survival and the possibility of a good future quality of life. Thank you.

Chairman HERGER. Thank you, Dr. Fleischman. Ms. Harris.

STATEMENT OF ROBERTA HARRIS, DEPUTY SECRETARY, WISCONSIN DEPARTMENT OF HEALTH AND FAMILY SERVICES, MADISON, WISCONSIN

Ms. HARRIS. Mr. Chairman, Members of the Subcommittee, thank you for this opportunity to provide information to the Subcommittee on this important topic. Children in the child welfare system, whether in their own homes or in some form of out-of-home care, are some of the most vulnerable children in our country. We must do everything that we can to ensure that these children are protected from any additional trauma. Clearly we need legitimate medical and other research. Significant advances are made every day as a result of well-designed and implemented research studies. In Wisconsin, we have not approved medical research on foster children or any subgroup of foster children as a class. In the child welfare system, we believe it is our responsibility to provide as much safe—as much of a safe and nurturing environment for the children in foster care as possible.

Today I would like to make some comments related to the lack of homogeneity of foster children, the problems with voluntary participation on the part of families, and the legal framework of our authority to consent to such research. Let me begin with lack of homogeneity. Research, whether medical or otherwise, should not be limited to a particular group unless there is some homogeneity within that group that is unique. In this regard, there is very little, if anything, that can be regarded as homogeneous among children in foster care other than that they have been removed from their homes.

As many of us know, children in foster care are there for a variety of reasons; abuse or neglect of themselves or their siblings, mental health issues of a severe nature, medical or developmental disabilities with special care and treatment needs that cannot be provided by their parents, and/or delinquency. Many of our children are also from low-income families. As has been mentioned here today, recent news articles have indicated that foster children have participated in medical studies related to research endeavors dealing with acquired immunodeficiency syndrome. It is true that some children in foster care have HIV or AIDS. It is also true that many children not in foster care have HIV or AIDS. To focus a study on medication related to that condition only on children in foster care where there are potential negative effects of those medications certainly leads to a perception that somehow foster children are valued less than other children.

In Wisconsin, our position on the involvement of foster children in research, especially medical research, is based in large part on a variety of ethical codes related to medicine, social work, and mental health. These codes place great emphasis on the voluntary nature of participation research. We believe that our children and our child welfare system are vulnerable, and it is our role to do what we can to ensure the safety and welfare of the children in our system. In addition, as I testified to earlier, many children in the child welfare system are economically disadvantaged. We must recognize this position and protect the family from giving consent under du-

ress. Voluntary consent goes to the heart of the nature of the relationships among children, their families, and the child welfare system. "Voluntary" is defined as acting or performing without external persuasion or compulsion.

Generally, out-of-home placements are ordered by the court. When the agency that has authority to determine when a child be returned to the parent recommends to that parent that the child's participation in medical research—recommends to that parent that that parent approve the child's participation in medical research, at least on a perceived basis it is questionable whether the parent would feel that his or her approval is truly voluntary.

This brings me to legal status. We need to look at the issue of who can approve the involvement of a foster child in any type of research, medical or otherwise. In the child welfare system, there are generally four types of legal relationship between a child and an individual agency acting on behalf of that child: physical custody, legal custody, guardianship and parental relationship. In most cases in Wisconsin, the legal custody of a child in foster care remains with the parent, because under Wisconsin statutes, there shall be a policy of transferring custody of a child from the parent only when there is no less drastic alternative.

If the parent's rights have not been terminated, and if guardianship has not been inferred on another party, then it is clear that the parent should make the medical decisions for the child. As noted previously, however, if the request for research participation comes to the parent through the agency having the authority to decide when the child is returned to the parent, one must legitimately question whether the approval of the parent is given freely and voluntarily. If a representative of the Wisconsin child welfare system has court-appointed legal custody or guardianship and has the authority to approve the participation of the foster child in medical research, it is our position that the approval for such participation should not be given solely on the basis of the child being a foster child.

We are not opposed to the participation of a child—of a foster child in appropriate and beneficial medical research on a case-by-case basis if a foster children meets the requirements for a medical research study based on some physical, mental, emotional or developmental condition; and the child's parent or parents were informed and, as is appropriate to their legal status, approved of their child's participation; and the child's personal physician, therapist and other qualified professional recommends to the system authority the child be involved in that research; and children with similar or related conditions will also participate; and the group of children, and other individuals in the study, include children outside of the child welfare system; and finally, the child is appointed an advocate with the express responsibility for determining whether participation is in the child's best interest, including, if possible, ascertaining the child's position. If all of these are met, we would consider granting that authority.

In summary, in Wisconsin, we believe it is our responsibility to help provide a safe, nurturing environment for the children in our foster care system so that they may become thriving, healthy adults. We are opposed to a foster child being involved in any such

research solely because the child is a foster children. It is inappropriate to single out foster care children as a group for medical research based simply on the fact that they are children in the child welfare system. Thank you again for your invitation to address this important issue. I trust that the legislative initiatives that will be forwarded will reflect the values Wisconsin uses with regard to foster child protection in medical studies.

[The prepared statement of Ms. Harris follows:]

Statement of Roberta Harris, Deputy Secretary, Wisconsin Department of Health and Family Services, Madison, Wisconsin

Thank you for this opportunity to provide information to the committee on this very important topic. Children in the child welfare system, whether in their own homes or in some form of out-of-home care, are some of the most vulnerable children in our nation. It is critical that child welfare professionals, child advocates, medical professionals, elected representatives, and the general public do all that we can to ensure that these children are protected from any additional trauma.

It is not my intent to denigrate the important work reflected in most legitimate medical and other research. Clearly, significant advances are made every day as a result of well designed and implemented research studies.

In Wisconsin, we have not approved medical research on foster children as a class, or any subgroup of foster children, because we believe it is our responsibility to provide as much of a safe, nurturing environment for the children in foster care as possible. The types of research that have unfortunately occurred in our nation in the past would also make it difficult for us to earn the trust and confidence of the families we are seeking to help, who desperately need the services we can offer.

As such, I would like to offer our comments on the topic related to the lack of homogeneity of foster children, the problems with voluntary participation on the part of families, and the legal realities of our authority to consent to such research.

1. Lack of Homogeneity

Research, whether medical or otherwise, should not be limited to a particular group, unless there is some homogeneity within that group that is unique. In this regard, there is very little—if anything—that can be regarded as homogenous among children in foster care, other than that they have been removed from their homes; in most cases, involuntarily.

Children in foster care are there for a variety of reasons: some have been abused or neglected or had siblings who were abused or neglected; some have mental health issues of a severe nature, sometimes as a result of the trauma of being removed from their homes, parents, and siblings; some are medically fragile or developmentally disabled with special care and treatment needs that cannot be provided by their parents; some children are delinquent. Certainly, many are from low income families.

Recent news articles have indicated that several states have allowed foster children to participate in medical studies related to research endeavors dealing with Acquired Immunodeficiency Syndrome (AIDS). It is certainly true that some children in foster care have HIV or AIDS. It is also true that many children **not** in foster care have HIV or AIDS. To focus a study, then, on medication related to that condition only on children in foster care, when there are known potential negative effects of those medications, certainly leads to a perception that somehow foster children are valued less than other children.

2. Voluntary Nature of Participation

In Wisconsin, our position on the involvement of foster children in research, especially medical research, is based in large part on a variety of ethical codes related to medicine, social work, and mental health. A major document forming the basis of our position is embodied in the The World Medical Association Declaration of Helsinki, originally adopted in 1964, and as amended in 1975, 1983, 1989, 1996, 2000, 2002, and 2004, which places great emphasis on the voluntary nature of participation in research.

Paragraph 1 of that document states, in part, that ". . . Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress. . . ."

We believe the children in our child welfare system are vulnerable based upon the trauma within their home, along with the distress that can be caused from being removed from their family and placed into foster care. We believe it is our role to do what we can to help ensure the safety and welfare of the children in our system. In addition, as I testified to earlier, many children in the child welfare system are economically disadvantaged. We must recognize their needs and protect the family from giving consent under duress.

To continue from the World Medical Association Declaration of Helsinki, Paragraph 20 states that "The subjects must be volunteers and informed participants in the research project."

Paragraph 23 states "When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship."

Paragraph 24 states that "For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons."

Paragraph 25 states that "When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative."

I raise these issues related to consent because, to a certain extent, they go to the heart of the nature of the relationships among children, their families, and the child welfare system. In the context noted above, two definitions of the term "voluntary" should be carefully considered:

> Voluntary: Done, given, or proceeding from the free or unconstrained will of a person. [The World Book Dictionary]
>
> Voluntary: Acting or performed without external persuasion or compulsion. [The American Heritage Dictionary of the English Language]

With the exception of some of the small percent of voluntary placements, out-of-home placements are ordered by the court. As such, when the agency that has the authority to determine when a child will be returned to the parent recommends that the parent approve the child's participation in medical research, at least on a perceived basis, it is questionable whether the parent would feel that his or her approval is truly voluntary.

3. Legal Status

This brings us to the issue of who can approve the involvement of a foster child in any type of research, medical or otherwise. In the child welfare system, there are generally four types of legal relationship between a child and an individual or agency acting on that child's behalf. These are physical custody, legal custody, guardianship, and the parental relationship, which are defined as the following:

Physical custody means actual custody of the person in the absence of a court order granting legal custody to the physical custodian. [s. 48.02(14)] In the context of this hearing, the foster parent would be a physical custodian only, because in Wisconsin, they would not generally have legal custody.

Legal custody is a status created by the order of a court, which confers the right and duty to protect, train and discipline the child, and to provide food, shelter, legal services, education and *ordinary* medical and dental care, subject to the rights, duties and responsibilities of the guardian of the child and subject to any residual parental rights and responsibilities and the provisions of any court order. [s. 48.02(12)] In most cases in Wisconsin, the legal custody of a child in foster care will remain with the parent because, under our statutes, ". . . there shall be a policy of transferring custody of a child from the parent . . . only when there is no less drastic alternative. If there is no less drastic alternative for a child than transferring custody from the parent, the judge shall consider transferring custody to a relative whenever possible." [s. 48.355(1)]

We believe that maintaining the parents' involvement, responsibility, and authority when a child is placed outside of the home is critical, if the goal is to reunify the child with the family.

Guardianship means a status granted by the court to a person who has the duty and authority to make important decisions in matters having a permanent effect on the life and development of the child and the duty to be concerned about the child's general welfare, including but not limited to:

- The authority to consent to marriage, enlistment in the U.S. armed forces, major medical, psychiatric and surgical treatment, and obtaining a motor vehicle operator's license.
- The authority to represent the child in legal actions and make other decisions of substantial legal significance concerning the child but not the authority to deny the child the assistance of counsel as required by this chapter.
- The right and duty of reasonable visitation of the child.
- The rights and responsibilities of legal custody except when legal custody has been vested in another person or when the child is under the supervision of the department of corrections . . . or the supervision of a county department . . . [s. 48.023]

The *parental relationship*, of course, is one in which the parent has all of the rights and responsibilities related to the care of his or her child which have not been otherwise altered by the action of a court.

Parental Authority for Participation. If parental rights have not been terminated, and if guardianship has not been inferred on another party, the parents retain the right to make medical decisions for the child.

System Authorization for Participation. Occasionally, a representative of the Wisconsin child welfare system is granted court-appointed legal custodianship or guardianship and would have the ability to approve the participation of a foster child in medical research. In these instances, it is our position that approval for such research participation should not be given solely on the basis of the child being a foster child, but rather reviewed on a case-by-case basis for medical benefits.

In other words, we are not opposed to the participation of a foster child in appropriate and beneficial medical research if:

- a foster child meets the requirements for a medical research study based on some physical, mental, emotional, or developmental condition *and*
- the child's parent or parents were informed and, as appropriate to their legal status, approved of their child's participation *and*
- the child's personal physician, therapist, or other professional recommends to the system authority that the child be involved in that research *and*
- children with similar or related conditions will also participate *and*
- the group of children and other individuals in the study include children outside of the child welfare system *and*
- the child was appointed an advocate with the express responsibility for determining whether participation is in the child's best interest (including ascertaining the child's position),

the representative may consider granting that authority. In Wisconsin, we believe it is our responsibility to help provide a safe, nurturing environment for the children in foster care so that they may become healthy, thriving adults. We are opposed to a foster child being involved in any such research solely because the child is a foster child. It is inappropriate to single out foster care children as a group for medical research, based simply on the fact that they are in the child welfare system.

Thank you again for your invitation to address this important issue. I wish you well and trust that legislative initiatives will be forwarded that reflect the values Wisconsin uses with regard to foster child participation in medical studies.

Chairman HERGER. Thank you, Ms. Harris. Dr. Speers to testify.

STATEMENT OF MARJORIE SPEERS, Ph.D., EXECUTIVE DIRECTOR, ASSOCIATION FOR THE ACCREDITATION OF HUMAN RESEARCH PROTECTION PROGRAMS, INC.

Ms. SPEERS. Good afternoon, and thank you for inviting me to speak about the roles of IRBs and protections for children when they are research subjects. IRBs have a broad responsibility to safeguard the rights and welfare of research subjects. Thus, they should be sufficiently qualified to review the research that comes before them and to ascertain the acceptability of proposed studies in terms of institutional commitments and requirements, applicable law and standards of professional practice. IRBs and institutions that receive funds from the Department of Health and Human Services or review research that the Food and Drug Administration regulates must abide by Federal regulations to protect research subjects and Subpart D, which provides additional protections for children participating in research. As stipulated in the regulations, IRBs must have at least five members with varying backgrounds to promote complete and adequate review of research. At least one member must have primary concerns in the scientific area, at least one member must have primary concerns in nonscientific areas, and at least one member must not be otherwise affiliated with the institution.

The primary role of the IRB is to determine whether a proposed study is ethically justifiable. The Federal regulations lay out seven criteria for IRB approval of research. They include risks to subjects are minimized; risks to subjects are reasonable in relation to potential benefits, including direct benefits to subjects and the importance of the knowledge that might be gained; subjects are selected equitably; informed consent is sought from each prospective subject or legally authorized representative and documented; and when appropriate, the research plan includes monitoring the data to ensure the safety of subjects and includes provisions to protect the privacy of subjects and to maintain the confidentiality of the data. IRBs use written procedures, checklists and other tools to assist them in complying with the regulations. During IRB meetings, an IRB member usually describes the proposed study, and all members discuss and debate the ethical and scientific issues relating to the protection of prospective subjects. In the end, they come to a conclusion to approve or disapprove the study, request more information, or require modifications of the study in order to approve it.

Involving children in research poses special ethical dilemmas. Aside from State laws governing the age of majority and who may consent on behalf of the child to participate in research, children, by nature of their developing cognitive abilities, are unable to give voluntary informed consent to participate in a study. IRBs consider this carefully in research involving children. IRBs must make specific determinations regarding the level of risk involved in a proposed study and whether there is a prospect of direct benefit to the individual subject. They may approve research only when it falls into one of four permitted categories. Research involving greater than minimal risk can only be approved when it meets certain regulatory criteria. These determinations are not easy to make because IRBs must interpret regulatory terms such as "minimal risk" or "minor increase over minimal risk."

One of the main protections for children is the requirement that IRB approve research in which investigators solicit assent from the child and permission from the parents or guardians, individuals who are authorized under law to consent on behalf of a child. Under the regulations, IRBs may approve research involving children who are wards. Depending on the level of risk and whether there is a possibility of direct benefit to the child-subject, a child advocate might be required. For example, in order to approve a study involving greater than minimal risk and no prospect of direct benefit to the individual subjects, IRBs must find that the research is related to their status as wards or is conducted in settings such as schools where the majority of children involved as subjects are not wards. Further, IRBs must require the appointment of an advocate for each child who is a ward, in addition to anyone who is acting on behalf of the child as a guardian.

In summary, there are a number of regulatory requirements to ensure that children participating in research are adequately protected. When IRBs and investigators implement these additional protections, the system works well. Thank you for the opportunity to address the Subcommittee.

[The prepared statement of Dr. Speers follows:]

Statement of Marjorie Speers, Ph.D., Executive Director, Association for the Accreditation of Human Research Protection Programs, Inc.

Good afternoon. My name is Marjorie Speers. I am the Executive Director of the Association for the Accreditation of Human Research Protection Programs—an organization that accredits institutional review boards, or IRBs, as part of a broader human research protection program. I was invited to speak about the roles of IRBs and protections for children when they are research subjects.

IRBs have a broad responsibility to safeguard the rights and welfare of research subjects. Thus, they should be sufficiently qualified to review the research that comes before them and to ascertain the acceptability of proposed studies in terms of institutional commitments and requirements, applicable law, and standards of professional practice.

IRBs in institutions that receive funds from the Department of Health and Human Services or review research that the Food and Drug Administration regulates must abide by federal regulations to protect research subjects and Subpart D, which provides additional protections for children participating in research.

As stipulated in the regulations, IRBs must have "at least five members with varying backgrounds to promote complete and adequate review of research," at least one member must have primary concerns in the scientific area, at least one member must have primary concerns in nonscientific areas, and at least one member must not be otherwise affiliated with the institution.

The primary role of the IRB is to determine whether a proposed study is ethically justifiable. The federal regulations lay out seven criteria for IRB approval of research. Briefly, they include: risks to subjects are minimized; risks to subjects are reasonable in relation to potential benefits, including direct benefits to subjects and the importance of the knowledge that might be gained; subjects are selected equitably; informed consent is sought from each prospective subject or legally authorized representative and documented; and when appropriate, the research plan includes monitoring the data to ensure the safety of subjects and includes provisions to protect the privacy of subjects and to maintain the confidentiality of the data.

IRBs use written procedures, checklists, and other tools to assist them in complying with the regulations. During IRB meetings, an IRB member usually describes the proposed study and all discuss and debate the ethical and scientific issues relating to the protection of prospective subjects. In the end, they come to a conclusion to approve or disapprove the study, request more information, or require modifications of the study in order to approve it.

Involving children in research poses special ethical dilemmas. Aside from state laws governing the age of majority and who may consent on behalf of the child to participate in research, children by nature of their developing cognitive abilities are

unable to give voluntary informed consent to participate in a study. IRBs consider very carefully research involving children.

IRBs must make specific determinations regarding the level of risk involved in a proposed study and whether there is a prospect of direct benefit to the individual subjects. They may approve research only when it falls into one of four permitted categories. Research involving greater than minimal risk can only be approved when it meets certain regulatory criteria. These determinations are not easy to make because IRBs must interpret regulatory terms, such as "minimal risk" or "minor increase over minimal risk."

One of the main protections for children is the requirement that IRBs approve research in which investigators solicit assent from the child and permission from the parents or guardians—individuals who are authorized under law to consent on behalf of a child. Under the regulations, IRBs may approve research involving children who are wards. Depending on the level of risk and whether there is a possibility of direct benefit to the child-subject, a child advocate might be required. For example, in order to approve a study involving greater than minimal risk and no prospect of direct benefit to individual subjects, IRBs must find that the research is related to their status as wards or is conducted in settings, such as schools, where the majority of children involved as subjects are not wards. Further, IRBs must require the appointment of an advocate for each child who is a ward, in addition to anyone who is acting on behalf of the child as a guardian.

In summary, there are a number of regulatory requirements to ensure that children participating in research are adequately protected. When IRBs and investigators implement these additional protections, the system works well. Thank you for the opportunity to address the Subcommittee.

Chairman HERGER. Thank you, Dr. Speers. Dr. Szilagyi to testify.

STATEMENT OF MOIRA SZILAGYI, M.D., Ph.D., FELLOW OF THE AMERICAN ACADEMY OF PEDIATRICS, ON BEHALF OF THE AMERICAN ACADEMY OF PEDIATRICS

Dr. SZILAGYI. Mr. Chairman, I am grateful for the opportunity to testify as this important hearing on children in foster care and clinical trials. My name is Dr. Moira Ann Szilagyi, and I am proud to speak on behalf of 60,000 primary care pediatricians, pediatric medical subspecialists and pediatric surgical specialists of the American Academy of Pediatrics. For the past 19 years, I have specialized in the medical care and developmental issues of children in foster care. I am an associate professor of pediatrics at the University of Rochester Medical Center in Rochester, New York; a medical director of Monroe County Department of Health's Foster Care Pediatrics Clinic. I also serve on the American Academy of Pediatrics Committee on Early Childhood, Adoption and Dependent Care. The academy has a deep and abiding interest in the health care provided to children in the child welfare system. In fact, the academy has numerous published policy statements, clinical guidelines and studies regarding children in foster care, including this, a 170-page handbook for pediatricians on health care standards for children in foster care. I was proud to chair the District II Task Force on Health Care for Children in Foster Care, which authored this resource manual.

The 540,000 children in foster care comprise one of many vulnerable populations to which the academy urges special attention in the provision of health care. Compared with children from the same socioeconomic background, children in foster care have much higher rates of serious emotional and behavioral problems, chronic physical disabilities, birth defects, developmental delays, and poor

school achievement. Typically these conditions are chronic, underidentified, and undertreated, and they have an ongoing impact on all aspects of their lives, even long after these children and adolescents have left the foster care system. As a result, children in foster care warrant special attention in all aspects of their health care. One aspect in which children in foster care deserve particularly close and special consideration is their inclusion in clinical trials. It is the position of the American Academy of Pediatrics that drugs be studied in children to determine their safety and efficacy in this age group. Indeed, the academy considers it a moral imperative to formally study drugs in children so that they can enjoy equal access to existing as well as new therapeutic agents.

Research participation is often beneficial to participants and may allow them access to care they could not otherwise receive. Therefore, children in foster care, as a population that tends to have a greater preponderance of special health care needs, should be afforded the same opportunities and access to safe and effective treatments. However, special consideration is necessary when allowing children in foster care who are in the care and custody of the State to take part in certain studies that may contain greater than minimal risk to the child.

The academy has developed extensive guidelines and standards related to the ethical conduct of clinical trials involving children. The academy also agrees with the Department of Health and Human Services' regulations governing the inclusion of children in clinical research. For the purposes of today's hearings, however, perhaps the most relevant standards deal with consent. Young children are, by definition, incapable of consenting to medical procedures. Consent must be given on their behalf by a parent, a legal guardian or an individual or institution acting in loco parentis; that is, in place the of the parent. In all cases, however, the overriding consideration must be the best interest of the child.

HHS regulations outline issues of consent. Consent must be obtained from the adult acting legally on behalf of the child. When developmentally appropriate, the assent of the child must be gained prior to participation in any clinical trial. The question, then, for children in foster care is whether adequate safeguards are established when consent is obtained for trials that contain above minimal risk to the child or when the research does not hold the prospect of providing direct medical benefit to the child him or herself.

For children in the foster care system, an important safeguard is a special advocate who can help the foster family or State agency navigate medical issues, ensure that the child's medical care needs are being met, assist the child in determining whether or not he or she should participate, and provide a source of continuity for the child and the legal guardians throughout the duration of the study. Even in cases of less than minimal risk or studies with prospect of direct benefit, an advocate, while not required, could play an important role in the child's support system. It is my understanding that the Subcommittee is concerned by press reports about the participation of children in foster care in clinical trials of HIV drug treatments that began in the late eighties. My own professional experience includes a number of cases of HIV-positive children in fos-

ter care in my community who received HIV multidrug treatments during the early nineties. When our patients took these drug combinations, we saw a startling improvement in lifespan and quality of life. Before the introduction of these combination drugs, our HIV-positive children in care were literally wasting away before our eyes.

There were some side effects with the drugs, but not that many, and the side effects were nothing compared to the devastation of the disease. I recall one 2-year-old child in particular who was literally dying. One year after receiving combination therapy, he was essentially indistinguishable from his healthy peers. He was able to go to preschool, live in a family instead of the hospital, and have hope for a longer life. He is still alive today and was eventually adopted by his foster family. Mr. Chairman, the decision to enroll a child in a clinical trial is never an easy one, even in a traditional family structure. While the headlines seem to suggest that children in foster care were somehow singled out as hapless guinea pigs, my experience indicates that children in foster care are actually less likely than other children to be considered for participation in a clinical trial. In fact, numerous barriers exist for children in foster care to even obtain routine health care and necessary health services. Participation in a clinical trial where access would be far more complex is even less likely to occur.

The American Academy of Pediatrics believes that children in foster care deserve to be offered the same opportunities as other children to benefit from newer drugs and treatment protocols, especially when a child's condition is so grave that there are few options available to them. Indeed, it would be unethical to do otherwise and systematically deny access to clinical trials that could have saved their lives or vastly improved the health of critically ill children in foster care. It is clear that children in foster care are a special population, and that they deserve additional protections when being considered for inclusion in clinical trials.

Mr. Chairman, and Members of the Subcommittee, I deeply appreciate this opportunity to offer testimony on behalf of the American Academy of Pediatrics. A more detailed version of my testimony has been submitted for the record. I stand ready to answer any questions you may have, and I thank you for your commitment to the health of the children of our Nation.

[The prepared statement of Dr. Szilagyi follows:]

Statement of Moira Ann Szilagyi, M.D., Ph.D., Associate Professor of Pediatrics at the University of Rochester Medical Center, Rochester, New York; Medical Director, Foster Care Pediatrics Clinic, Monroe County Department of Health; and Member, Committee on Early Childhood, Adoption and Dependent Care, American Academy of Pediatrics

Mr. Chairman, I am grateful for the opportunity to testify at this important hearing on children in foster care and clinical trials. My name is Dr. Moira Ann Szilagyi, and I am proud to speak on behalf of the 60,000 primary care pediatricians, pediatric medical subspecialists, and pediatric surgical specialists of the American Academy of Pediatrics. For the past 19 years, I have specialized in medical care and developmental issues of children in foster care. I am an associate professor of pediatrics at the University of Rochester Medical Center in Rochester, New York and Medical Director of the Monroe County Department of Health's Foster Care Pediatrics clinic. I also serve on the American Academy of Pediatrics' Committee on Early Childhood, Adoption and Dependent Care.

The Academy has a deep and abiding interest in the health care provided to children in the child welfare system. In fact, the Academy has published numerous policy statements, clinical guidelines, and studies regarding children in foster care, including a 170-page handbook for pediatricians on health care standards for children in foster care. I was proud to chair the District II Task Force on Health Care for Children in Foster Care, which authored that resource manual.

The 540,000 children in foster care comprise one of many vulnerable populations to which the Academy urges special attention in the provision of health care. Compared with children from the same socioeconomic background, children in foster care have much higher rates of serious emotional and behavioral problems, chronic physical disabilities, birth defects, developmental delays, and poor school achievement.[1] Typically, these conditions are chronic, under-identified, and under treated, and they have an ongoing impact on all aspects of their lives, even long after these children and adolescents have left the foster care system.[2] As a result, children in foster care warrant special attention in all aspects of their health care.

One aspect in which children in foster care deserve particularly close and special consideration is their inclusion in clinical trials. It is the position of the American Academy of Pediatrics that drugs must be studied in children to determine their safety and efficacy in this age group. Indeed, the Academy considers it a *moral imperative* to formally study drugs in children so that they can enjoy equal access to existing, as well as new, therapeutic agents.[3] Research participation is often beneficial to the participants, and may allow them access to care they could not otherwise receive. Therefore, children in foster care, as a population that tends to have a greater preponderance of special health care needs, should be afforded the same opportunities and access to safe and effective treatments. However, special consideration is necessary when allowing children in foster care who are in the care and custody of the state to take part in certain studies that may contain greater than minimal risk to the child.

The Academy has developed extensive guidelines and standards related to the ethical conduct of clinical trials involving children. The Academy also agrees with the Department of Health and Human Services' (HHS) regulations governing the inclusion of children in clinical research (CFR 45 Part 46, Subpart D). For the purposes of today's hearing, however, perhaps the most relevant standards deal with consent. Young children are, by definition, incapable of consenting to medical procedures. Consent must be given on their behalf by a parent, a legal guardian, or an individual or institution acting *in loco parentis* —that is, in the place of the parent.

The Academy's foster care handbook, Fostering Health, dedicates an entire chapter to medical consents for children and adolescents in foster care.[4] States and localities have varying laws and detailed policies related to the ability of individuals involved in a child's care to consent to medical care or procedures. Many localities have convened multidisciplinary teams to determine what is in a child's best interest when confronted with complex health issues for children in their care. In general, legal guardianship remains with the birth parents (a term which includes legal guardians) unless a child is freed for adoption. There have certainly been cases when children who are in foster care are enrolled in clinical trials with the full consent of their birth parents. In certain cases when the birth parents are unavailable or uncooperative, agencies may approve or seek a court order for medical procedures—such as participation in clinical trials—for which written consent is required and which are deemed to be in the best interests of the child. Once a child is freed for adoption, the state agency assumes sole responsibility for consenting for a child's medical care.[5] In all cases, however, the overriding consideration must be the best interest of the child.

HHS regulations outline issues of consent: consent must be obtained from the adult acting legally on behalf of the child, and, when developmentally appropriate, the assent of the child must be gained prior to participation in any clinical trial. The question, then, for children in foster care is whether adequate safeguards are established when consent is obtained for trials that contain above minimal risk to the child, or when the research does not hold the prospect of providing direct med-

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[1] Committee on Early Childhood, Adoption and Dependent Care. "Health Care of Young Children in Foster Care." *Pediatrics*, Vol. 109, No. 3, March 2002.

[2] Task Force on Health Care for Children in Foster Care. Fostering Health: Health Care for Children in Foster Care. 2nd ed. American Academy of Pediatrics, 2005.

[3] Committee on Drugs. "Guidelines for the Ethical Conduct of Studies to Evaluate Drugs in Pediatric Populations." *Pediatrics*, Vol. 95, No. 2, February 1995.

[4] Committee on Drugs. "Guidelines for the Ethical Conduct of Studies to Evaluate Drugs in Pediatric Populations." *Pediatrics*, Vol. 95, No. 2, February 1995.

[5] Task Force on Health Care for Children in Foster Care. Fostering Health: Health Care for Children in Foster Care. 2nd ed. American Academy of Pediatrics, 2005.

ical benefit to the child him or herself. For children in the foster care system, an important safeguard is a special advocate who can help the foster family or state agency navigate medical issues, ensure that the child's medical care needs are being met, assist the child in determining whether or not he or she should participate, and provide a source of continuity for the child and legal guardians throughout the duration of the study (section 46.409). Even in cases of less than minimal risk or studies with prospect of direct benefit, an advocate, while not required, could play an important role in the child's support system.

HHS regulations state—and the Academy concurs—that children in foster care should not be considered for studies which contain the prospect of greater than minimal risk *and* in which there is no direct benefit to the child him or herself (46.406–407). For these studies, it is only appropriate to consider using children in foster care under certain circumstances, such as if the research is related to their status as wards of the state. In other words, they should only be included when involvement of children in foster care is necessary since the research aims to answer a question related to conditions specifically affecting children in foster care. In these rare instances, it is imperative that an advocate be appointed to act on behalf of the child for the duration of the study to assist the child and foster family for the reasons stated above: to navigate medical issues, ensure that the child's medical care needs are being met, assist the child in determining whether to participate, and provide a source of continuity for the child and legal guardians throughout the duration of the study.

It is my understanding that the subcommittee is concerned by recent press reports about the participation of children in foster care in clinical trials of HIV drug treatments that began in the late 1980s. While attention has been paid specifically to these HIV drug trials, children in foster care have been known to participate in other types of clinical trials, including those focused on cancer treatment. My own professional experience includes a number of cases of HIV-positive children in foster care in my community who received HIV multi-drug treatments during late 1980s and early 1990s. When our patients took these drug combinations, we saw a startling improvement in lifespan and quality of life. Before the introduction of these combination drugs, our HIV-positive foster children were literally wasting away before our eyes. There were some side effects with the drugs, but not that many. I recall one two-year-old child in particular who was literally dying. One year after receiving combination therapy, he was essentially undistinguishable from his healthy peers. He was able to go to preschool, live in a family instead of the hospital, and have hope for a longer life. He is still alive today and was adopted by his foster family.

Mr. Chairman, the decision to enroll a child in a clinical trial is never an easy one, even in a "traditional" family structure. While the headlines seem to suggest that children in foster care were somehow singled out as hapless guinea pigs, my experience indicates that children in foster care are actually less likely than other children to be considered for participation in a clinical trial. In fact, numerous barriers exist for children in foster care even to obtain routine health care and necessary services. Participation in a clinical trial, where care would be far more complex, is even less likely to occur.

The American Academy of Pediatrics believes that children in foster care deserve to be offered the same opportunities as other children to benefit from newer drugs and treatment protocols, especially when a child's condition is so grave that there are few options available to them. Indeed, it would be unethical to do otherwise and systematically deny access to clinical trials that could have saved the lives or vastly improved the health of critically ill children in foster care. It is clear that children in foster care are a special population, and that they deserve additional protections when being considered for inclusion in clinical trials.

Mr. Chairman and Members of the Subcommittee, I deeply appreciate this opportunity to offer testimony on behalf of the American Academy of Pediatrics. I stand ready to answer any questions you may have, and I thank you for your commitment to the health of the children of our nation.

Chairman HERGER. Thank you, Dr. Szilagyi. The gentleman from Colorado Mr. Beauprez to inquire.

Mr. BEAUPREZ. Thank you, Mr. Chairman. Doctor, let's just start with you, if I might. I am intrigued by your testimony and especially, I think, your closing assertion that the very children

that may need the opportunity to participate in these trials, may need good health care in general, are ones that, perhaps, are being denied, foster children. I am concerned that perhaps in our zeal to do something, we maybe do too much. Congress sometimes can do that. If you can enlighten me a little bit, what maybe should we be doing; and even more specifically, since we're focused on HIV/AIDS, and that seems to be a situation that occurred quite a few years ago, tell me from what you know, and you would appear to be a pretty good expert at this, what sort of clinical trials are going on today? We're talking a lot of about what went on 10 or 15 years ago. What is going on today, and what, in your opinion, should Congress do?

Dr. SZILAGYI. Are you asking me about specifically what clinical drug trials or what types of trials?

Mr. BEAUPREZ. What type of trials?

Dr. SZILAGYI. I think most of the research that is centered on children in foster care from the health perspective now has to do with mental health interventions for children, and possibly developmental interventions for children; visitation, mentored visitation interventions. I put those in health because I look at health as a very global issue for children in foster care. There are still occasionally children who might be enrolled in a drug trial, but those are usually children with rare illnesses, childhood cancers that haven't responded to more traditional therapies, and that they be offered the same opportunity as any other child to become involved in a therapeutic drug trial, that may be their own only last best option for life. That is an extremely rare event. It has happened—I have taken care of probably close to 9,000 children in foster care over the last 19 years of my practice, and, you know, that number—those faces change all the time because of the nature of my practice. I have really only had occasion to have that situation outside of the HIV situation come up probably two other times. So, it is not—you know, we don't have vast numbers of children involved in these randomized controlled clinical trials.

Mr. BEAUPREZ. Ms. Harris, near the end of your testimony, I think it is on page 4 of your written testimony, you outlined, I believe, six different criteria for a child—a foster care child to be included in a clinical trial. Are any of those—do all of those have to be met in the affirmative in order for a child to be included?

Ms. HARRIS. Yes, as stated.

Mr. BEAUPREZ. Which raises, actually, another question, and I fully understand and appreciate how we could get to that point. Another concern I actually had raised to me about the very point you're talking about, about making these kind of opportunities available, not precluding foster children from the population, is that perhaps in our concern about making sure the wrong thing doesn't happen to the wrong child for the wrong reasons, that by an abundance of regulations and hoops to jump through we actually do just that; that it is not a very attractive target—a very attractive population, excuse me—a very attractive population to even look at for clinical trials because of the regulation burden we put in front of them.

Ms. HARRIS. Well, my guess is that most of these criteria, with the exception of appointing an advocate, would be applicable to all children that are going to be involved in medical trials.

Mr. BEAUPREZ. So, in my case, if it were one of my children, it would be another advocate. Would there—since I am the parent, the biological parent, I have legal custody, we wouldn't be setting up another hurdle, would we?

Ms. HARRIS. No, not with respect to the advocate.

Mr. BEAUPREZ. I am not suggesting the advocate go away. Actually, Dr. Fleischman, I wanted to pursue that a little bit with you. What exactly did you do in the Bronx? I want to be sure and ask, I think, two related questions: Why is this— if most of this occurred—most of what we read in the press occurred 10, 15 years ago, why are we just now kind of hearing about it? It is being brought to light, and I think HHS regulations neither preclude now nor mandate certainly that there be any payment made, but are you familiar with payments ever being made; and, if so, who gets paid for these clinical trials?

Dr. FLEISCHMAN. The why now question, I think you're going to have to ask people other than myself. I have no idea why now. I find no rational reason for what I thought was a rewriting of history in much of the media circus. In terms of the question of why, what we did in the Bronx, we did appoint a physician advocate who was in one of our public hospitals to share his views on these trials with each of the foster families, and we did use his expertise to help the foster families, help decide whether the child ought to be in the trial after the other steps had been gone through of individualized consent from the agency, legal guardian or parent, review. This was an adjunct, an added thing, that we at the Albert Einstein College of Medicine felt was important. In terms of the payment, families who enroll children in clinical trials generally do receive some compensation for their efforts in bringing the child to the clinic; transportation, time away from work, things of that sort. To my knowledge, there were no dollars in true payment for using children or commodifying children in such clinical trials, and most IRBs would not tolerate such.

Mr. BEAUPREZ. Good.

Chairman HERGER. The gentleman's time has expired.

Mr. BEAUPREZ. Thank you, Mr. Chairman.

Chairman HERGER. The gentleman from Washington Mr. McDermott to inquire.

Mr. MCDERMOTT. Thank you, Mr. Chairman. As I listen to this panel, I come away with a question. I guess it sounds like in Wisconsin you wouldn't get into a clinical trial like this; is that correct?

Ms. HARRIS. With foster care children as a class. We are not saying that we don't think foster care children should be eligible for clinical trials. If they are eligible, they should be treated as any other child and have parental consent or consent of the legal authority that has legal custody of the child.

Mr. MCDERMOTT. I asked my staff after I listened to all of you, why are we here? Not exactly Mr. Beauprez's question. I read these articles from the Newsday and from the New York papers that covered this issue. I tend to agree with Dr. Fleischman. There seems to be a—this was a long time ago, and a whole different scene.

What I would really like to hear from you, you all are advocates for children, all of you. Is there anything that we should do to make a uniform system across the country so that there is no real magical difference? This whole question about should we override what goes on at the State level, is that a good idea in this area? Or do you see something where there is a Federal role that we should do? None of you made any recommendations. I don't know whether that was because you didn't have any or didn't think there should be any changes, or it was all perfect out there. So, Dr. Fleischman?

Dr. FLEISCHMAN. I, individually, myself, had three opportunities through service to the government to review the regulations for children, and in each of those times, we felt those regulations were adequate. The National Bioethics Advisory Commission, Dr. Shalala, Secretary Shalala's Human Research Protections Advisory Committee, and the now Secretary's Advisory Committee have all suggested, as well as the IOM Institute's reports, the Institute of Medicine reports, all suggested that we would benefit in this country, not specifically in the foster care, only in foster care, in a basic data collection system that would assist us in understanding who are the subjects of research in our country, what are the criteria that IRBs are using in approving research, and what are the outcomes based in those research studies. The Office of Human Research Protection has not requested that. They feel, I believe, that they don't have the authority to do that. I don't speak for them, but we would be well served by having a database that at least gives us the baseline information about such. That is one. Two, all of those groups have recommended that there be expertise in pediatrics—you can call it advocates or experts in pediatrics—on any IRB that is reviewing things related to children. It isn't required in the regulations. It could be strongly urged, or it could be required. All of those learned groups have made those recommendations, and I believe for the most part IRBs fulfill those recommendations. In these cases, since these were—these research prospects were in AIDS clinical trials centers, centers of excellence in our cities, all of those IRBs had advocates for children and had children's experts on them. In general, if we are looking to fix, or help, or support the present regulatory structure of the data collection system and expertise in the areas related to the kinds of subjects who are being reviewed like prisoners, or children, or mentally ill people, or retarded people, or people of any variety——

Mr. MCDERMOTT. Any of the others of you have a comment?

Dr. SZILAGYI. I probably have a broader perspective on the whole issue of health care for children in foster care than the more narrowly defined. I agree with everything Dr. Fleischman said. Let me start there. I think that children in foster care have huge health care needs. Forty-five percent of them have chronic medical illness. Sixty percent of children under the age of 5 have developmental disabilities. Forty-five percent of our school-age children are in special education placements, and eighty percent of children over the age of 4 have mental health needs. Their access to health care services is abysmal in this country. There are multiple barriers. One of you asked about barriers before. Those barriers include their high mobility in and out of the system; the high mobility of

professionals in the system; Medicaid as a funding resource, which, while it offers some benefits in terms of routine preventive care, is a barrier to many other types of care. The whole system is underfunded and under-resourced, and I would suggest that every child in foster care deserves to have a medical home where they receive high-quality care that is comprehensive, well-coordinated, and that works very closely and in collaboration with the child welfare system. I think that that would afford a high level of protection in terms of enrolling children in clinical research trials. In our community, whenever a question comes up about an end-of-life issue for a child, a surgical procedure that is being offered to a child, bone marrow transplant or child with cancer who needs a more advanced protocol than is currently available as a standard of care, those questions come back to our office where we are the primary care doctor in the medical home. I think trying to change the whole system of care for our kids so that it was much more modeled on a medical home model would go a long way toward preventing these types of issues.

Dr. FLEISCHMAN. Well said.

Mr. MCDERMOTT. If the Chairman would just give me 1 more second. The database you are talking about, I remember when I did some research when I was in my residency, and I found the databases could give me two left-handed plumbers living in towns of less than 20,000 people. Are you suggesting a national database for all health care data so that we would then have that capacity to do that kind of research? Do you think politically that is possible?

Dr. FLEISCHMAN. No. I am suggesting that we have a database on all subjects of research in this country.

Mr. MCDERMOTT. Oh, just research.

Dr. FLEISCHMAN. That we ask IRBs to review research, and we ask investigators to tell IRBs and then tell the government how many subjects, what was the kind of research, what were the criteria in which the IRB reviewed the research, and move forward with it.

Mr. MCDERMOTT. Thank you, Mr. Chairman.

Chairman HERGER. Thank you. The gentleman from California Mr. Becerra to inquire.

Mr. BECERRA. Thank you, Mr. Chairman. Thank you all for your testimony. I want to go back to the gentleman of Washington's question, because I think it is the correct one. Is there something we should be doing? My sense is that we are trying to find out if there is this purgatory where children are where it is not clear if they really should participate in these clinical trials, and we are concerned that they actually may be used as a commodity in some of these clinical trials. I am not sure if you have answered that question for us to leave us with a feeling that there is something we can do, or we needn't do anything. So, if you can give us some clarity, is there something we should do? If you say yes, please try to give us a specific.

Ms. HARRIS. I think one of the questions that comes to mind is is the determination of whether research carries minimal risk and the child would directly benefit subjective? Who makes that determination? What are the criteria? That is one of the questions I

think that is unanswered, and that was sort of central to some of the HIV/AIDS research.

Mr. BECERRA. Before anyone goes on, Ms. Harris, let me ask, are you saying then that Wisconsin, since you are more restrictive than other States, and I think my State of California is also very restrictive in requiring some judicial order to allow a child, a foster child, to participate, are you saying that there is a concern that, in fact, there might be a problem in protecting that child sufficiently through the IRB process without a child advocate?

Ms. HARRIS. Yes, and if there is, if there is, that right now within the IRB process, there is lack of clarity with—in that determination.

Mr. BECERRA. Thank you.

Ms. SPEERS. I would suggest three items. One is to just reinforce what Dr. Fleischman suggested, which is any IRB that is reviewing research involving children, that IRB should have expertise in pediatrics; but more than just pediatrics, in the interests of children so that it might not be a pediatrician. It might be a social worker. It might be an individual school, someone who understands the needs of children. That is not a requirement in the Federal regulations at this time. Secondly, the additional protections pertaining to children in Subpart D are not universally adopted across the Federal agencies that conduct or sponsor human research. Subpart D is followed by the Department of Health and Human Services. It was added in 2001 to the Food and Drug Administration regulation.

Mr. BECERRA. Who else would be part of that, what other agencies?

Ms. SPEERS. There are 16 other agencies.

Mr. BECERRA. Can you give us those you believe should fall under the jurisdiction of Subpart D?

Ms. SPEERS. I want to say also that the Department of Education does have Subpart D. Those are the three that do, but the other ones, in particular one is the National Science Foundation.

Mr. BECERRA. Do me a favor. If you could just submit those so that way you can get to your third part, because otherwise I am going to run out of time.

[The information was not received at time of printing.]

Ms. SPEERS. The third is I wanted to suggest that there should be an education requirement for IRBs. IRB members now have no education requirement under the Federal regulation. It would be much easier for IRBs to follow the regulations and understand the regulations if they had some type of education requirement.

Mr. BECERRA. Dr. Szilagyi, I hope I pronounced that correctly, do you have anything you would like to add?

Dr. SZILAGYI. No.

Mr. BECERRA. A quick question then before I run out of time. Is there any standard throughout that is applied, that should be applied, a best practices standard that we could use?

Ms. HARRIS. I am not aware of an existing best practices.

Mr. BECERRA. Is it good policy to allow the various States to come up with what they believe is the best practice for these decisions in regards to foster children?

Dr. FLEISCHMAN. One very powerful method is that Office of Human Research Protection has the ability to give guidance to all IRBs around the country.

Mr. BECERRA. Does it do so?

Dr. FLEISCHMAN. They do. They have not yet done that in this area. The Secretary has an advisory committee to that office on human research protection.

Mr. BECERRA. Should they do so?

Dr. FLEISCHMAN. I believe they should, as well as to clarify for Ms. Harris the definitions of minimal risk, and minor increase over minimal risk, and prospect of direct benefit, which the Subcommittee on children has already provided and requested that a guidance be produced.

Mr. BECERRA. One last question as my time runs out. If the best interest of a child is not upheld, who should be responsible?

Dr. FLEISCHMAN. Everyone. Starting with the investigators, starting with those people in agencies who are responsible for those children, and going back toward the IRB, the institution that conducted that IRB. Ultimately, at the Federal level, there is some responsibility. The real responsibility stands at the local level.

Mr. BECERRA. Anyone else?

Chairman HERGER. Thank you. The gentleman from California Mr. Stark may inquire.

Mr. STARK. Thank you, Mr. Chairman. Just a couple of comments. Dr. Szilagyi, I am a little bit concerned. I appreciate your idea that it is through experiments, and the poor children can get health care, but I wonder is it right in this country, and this is just an aside, should they have to be guinea pigs to get health care? I think that is wrong.

Dr. SZILAGYI. I don't believe I said that.

Mr. STARK. Well, you didn't say that. To me it implies that. One of the good things about getting foster children into these programs is that they wouldn't get health care otherwise. I am suggesting to you that that is a travesty. It is has nothing to do with these rules, but that is one of the travesties of having uninsured children.

Dr. SZILAGYI. Then I would like to clarify. What I intended to say was that for some children in certain circumstances, and the HIV/AIDS phenomenon of the early 1990s was one of those——

Mr. STARK. Let's move ahead, though. Dr. Szilagyi. ——the only way for them to get certain kinds of care was actually for them to be enrolled in studies because that was the only way to obtain these drugs.

Mr. STARK. Going back, very quickly, and, Mr. Chairman, I ask unanimous consent to put both subpart C and subpart D of 45(c) in the record.

[The information is pending:]

Basically, there is a difference. Young was wrong. There are additional protections for prisoners; and basically, if I can just paraphrase in the time allowed, it says that all regulations relative to prisoners will be enforced regardless of other regulations in this subpart. It goes on to say that because prisoners may be coerced, they have got to have an advocate; yet subpart D for kids, and that is not there. There is in my mind a question. If you still had an Eloise Anderson around someplace, she would sacrifice children

for—you don't know who she was, do you? You dumped her from Wisconsin, did the California, thank you very much, send her back and give you three free kicks. There is a question that perhaps foster children are—present company completely excepted—you and the Committee are an easy target because they are there, and they may not have to go through as much pleading with the parent and explaining because it is a much more institutionalized group of children, and you are able to find research subjects in that population. That worries me. It would be a simple thing, it seems to me, for us—what is good enough for Haldeman, Erlichman or Martha Stewart ought to be good enough for my kids, right? Prisoners can have an advocate required; it doesn't seem to prohibit us from using prisoners in these cases. I think maybe we could make some simple changes, which—in States other than the ones represented here which don't have such good protection. I think there are some States, Mr. Chairman, where we find it has been more casual in their outlook as to how foster children are protected. I don't think we would impose any great impact or regulatory burden by considering in this Subcommittee whether we might coordinate the requirements for prisoners and children. I hope you all will have staff look at these requirements, and we could ask the witnesses perhaps to respond to us later whether the prisoner requirements would unduly hamper research and the opportunity for children to participate in these programs. Then we could sleep a little better at night knowing that at least we put in the requirement, the children would have adequate advocates in the program. If anybody wants to disagree with that, that is fine with me, but that is what I am reading here.

Dr. FLEISCHMAN. As long as you are aware of that, the Office of Human Research Protection has just created the Institute of Medicine broad-based study on prisoners research, and the Secretary's Advisory Committee is taking up that issue as well. There is a broad-based review of research with prisoners that is going on as we speak. We need to be sure to coordinate that thinking with whatever thinking you have.

Mr. STARK. I think, Mr. Chairman, with foster kids, they don't have the complete freedom, just as a prisoner doesn't, and it is that minor extra protection that we might want to consider in any legislation that you might consider, Mr. Chairman. I thank all of you for taking the time, and your concerns. I thank you all for everything, except Eloise Anderson. You can have her back.

Chairman HERGER. I thank the gentleman. Ms. Harris, beyond participation in clinical trials, could you tell me about drug use of children in foster care more generally? For example, who decides whether children are to receive medications such as antidepressants or stimulants, the doctors, foster parents, caseworkers, all of the above? What do we know about the medications provided children in foster care; for example, what share are on medication and for how long?

Ms. HARRIS. I can't speak specifically to certain medications. We can certainly get that information to the Subcommittee. The determination is parents retain the rights of any other parent with respect to children in Wisconsin's foster care system, unless the parent is incapacitated or for some other reason incapable of mak-

ing that decision. Then the court can grant authority for decision-making, either a temporary—through temporary guardianship through the system. Generally, even if the child is not physically placed with the parent, the parent retains the right to make all decisions with respect to all medical decisions.

Chairman HERGER. Thank you. Dr. Fleischman, the purpose of this hearing this afternoon is that there has been some very serious allegations made recently, especially about the treatment of children in New York City, in clinical trials for AIDS medicines in the late 1980s and 1990s. These go to race and whether certain children were targeted because of their race or their being in foster care. Our purpose today is to review whether current protections are adequate or not. Obviously, we are concerned about the allegations that have been raised. You were not only there, but you treated many of these children and sat on the Institutional Review Boards, whose purpose was to determine the propriety of their participation. Would you care to comment directly about some of the more inflammatory charges that have been made of late?

Dr. FLEISCHMAN. The charges saddened me. I thought they were extremely inaccurate; that the doctors, the Institutional Review Boards and the institutions caring for children with HIV and AIDS were extremely sensitive to the areas of cultural sensitivity, race, ethnicity, the concerns of poverty. Our children, all of our children with HIV, the vast majority, were from poor families and minority families. We were very sensitive to those issues. The IRBs were extremely concerned. We believe we developed procedures that protected their interests and enhanced their quality of life and their lives in general.

Chairman HERGER. Thank you. I want to thank each of our witnesses this afternoon for taking the time to appear here today. I appreciate your help in understanding this issue further. With that, the Subcommittee stands adjourned.

[Whereupon, at 3:55 p.m., the hearing was adjourned.]

[Submissions for the record follow:]

Statement of Sheila Matthews and Gloria M. Wright, Ablechild.org, New Canaan, Connecticut

Wards of the State: Protection of human subjects "Special Population"

Ablechild Background: a non-profit 501C–3 organization whose Board of Directors consist of doctors, teachers, psychologists, and other mental health providers dedicated to protecting the health and well-being of children. These true professionals wholeheartedly support parental rights, informed consent (full disclosure), and a parent's right to choose regardless of legal status.We have spoken out on this issue in many media outlets: CNN Today Show, CBS Evening News, Good Morning America, Hannity & Colmes, A&E Investigative Reports, Montel Williams Show, John Walsh Show, Discovery Health Gary Null Show, WXIA TV NBC Atlanta, NBC Health Page, Time Magazine, New York Times, USA Today, G. Gordon Liddy Show, Sean Hannity Radio Show, Armstrong Williams Show, Martha Zoller Show, WDUN, The Riley Report Many Other Shows and Publications Numerous Websites.

My name is Sheila Matthews and I am a Connecticut mother who testified before the public health committee on the first law to prohibit schools from recommending psychotropic "medication" to children as a requirement for attending school. I am also the National Vice President and Co-founder of Ablechild.org a non-profit national parent organization that works on educating the public on the issues of informed consent and the right to refuse psychiatric "treatment".

Our organization is very concerned with the outcome of this hearing because we hear directly from parents victimized by the trafficking of their children into clinical drug trials while in state custody. Ablechild has documented cases of children that have been placed on drugs, completely unaware if they are participating in a clinical drug trial, and without knowing that they have the right to "opt out" of participating. The fact is, the State holds the responsibility of providing informed consent to parents and children, and lacks any procedure to protect and safeguard this right.

A clear conflict of interests exists between the pharmaceutical industry and the experimentation occurring on children within state custody. This fact is clearly demonstrated by workshops sponsored by the pharmaceutical and biotechnology industries designed to optimize strategies for drug development and trials in children. One such workshop was held in New Haven, Connecticut on May 19th–21st, 1997 and brought together representatives of the drug industry, government, and the academia.

The workshop was specifically designed to focus on "New Pediatric Regulations," "Vaccine Development," "Strategies for Identifying New Gene Targets," "Novel Drug Delivery Systems," and "Neuro-Behavioral Disorders". What this workshop failed to focus on was the informed consent process, the right to refuse process, and the special rights afforded to the vulnerable population, "Wards of the State".

Sponsors included Yale Department of Pediatrics and Yale Child health Research Center New Haven CT, Yale Child Study Center, New Haven Connecticut, National Institute of Child Health and Human Development, and NIH Bethesda, MD. Corporate Sponsors included Bayer Corporation, Pfizer, Inc., SmithKline Beecham Pharmaceuticals, Biological Division, Wyeth-Lederle Vaccines, and Pediatrics.

Our organization points out the problems that resulted from strategies designed to target and exploit these children, strategies that were highlighted at the workshop in 1997.

*The Connecticut Advocate reported these resulting problems in its June 5th, 2001 article, "**Study Calls for Review of Psychiatric Drugs Prescribed to Kids.**"* Within this news story, the authors of a new study questioned why **396** children under 4 years old covered by Medicaid were prescribed psychiatric drugs. Some of these children were less than 1 year old.

Trafficking children into clinical drug trials is a violation of basic human rights. Past history of this United States human rights violation is clearly illustrated by one landmark case, Willowbrook that was brought to public light in 1987. This case addressed the right to informed consent of any institutionalized person. It is our hope that these hearings will reform this human rights violation and uphold their rights.

Ablechild.org
Hendersonville, NC 28791
May 18, 2005

Congressman Wally Herger
2268 Rayburn House Office Building
Washington, DC 20515

Dear Congressman Herger:

As a grandparent and a member and officer of **Ablechild**, a 501(C) 3 organization, I wish to bring to your attention our cry for the *protection of human rights of foster children across America*!

Our organization frequently hears from parents across the nation that implore us for assistance in the matter of the clinical trial/experimental drugging of their children while in state custody and in foster care. These children have been placed on clinical trial drugs without a legal advocate responsible for safeguarding their health, nor their life. As minors these children are unable to opt out of these tests/experiments, the parents have been denied their right to dissent and there obviously are no procedures in place to safeguard the rights of the children.

Ablechild is aware of your committee's investigative hearings into Child Protective Services which was held in March 2004. Wreckless endangerment of children in the custody of most states across the nation became fairly apparent during those hearings. Illegal seizure of many children was noted. Methods used and justification to seize children from the safekeeping and love of their parents and thus placing them in foster care was well exposed at that time. Now these very children are being forced into clinical trials—or experimentation—*while being forced to SURRENDER THEIR HUMAN RIGHTS while at the same time endangering their present/future health*.

Congressman Herger, **Ablechild** calls upon your committee to *enact a law whereby all pediatric clinical trials, without express consent of the parents, be prohibited. This law should include children in foster care and should not preclude those children who are at home with their parents or custodial family members*. Congressman, the importance of such legislation goes beyond the giving of a pill to a child. **This matter is about Human Rights—and those rights of children have been gravely sacrificed and the health and future of these children may have been imperiled.**

Ablechild stands ready to support you and your committee on behalf of America's children and we would appreciate having dialogue with you and/or your committee members in this matter and others that greatly impact our America's children and their families.

Sincerely,

Gloria Wright
NC Vice President

Statement of Vera Hassner Sharav and John H. Noble Jr., Ph.D., Alliance for Human Research Protection, New York, New York

On March 10, 2004, The ALLIANCE FOR HUMAN RESEARCH PROTECTION (AHRP) filed a complaint with both the Food and Drug Administration and the federal Office of Human Research Protection (OHRP) when we learned that 36 Phase I and Phase II AIDS drug experiments had been conducted on infants and children who were under the guardianship of the New York City Administration for Children's Services (ACS). The children were living at Incarnation Children's Center, a foster care facility under contract with ACS and the Catholic Archdiocese. We had reason to believe that the experiments were unethical, illegal, and coercive—and that federal regulations have been violated. We did not know at the time that children in foster care nationwide were subjected to research exploitation at prestigious medical research institutions.

Historically such children have been abused and exploited in medical experiments—for that reason, federal regulations were enacted to restrict the use of foster care children in research. The Associated Press confirms that for more than two decades, government officials colluded with hospitals and researchers to facilitate the enrollment of children who were in the care of the state for experimental drug trials. Nationwide, an estimated 698 to 1,388 foster children were used to test experimental AIDS drugs—at least 465 of those children were in the care of NYC's ACS—almost all were children of color. How ironic it is that children, who were placed by the courts into the protective custody of foster care agencies pursuant to the provisions of the Adoption and Safe Homes Act of 1997, should end up further victimized by their caretakers.

These children were exposed to pain, risks, and potentially harmful experimental drugs—the children suffered, some died. In some cases the children were diagnosed with HIV infection—in other cases infants were merely "presumed" to be HIV-infected.

The Code of Federal Regulations (45 CFR 46.409 and 21 CFR 50.56) prohibits subjecting children who are wards of the state to experiments involving greater than minimal risk:

(a) Children who are wards of the State or any other agency, institution, or entity can be included in research approved under 46.406 or 46.407 only if such research is:

(1) related to their status as wards; or

(2) conducted in schools, camps, hospitals, institutions, or similar setting in which the majority of children involved as subjects are not wards.

(b) If the research is approved under paragraph (a) of this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis.

The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

The Phase I and Phase II experimental drug and vaccine trials in question were unrelated to their status as wards—the NYC-ACS enrollment guidelines applied to foster care children only. The ACS guidelines falsely stated that the trials posed

"minimal risk," and the guidelines clearly focused on facilitating rapid enrollment of as many foster children as possible—rather than ensuring that the trials were in the children's best interest: [Attached]

"ACS will review clinical trial protocols for HIV-infected children as soon as such protocols become available, before a specific hospital decides to participate in the study. The National Institutes of Health (NIH) and pediatric AIDS specialists throughout New YorkState will make ACS aware of protocols as soon as they are in final form, before hospitals are ready to enroll children. This procedure will expedite ACS' decision-making even before physicians are ready to start treating children in the protocols."

The Associated Press confirmed our suspicion that most of the children in the care of ACS did not have a personal advocate—as required under federal regulations. Indeed, of the 465 NYC children in the experiments, only 142 had an advocate. Furthermore, ACS even waived the requirement for individual consent for these children—encouraging them to be herded en masse into drug trials as if they were animals.

Phase I and Phase II drug experiments involve the highest level of risk, uncertainty, and discomfort—the safety and toxicity of drugs as well as maximum dose tolerance are tested in these trials. Experiments at that testing stage are unlikely to have any direct benefit for the children in whom the drugs are tested. In some trials children were diagnosed with HIV infection—in some cases infants were merely "presumed" to be HIV-infected:

#292: A Double-Blind Placebo-Controlled Trial of the Safety and Immunogenicity of a Seve n Valent Pneumococcal Conjugate Vaccine in Presumed HIV–Infected Infants

#345 A Study of Ritonavir (an Anti-HIV Drug) in HIV–Positive Infants and Children, last amendment 3/13/2000.

"Replacement infants . . . are either presumed HIV infected or have already been shown to be HIV-infected . . ."

Infants and children were exposed to experimental HIV vaccines—which have never been successful:

#218 A Placebo-Controlled, Phase I Clinical Trial to Evaluate the Safety and Immunogenicity of Recombinant Envelope Proteins of HIV–1gp160 and gp120 in Children >=1 Month Old with Asymptomatic HIV Infection.

Although more than 4 AIDS drugs had never been tested in children, foster care children were exposed to an 8 drug cocktail "some at higher than usual doses" (which was reduced to 7 drugs because of "significant toxicity" 11/9/2001).

#1007 Multi-Drug Antiretroviral Therapy for Heavily Pretreated Pediatric AIDS Patients: A Phase I Proof of Concept Trial

Among the drugs tested in foster care children, is Nevirapine, a drug whose safety has been the center of controversy. [AP] Because Nevirapine confers resistance following even a single (low) dose, its manufacturer cautions that its use should be restricted to "previously untreated women with HIV infection who present at labor" for the prevention of mother-to-child transmission of HIV. Yet, 4 to 17 year old children in foster care were exposed to Nevirapine.

A Phase I trial of a Glaxo Wellcome drug, Valacyclovir hydrochloride was terminated in 1997—Why? Typically, trials terminated at such an early stage show unacceptable levels of toxicity.

The Associated Press reported: "Some foster children died during studies, but state or city agencies said they could find no records that any deaths were directly caused by experimental treatments." It is not for those city agencies to decide the cause of death. ACS Commissioner, John B. Mattingly, testified before a City Council General Welfare Committee, that he knows of just 19 children—out of 465—who remain within the NYC foster care system.

In addition, a series of recent investigative mediareports from Texas, Florida, Ohio, New York, California, Illinois, raise concerns that over 50% of all children in foster care are currently being prescribed untested, experimental combinations of powerful, mind altering, psychotropic drugs—including antipsychotics (e.g., Risperdal, Zyprexa), anticonvulsants (e.g., Depakote, Neurontin), antidepressants (Zoloft, Paxil, Prozac, Celexa and others), tranquilizers (Klonopin, Xanax), stimulants (Ritalin, Adderall), as well as heavily sedating drugs such as the anti-hypertensive medication clonidine. These prescribing patterns are essentially uncontrolled experimental drug trials. [See: The Columbus Dispatch series by Encarnacion Pyle. Forced medication straitjackets kids, Sunday, April 24, 2005 http://www.dispatch.com/reports-story.php?story=dispatch/2005/04/24/20050424-A1-00.html.

Clinical trials approved by the FDA study only a *single* drug given in tightly controlled dosages. Combinations of two and three or more different psychotropic

drugs have simply never been studied in a rigorous and responsible manner. Furthermore, the foster parents and social workers who are mostly entrusted with supervising these children have less than rudimentary knowledge about these drugs' adverse effects, and even less skills in monitoring these children to avoid dangerous drug reactions. This is of course less than the protection afforded subjects in ordinary clinical trials. It is worth repeating: none of these idiosyncratic drug combinations—called polypharmacy—have ever been studied by any responsible government or other agency, and the children receiving them may be considered guinea pigs in a gigantic uncontrolled medical experiment.

How can the Congress fail to take strong corrective action?

The public has a right to know:

- How many children in foster care have been enrolled in clinical trials?
- What happened to foster children who were used as human guinea pigs?
- What adverse effects did the children suffer during and after participation?
- How many children died during the experiments?
- A question has been raised about the size of the cemetery plot in which children in ACS custody are buried: Were any children buried in mass graves?
- What were the specific sources of funding for these Phase I and Phase II clinical trials?
- Did the foster care agencies or foster families receive payment, fees, or other rewards for enrollment of the children in these trials?
- How much money was paid to the researchers and participating hospitals?
- What happened in 2001 that the AIDS drug trials in foster children were stopped?
- What other drug trials are being conducted on foster children?

The other questions we pose below suggest that there may have been a breakdown in the implementation of the Adoption and Safe Families Act and/or related federal law governing the protection of children in foster care. Our questions, by extension, suggest that the Council on Accreditation of Family and Children Services (COA), and one of its two founding organizations, the Child Welfare League of America (CWLA), may not be meeting their obligations.

Child protection falls within the purview of the juvenile and family court system, which remands abused and neglected children into the care of public and private, non-profit foster care agencies. In our view, the courts have ultimate jurisdiction and responsibility for what happens to these vulnerable children.

The Congress may want to consider a dual approach in dealing with the issues at hand. Child welfare laws operate by regulating the care-givers. Child abuse reporting laws, for example, require health, school, and social service personnel to report suspected child abuse. If such laws were to define "suspected child abuse" to include enrollment of foster children in Type I and Type II clinical trials, in violation of the protections afforded by 45 CFR 46.409 and 21 CFR 50.56), there would be many more eyes watching to protect children from overreaching biomedical researchers who, history has shown, have abused their authority to exploit children in foster care.

- Were there violations of the provisions of the Adoption and Safe Families Act and/or related child welfare legislation by officials of the foster care agencies that permitted enrollment of foster children in Phase I and Phase II clinical trials?
- Should not the supervising foster parents and/or social workers have reported suspected child abuse in these high risk, Phase I and Phase II clinical trials of experimental drugs and vaccines?
- What training, if any, is provided to supervising foster parents and/or social workers about the conditions that must be satisfied by reference to 45 CFR 46.409 and 21 CFR 50.56 in order to justify enrollment of foster children in ANY biomedical research involving greater than minimal risk?
- Is there a need for new federal legislation that would amend the Adoption and Safe Families Act and/or 45 CFR 46.409 and 21 CFR 50.56 to expressly define children in foster care a "protected class," whose enrollment in ANY biomedical research would trigger appointment of an independent research ombudsman under the supervision of the juvenile or family court that remanded the foster child into state custody?

Finally, if, as we argue, the courts have ultimate jurisdiction and responsibility for what happens to children whom the courts remand to the protective custody of state and private, non-profit foster care agencies, then the Congress might wish to consider amending the existing requirement for the appointment of a child advocate by the IRB pursuant to 45 CFR 46.4.09 and 21 CFR 50.56 to require instead that

the child advocate be appointed by and be held accountable to the court of original jurisdiction for foster children who may be subjected to biomedical research involving greater than minimal risk. The courts, we believe, are the last recourse that foster children have to protect them from the predatory practices of those who would exploit and take advantage of their vulnerability. We should remind ourselves that the measure of a society is how it treats its most vulnerable citizens.

Statement of Cheri Carlene Campbell, American Family Rights Association, Morongo Valley, California

This information has been assembled to help equip those attending [and those who will influence the outcome of] the hearing on June 9, 2005 in an effort to protect the greater society. You must look closely at the problems surrounding Dept. of Children's Services [DCS] to discover that the real problem has nothing to do with how funding is related to outcomes for children. It is your moral duty to find a solution to this Nationwide dilemma which has been plaguing America for decades.

On March 13, 2004 U.S. Congressman Joe Baca gave the victims of DCS a voice and sent 163 evidence books to Washington. The people need to know what our elected officials have done to protect us and our Posterity since receiving the documents proving the ministerial ineffectiveness of DCS.

Victorville, CA—Daily Press: "United States Accuses 14 Nations of allowing Modern Day Slavery" reads: U.S. criticizes 14 other nations of not doing enough to stop the modern day slave trade (prostitution, child sex rings, and forced laborers) involving 800,000 annually. Condolezza Rice stated, "The U.S. has a particular duty to fight this scourge because trafficking in persons is an affront to the principles of human dignity and liberty upon which this nation was founded. U.S. spends $96 million to help other countries combat trafficking." The U.S. is not included on the list although R. Miller said the country is far from immune . . . and includes the U.S.—June 4, 2005

American children and their families are the victims I speak of. Children are routinely seized by DCS agents who blatantly violate Laws in place to protect the familial bond which include the California and U.S. Constitutions! DCS hides their practices under the confidentiality clause, which was designed to protect families receiving public assistance from embarrassment, not hide their devious practices. DCS is a Government sanctioned agency that receives federal and state funding in advance for obtaining children, which clearly makes this a problem for each branch of Government.

I agree with Congressmen Herger who believes there should be better outcomes for the safety and well being of our children. However, even after thousands of complaints from victims of abuse under color of law by DCS, our elected officials continue to look for a solution in the wrong place.

Congresswoman Nancy L. Johnson shared the reasonable solution of frontloading the money to help keep the family in tact. This would not only save the government billions of dollars, it would effectively spare the greater society a whole generation of shattered children and adults who have no confidence whatsoever for those in authority.

The problem is multi-faceted and although they appear to be complex, these issues are simple to correct. Cross references from legal authorities have been used to substantiate the current immoral practices and motives used to obtain, detain and adopt our children without Due Process which include: California Benchguide [CAB] 100 Juvenile Dependency Initial or Detention Hearing—revised 2003; Welfare and Institutions Code [WIC]; California Rules of Court [CRC]; CA Dept. of Social Services Manual—Child Welfare Services Program [CWS]; Family Code [FC]; National Association of Social Workers—Code of Ethics [NASW].

Removal of a child: Federal Law mandates there must be a court order or voluntary surrender. Cathy Cimbalo [San Bernardino Director of DCS] states her social workers must have the agreement of a police officer and a court order. When I offered to show the court order during the unjust removal of our grandchildren, Deputy Porter stated "I don't care what papers you have, we're taking the children!" Out of thousands of 'removals,' no victim has ever seen a court order and they have not voluntarily surrendered their child! In fact, many have been arrested for verbally trying to dissuade the police officer during the unjust removal of their children! CWS 361(b) no dependent child shall be taken from his parents/guardian where he resides unless the juvenile court finds clear and convincing evidence of: (1) substantial danger; no reasonable means child can be protected without remov-

ing him; WIC 300(e) [child has suffered severe physical abuse] shall constitute prima facie evidence minor can not be safely left in custody of parent/guardian with whom the minor resided at the time of injury. Most children have no injuries, which is proven during the medical exam performed after removal. This exculpatory evidence is deliberately withheld, and is punishable pursuant to Government Code 820.21 which strips away supposed immunity! CAB—100.9 Initiating the Hearing—If the social worker determines that the child is to be detained, a petition must be filed with the Juvenile Court [JC] clerk, who must set the matter for hearing on the detention hearing calendar . . . WIC 311(a) Filing petition for retention of custody . . . Confrontation by and cross-examination of witnesses [Due Process] Most [if not all] parents/guardians do not contest due to threat ["if you contest termination of guardianship, your children will be separated, adopted out and you'll never see them again!"], duress and coercion; CRC 1442(b)—Time limit on custody, filing petition—A detained child must be released within 48 hours . . . if no petition has been filed. The contents of the petition are prescribed by WIC sect. 332—A petition to commence proceedings . . . to declare a child a ward or a dependent child of the court shall be verified . . . and CRC 1407—The petition shall be verified and may be dismissed without prejudice if not verified. An unverified petition may be dismissed without prejudice. The laws are in place, but they are constantly violated! An internal review is DCS' only watch dog, as they claim confidentiality prohibits 'outside' review.

Perverse financial incentive: WIC 319(c) If the matter is continued pursuant to Section 322 or for any other reason, the court shall find that the continuance of the child in the parent's or guardian's home is contrary to the child's welfare at the initial petition hearing or order the release of the child from custody. CAB JUDICIAL TIP: Failure to make this finding [contrary to the child's welfare] may cause permanent loss of federal funding for foster care. Herein lies the problem: financial incentive; empires being built off the backs of our children of tender years!

Prima Facie Evidence: Most Americans still trust the Justice System even though millions of its victims exist. CRC 1445(a) Requirements for detention—(1) a prima facie [Latin for: at first view] showing has been made that the child is described by WIC 300 [child abuse, neglect, etc], (2) One or more of the grounds for detention in CRC 1446 is found; CRC 1446(a) Grounds for detention—There is a substantial danger to the child's physical health, or the child is seriously emotionally damaged and removal is the only way to protect the child. DCS agents have created "emergencies" believing they will never be forced to prove the petition's allegations. Most court reports and verbage are almost identical in all cases.

Furthering the destruction of the familial bond without Due Process is demonstrated in: CRC 1447 Detention hearings; prima facie hearings (d) [Hearing for further evidence; prima facie case—If the court orders the child detained, and the child, a parent, a guardian or counsel requests that evidence of the prima facie case be presented, the court shall set a . . . hearing within three court days to consider evidence of the prima facie case, or set a jurisdiction hearing within 10 court days. If at the hearing petitioner fails to establish the prima facie case, the child shall be released from custody. WIC 321 If the minor, a parent or guardian or the minor's attorney . . . requests evidence of the prima facie case, a rehearing shall be held within three judicial days to consider evidence . . . if [it] is not established, the minor shall be released from detention. Most victims do not have a clue these laws exist until it is too late and although Cathy Cimbalo continues to say "we must trust the justice system" and that her "460 'professionals' only do what the court says," we have found this to be a deadly combination. Social worker's libelous reports are not challenged and are 'found to be true' at the next hearing, we are rarely allowed to speak in court and our public defenders do not defend our rights!

In 2004, the Federal Government provided more than $7 billion in dedicated funds for child protection. The bulk of these funds [almost $5 billion] supported children who had been removed from their homes. All this money spent to "protect" those in foster/adopt/group homes where far too many children have been killed or tortured, proves that more money is not the solution. Maybe it's time to try a new approach. Carefully consider what you have read. Our right to fair and honest government, government accountability to the people, and redress has thus far been denied. More importantly, our God given inalienable rights have been violated!

You must invoke the power to open DCS files for the sake of investigating the current immoral and illegal practices [full Thesis available connecting the above Legal references]. We the people nominate expert family advocate Bill Tower and Jane Flickinger at Pacific Justice Institute as overseers of this Commission.

We have sought redress from the proper chain of command and found no remedy. San Bernardino [S.B.] County Board of Supervisors were duly noticed regarding DCS practices of non-compliance to State and Federal mandates; were informed that

DCS' ministerial ineffectiveness is causing irreparable damage to the greater society; and Chairman Dennis Hansberger publicly stated 'his hands are tied'. S.B. Grand Jury received 13 official complaints against DCS via certified mail in 2004 and replied, "After a thorough review [of complaints, evidence], we have decided not to investigate." S.B. Assistant District Attorney Mike Risley was given copies of these complaints, but no remedy or acknowledgement has been given to date.

In conclusion, I must remind you that the U.S. has a particular duty to fight this scourge. Trafficking in persons is an affront to the principles of human dignity and liberty upon which this nation was founded. The following questions remain unanswered: How will this Government offer a gentle return of our children when the mask is torn off these "child protectors"? How many more Logan Marr's will have to die or be tortured while in the State's care before DCS is completely reformed and held accountable? June 9th is our granddaughter Rainya's 7th birthday and almost 2 years since we've seen our beautiful grandchildren . . . today is a great day to start protecting your constituents!

Thank you for your quick resolve in stopping this egregious silent epidemic that is now shouting for remedy. Your response, nomination of Bill Tower and Jane Flickinger to oversee the investigation of DCS and its inter-related service practitioners, and an outline of remedy will be expected within 20 days of this communiqué. We are not just a few disgruntled people, we are millions that are growing weary. We will not be comforted for the unjust loss of our Posterity. You must assure the people that our Nation's officials are going to stop this modern day domestic terrorism and pledge to restore democracy in our own backyard.

Statement of Linn Asplund, Waterbury, Connecticut

Thank you for considering my testimony. When me son was 10 years old, he was attending Washington School in Waterbury, CT. He started having problems in the beginning of third grade, September 1999. He was being picked on and bullied by the other children. His grades started suffering and he too started having discipline problems. This bullying was brought to the schools attention, but it still went on. The principal suggested a PPT. I agreed and at the first PPT I agreed to have him tested. I was then told he was "LD" (Learning Disabled), but it 'was not that bad.' I told the school I wanted him to go to a school where they had smaller classes in which he could learn at his own pace and not be picked on. I knew of schools with such classes. I was denied this and told by the Special Education Supervisor there was no such class. Next they told me they wanted him to see a psychologist for a psychological evaluation, I agreed. I obtained a copy of the evaluation. My son told the Doctor that he had no friends at school. He liked it better at home and would wake up repeatedly at night with thoughts of how to quit school. By this time Dr. Abramavich said my son was psychotic and needed to be medicated. I refused. The next thing I knew, DCF (Department of Children and Families) was at my door telling me the school said my son has special needs that need to be taken care of. I still refused the psychiatric drugs. I brought him to "child guidance" and was told that he was a normal child.

After several visits form DCF I still refused to drug my son. On March 16th 2000, I found court papers on my doorstep. In them my husband and I were charged with abuse and neglect and were informed that DCF was going to take our son from us. Later that day a social worker and police officer arrived and took him away.

Two weeks later, DCF placed him in Waterbury Hospital where Dr. Edwards gave my son Haldol and Attavan—mind altering drugs not approved for use in children. A few days after this, Dr. Mennessen put him on 100 mg of Wellbutrin a day; also not FDA approved for use in children. When I asked Dr. Mennessen why he was giving my son this drug without my consent, his reply was "we need a number of cases to get it FDA approved." Some of the side effects I saw were loss of hair, dry & scaly skin, large hive like rashes and very pale skin. While in DCF's care my son lost weight and appeared malnourished.

There were numerous, outright lies in the documents that DCF had from the initial "anonymous" report from the school, I can provide this information and numerous other internal DCF documents regarding my sons "treatment" should you require it. This of course is a very brief summary of what happened to my family. I finally got my son back from DCF in August of 2002. This entire nightmare began because I refused to put my son on dangerous, mind-altering drugs.

Statement of Alexandra Yoffie, Child Welfare League of America

CWLA STATEMENT ON PERMISSIONS FOR CHILDREN IN FOSTER CARE TO PARTICIPATE IN TREATMENT RESEARCH FOR HIV INFECTION

The Child Welfare League of America and its nearly 900 member agencies believe every child and youth is unique, has an intrinsic value to society, and is entitled to have their basic care needs met, to be nurtured and protected, to heal when harm is done, and to have the opportunity to develop to his or her potential. Ensuring that each child receives needed primary and preventive health care is an essential part of meeting these universal needs.

CWLA's *Standards for Health Care Services for Children in Out-of-Home Care* serve as a guide for the delivery of routine and specialized health services to children in foster care and assert that these children have human rights that should be protected. Because of the vulnerability of children in foster care and the responsibility of the child welfare agency toward children in its care, recognition and safeguarding of these rights are foremost considerations.

Concerns have been expressed regarding states that have allowed children in foster care to receive experimental treatments for HIV infections without adequate safeguards. CWLA's *Standards of Excellence for Family Foster Care Services* provide guidance in this area, stating, "The foster care agency should obtain written consent [for medical care] from the child's parents, or alternatively, from the court. . . . Parents should grant written consent for their child's medical care," and for those children whose parent's rights have been terminated, the agency "should obtain written consent from the courts." This provision applies to all forms of medical care, including treatment for HIV infection.

Allowing children in foster care to receive experimental drugs for the treatment of HIV infection without providing an independent advocate to protect and ensure the child's safety and well-being-, is contrary to CWLA's *Standards for Health Care Services for Children in Out-of-Home Care* and our *Standards of Excellence for Family Foster Care Services*.

As of December 2002, 821,470 adults and adolescents, and 8,804 children under age 13, had been diagnosed with HIV/AIDS in the United States. Many children, particularly those with HIV/AIDS, lack the kind of health care coverage that would allow them to receive state-of-the-art medical care. Children in foster care should not, as a matter of course, be denied access to appropriately reviewed and approved treatment research. Nonetheless, it is in their best interests for the parents or guardians and the child, when appropriate, to participate to the fullest extent possible in the development and implementation of the health care plan so that each child's unique needs and concerns are considered in any treatment decision.

We encourage all concerned to take this opportunity to more comprehensively examine the health care needs of children in foster care, including those who are disabled or have mental health needs. In many instances, these children are without adequate care to address their treatment needs. Priority must be given to providing the advocacy and protections that would help ensure all children in foster care receive needed services so they might best heal from the harms of child abuse and neglect

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Jacobi Medical Center
Bronx, New York 10461
May 17, 2005

Congressman Wally Herger
Chairman, Subcommittee on Human Resources
Committee on Ways and Means

To the Committee:

I am currently the Director of Pediatric HIV Services at Jacobi Medical Center, a member of the NYC Health and Hospital Corporation, located in the Bronx, New York and have a pediatric HIV provider in the Bronx for over 20 years. Our program is one of the largest single site programs in the United States and provides integrated, comprehensive, multidisciplinary care to HIV infected children and HIV-exposed, uninfected children as well as integrative care for infected adults and other family members. As the Director of a recognized HIV Center of Excellence, our program has worked closely with foster care agencies and the NYC Administration for Children's Services in managing the healthcare of infected children in foster care.

In addition, I have been involved in clinical trials involving HIV-infected children as a member of the NIH funded Pediatric AIDS Clinical Trials Group (PACTG)as

well as a site investigator in clinical trials sponsored by pharmaceutical companies. I am currently the Chairperson of the PACTG Primary Therapy Research Action Committee which oversees HIV therapeutic treatment protocols sponsored by the PACTG and NIH.

I would like to present a brief personal historical synopsis of how therapies for HIV-infected children have evolved since the first description of the pediatric HIV-epidemic since its inception in the early 1980's. At that time, most HIV-infected children entered care as a result of clinical conditions which resulted from their HIV associated immunodeficiency. Treatment focused on the child's clinical symptoms such as anti-fungals for thrush, nutritional support for weight loss and antibiotics for bacterial infections or pneumocystis carinii pneumonia (PCP) but without therapies directed at the underlying illness (now known to be HIV), the immunodeficiency progressed, the child deteriorated and, frequently, death ensued. For example, in 1989, I personally attended 1–2 funerals per month for children or their parents who were in our care.

Late in the 1980's, there were rays of hope as new therapeutic agents, with limited but real efficacy, began to emerge. Unfortunately, due to many fiscal, practical and regulatory reasons associated with drug development for FDA approval, children did not have availability to these agents for 1–3 years after they were available for use in adults. The only way for an HIV-infected child to gain access to AZT (zidovudine, Retrovir) was through a compassionate access protocol sponsored by the manufacturer, which required an informed consent by a guardian or parent. While this agent, as monotherapy, has extremely limited efficacy, for many, especially those who were very ill and rapidly deteriorating, the alternative therapy was no therapy. I can remember giving out the first pediatric AZT bottles to children and their families during our 1989 Christmas party and the joy, tears and hugs that accompanied this "gift." To the families and children, it was the first concrete impression that there was hope that this therapy, or future ones, would significantly prolong lives. At that time, if there was no mechanism available for obtaining consent, many children in foster care would not be afforded this therapy, subsequent therapies and, the hope, for clinical improvement and life extension.

In fact, this hope has been born out as demonstrated by HIV survival data (both pediatric and adult) throughout the medical literature as well as statistics from the CDC. On a more local level, our program is providing care to over 250 HIV-infected children; over the past 12 months only 1 child has died. Some 50% of children in our care have "undetectable viral loads" which suggests suppression of HIV replication and, in general, the majority of children in our care, are immunologically (as measured by CD4 numbers and percentages) healthier now than they were in 1993. While all therapies have potential and real toxicities, especially HIV medications, these children are significantly healthier now than in the past and most are fully involved in school, after school and other activities shared by healthy children.

I am in total agreement with the need for well defined systems to protect the rights of children in foster care systems including the appointment of an independent advocate for the child. However, I strongly believe as a health care professional caring for children with a chronic, life threatening illness, that a reactionary posture in response to localized cases where some administrative oversight has been missed would be an ethically unacceptable position for our society. How can one refuse therapy to a child of a therapy which has been demonstrated, in rigorously controlled clinical trials, to be effective, simply because there is no one legally capable of signing consent for a trial which makes that therapy available? If you are HIV infected, severely immunocompromised and resistant to all available therapies, shouldn't society be able to provide a mechanism which balances the potential for clinical improvement and well-being for this child with a mechanism that respects their rights as a participant in a clinical trial? As an HIV clinician, I have experienced the pain and suffering associated with the lack of access of therapies.

I would also like to quickly comment on some of the allegations about the content of many of the clinical trials in which children in foster care may have been participants. In NYC, the ACS had strict guidelines for approving clinical trials for children: the bottom line was that the trial had to provide the potential of benefit for that individual trial. For example, foster children in NYC, in the absence of maternal consent, were not allowed to participate in the PACTG 219 study which was a long-term, natural history study where data was collected during regularly scheduled visits. While the result of this study has benefited HIV infected children, there clearly was no benefit to the individual child.

However, the Alliance for Human Research Protection listed in their 3/10/05 letter to the OHRP and FDA that foster children were inappropriately enrolled into numerous NIH–PACTG trials. Included in this list was PACTG 377 of which I was the co-chairperson. This trial, a Phase I/II (not purely a Phase I) trial, strategically

compared a number of therapeutic regimens for advancing the treatment of HIV infected children when contrasted with standard of care. This study was linked to PACTG 338 which demonstrated that a protease inhibitor containing regimen was superior to the existing standard of care (two nuclosides). Importantly, these studies were invaluable as they contained provisions that the first 8 children in each arm participate in an intensive pharmacokinetic (pk) evaluation to ensure that the dosing was appropriate when compared to drug exposure that had been demonstrated, in adults, to be safe and effective. This component of the study, which required it to be partially labeled a Phase I study, protected the study participants as demonstrating the correct dose prevented the overdosing of children which would lead to increased toxicity or underdosing the child which would lead to inadequate drug exposure and rapid development of resistance to that therapy and, potentially, other agents in that treatment (i.e.; protease inhibitor) class. These studies clearly demonstrated that children metabolize many of these agents much more rapidly than adults and that to achieve equivalent efficacy with adults, drug dosing in children needed to be higher than one would expect.

In fact, it was data from this study and other studies which were important in the signing, by President Bush on 12/3/03, the Pediatric Research Equity Act of 2003 (S. 650/H.R. 2857), which restores the protections of the Food and Drug Administration's (FDA) 1998 Pediatric Rule. This legislation was hailed as a necessary safety net for children.

In addition to ensuring that the dosing was correct (the protocol provided provisions for dose modification if needed from the pk evaluation), these studies also contain extensive, real time, safety evaluations and patient management requirements to protect the health of children on the study. The information concerning the safety, dosing and efficacy of therapies included in this study, and others, has significantly advanced our knowledge about treating pediatric HIV infection. This information has been essential for advances in care which have been translated into improved health and survival for children residing in the developed world. This, I see, every day, when I walk into our outpatient pediatric HIV clinic and am greeted by healthy looking, HIV-infected children, adolescents and young adults. Without early access to therapy for all, including those in foster care, I do not believe that this would have been possible.

The proper response for future children living in foster care with chronic, terminal illnesses should not be to have policies which prohibit and withhold therapies. In 1986, there were only a handful of people who thought that an HIV-infected child would survive to adulthood. This is now common in the Bronx.

We just need to be more diligent in ensuring that successful policies and procedures are in place to protect the rights of these children. Their rights, however, include having access to therapies that provide hope.

If needed, I am willing to work with this subcommittee, on this or any related matter.

Sincerely,

Andrew Wiznia
Director of HIV Services

Johns Hopkins Bloomberg School of Public Health
Baltimore, Maryland 21205
May 31, 2005

Representative Wally Herger, Chairman
Representative Jim McDermott, Ranking Member
Subcommittee on Human Resources
Ways and Means Committee
United States House of Representatives
Washington, DC

Dear Chairman Herger and Ranking Member McDermott,

We are aware that the Subcommittee on Human Resources of the House Ways and Means Committee is reviewing the required procedures for protecting children, including children who are wards of the state, when they become subjects in research studies. I am writing to describe briefly the procedures used by the Institutional Review Boards (IRBs) of this School to ensure that all children, including wards, receive the additional protections required because of their vulnerable status. I also wish to convey our strong support for the current federal regulations that govern research that involves children (45 CFR 46, Subpart D).

It is the understanding of our IRBs that the principle of *justice*, as described in the *Belmont Report*, requires that all populations, including children, have the opportunity to take part in research and to share in its benefits. Furthermore, we support the strong recommendations of both the American Academy of Pediatrics and the FDA that research on children is essential in order to determine how new findings can be safely and most effectively used for their benefit.

To achieve these objectives our IRBs require that children be included in all of this School's human research activities unless there are specific scientific or ethical reasons for excluding them. Following the principle of *justice*, we also require that *all children* have equal opportunity to take part in research unless, again, there are scientific or ethical reasons for excluding particular individuals or members of specific groups or populations.

When reviewing proposed research that would include children our IRBs follow very carefully the requirements of Subpart D to determine the category of research and the requirements for consent and assent (46.404, 46.405 or 46.406). The IRBs focus especially on the assessment of risk to the child and on the prospect for direct benefit for the child. Our assessment of risk is, if anything, overly cautious in favor of the child, and the prospect for direct benefit, if any, is consistently weighed against this cautious assessment of risk. We believe that the categorizations made by our IRBs are consistent with the federal requirements and, more importantly, ensure appropriate protections for each child.

In accord with the position described above, we firmly believe that children who are wards of the state deserve the opportunity to participate in research, and especially so when they suffer disproportionately from the condition being studied, an example being HIV/AIDS. We would emphasize, however, that wards are not targeted for inclusion. Rather, their status as wards is simply coincidental to their being eligible for enrollment in the study. We also share the view that children who are wards of the state require special protection because of their uniquely vulnerable situation. We believe, however, that this is adequately ensured by the requirements outlined in 46.409, which require an advocate for each child involved in a study categorized as involving greater than minimal risk and having no prospect of direct benefit for the child (46.406). In our view, extending the requirement for an advocate to studies that are greater than minimal risk but having the prospect for direct benefit for the child (46.405) would create a substantial barrier to conducting such studies while providing no clear added protection for the child.

We hope that these comments and our strong support for maintaining the current federal regulations concerning protection of children will be of help to the Subcommittee in its deliberations. I would, of course, be pleased to respond to any specific queries that may arise.

Sincerely,

Alfred Sommer, MD, MHS
Dean

National Institute of Allergy and Infectious Diseases
Potomac, Maryland 20854
May 9, 2005

The Honorable Daniel R. Levinson
Inspector General
U.S. Department of Health and Human Services
330 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Mr. Levinson:

I am writing you in fulfillment of my obligation as a federal employee of the National Institutes of Health to report possible waste and fraud under Executive Order 12674 and 12731, and NIH Policy Manual, Section 1754(C)(1)(a),(b) and (c). Currently I am the Director of the Office of Policy in Clinical Research Operations (OPCRO) in the Division of AIDS of the National Institute of Allergy and Infectious Diseases (NIAID).

On Wednesday, May 4th, the Associated Press (AP) reported:

Government-funded researchers tested AIDS drugs on hundreds of foster children over the past two decades, often without providing them a basic protection afforded in federal law and required by some states.

The basic protection denied these foster children was the appointment of an advocate "to act in the best interests of the child," as explicitly required by 45 CFR 46.409:

§ 46.409 Wards.

(a) Children who are wards of the State or any other agency, institution, or entity can be included in research approved under § ***46.406*** or § ***46.407*** only if such research is:

(1) related to their status as wards; or

(2) conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

(b) If the research is approved under paragraph (a) of this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

The *AP* report further states:

The research was conducted in at least seven states—Illinois, Louisiana, Maryland, New York, North Carolina, Colorado and Texas—and involved more than four dozen different studies. The foster children ranged from infants to late teens, according to interviews and government records.

These clinical research studies were funded primarily through grants awarded to researchers by the Division of AIDS (DAIDS).

I would like to bring to your attention that according to the NIAID Clinical Terms of Award: ***All*** clinical research supported by NIAID ***must comply*** with applicable Parts of U.S. Code of Federal Regulations, Title 45, Part 46 "Protection of human subjects." (Emphasis added)

The failure of numerous DAIDS/NIAID-sponsored researchers and their institutions to assure that foster children enrolled in their research were appointed individual advocates even where a foster parent exists constitutes a violation of the terms of their grant awards. By any definition, this is a severe violation because it directly impacts the health and safety of foster children, among the most vulnerable populations in our society.

Please be advised that 45 CFR 46.409 ***contains no exceptions*** to the requirement that foster children enrolled in research must be provided with advocates, although an advocate may serve more than one child.

The claim by some researchers that "oversight boards may decline to appoint advocates if they conclude the experimental treatment affords the same or better risk-benefit possibilities than alternate treatments already in the marketplace" is simply false. ***There is no provision in either law or regulation that allows researchers or their oversight boards to waive the rights of children in clinical trials to have advocates.***

I ask that the your office immediately conduct an investigation to determine which foster children were denied their rights under the law and to seek a full recovery of grant funds from the researchers responsible for this lapse.

Furthermore, I respectfully suggest that your review include a comprehensive financial and protocol audit of each of the research entities and clinical trial sites involved in these studies. As part of this inquiry, the medical and study records of each foster child enrolled in their respective AIDS clinical trial should be examined to determine whether any of these children were subjected to unnecessary risk or injury owing to the toxicity of the drugs administered to them, and whether the researchers complied with their obligations to report all adverse events.

Your office should be aware that DAIDS/NIAID currently is soliciting applications for HIV/AIDS Clinical Trials Networks and Clinical Trial Units. Applications are due this month and in July, 2005, respectively. Funding for both is expected to total up to $300 million for the first year and may continue for up to seven years. (See: ***http://www2.niaid.nih.gov/newsroom/Releases/ctu2005***).

It is expected that many of the investigators and their institutions responsible for enrolling foster children in AIDS clinical trials without the appointment of advocates will be competing for the upcoming award.

It is wholly inappropriate for DAIDS/NIAID to consider making awards to any of these applicants who have violated basic human research protections until a full, open and independent investigation has concluded and full restitution is made to both the government and the victims of these unlawful experiments.

Thank you for your time and attention to this important matter. Please feel free to contact me at my home telephone number, 301/983–4370 if I can be of further assistance.

Sincerely,

Jonathan M. Fishbein, M.D.
Director
Division of Aids
Office for Policy in Clinical Research Operations

Submission of John Mattingly, New York City Administration for Children's Services, New York, New York

Good afternoon Chairman Herger and Members of the Subcommittee. I am John Mattingly, Commissioner of the New York City Administration for Children's Services (Children's Services) and I submit this testimony on behalf of Children's Services regarding participation of children in foster care in HIV/AIDS clinical trials during the late 1980's and early 1990's.

As a professional whose career has been focused in child welfare for over 30 years, I want to begin by stating that it is imperative—both in terms of our own institutional integrity and our critically important relations with the communities we serve—that the serious questions that have been raised regarding inclusion of children in foster care in HIV clinical trials are fully explored, and that that review process be transparent to the public and conducted with due diligence.

That is why I have asked the Vera Institute, a New York-based not-for-profit research institute which works with government to study a variety of social issues, to conduct a comprehensive analysis. An independent Medical Oversight Committee, consisting of nationally known experts in pediatric AIDS, medical ethics, and the taxonomy of clinical trials, will review, respond to, and provide guidance to the Vera Institute's review of cases. Having said that, I want to make equally clear that I have seen no evidence to date of any wrongdoing or malfeasance in regard to these clinical trials, and much of what I've seen speaks to the good faith of those who had decision-making authority at that time.

History of Clinical Trials in New York City

Along these lines, I would first like to bring us back to the calamity that befell New York City and its children in the late 1980's and early 1990's with the arrival of the AIDS epidemic in the lives of infants and children.

At that time, HIV/AIDS, fueled in part by the crack crisis, had reached epidemic levels in New York City, and no effective treatment or medical regimen to manage the disease had yet been found for children, nor did such treatment appear imminent. The mortality rate for those who suffered from full-blown AIDS was 100 percent. Newspapers and scientific journals, as well as doctors, social workers and administrators in the child welfare system, hospitals and beyond, struggled with stemming the ominous tide of a disease that, at that time, had no end in sight.

The impact the disease was having on many of the City's children and families was devastating. Media accounts from those years described the funerals of children who had died of AIDS, of children desperately trying to hide from their friends the fact that they had been infected with the HIV virus, and of boys and girls who were spending their early years in and out of the hospital, suffering from repeated bouts of pneumonia and other illnesses as a result of their HIV infection. All this suffering occurred without any medical regimen available to even begin addressing their illness.

At that same time, the scientific community was advocating strongly for making available to children those HIV/AIDS drugs that were beginning to make a difference for adults afflicted with AIDS and the HIV virus. The journal Science, one of the most respected scientific publications in the world, published an October 1989 article on the subject. The author described as "heartrending," the lack of availability of AIDS drugs for children, who were characterized as "being left out in the cold."

Some of the doctors and nurses who treated children infected with HIV/AIDS as well as social workers who cared for many of them have told us about the heartbreak they experienced, as they watched children suffer and die. They also told us of their heartrending frustrations that there was so little they could offer by way of treatment.

The cold numbers bear out what the written historical record reveals: in March 1987, 183 children under the age of 13 with full-blown AIDS had been reported to

the City's Department of Health (DOH). In 1991, just four years later, DOH reported that the number of children in the City with the disease had nearly quadrupled, to 745. By then, these reported cases comprised 26 percent of the nationwide pediatric caseload. Even more alarming was the fact that City health officials at the time believed that there were far more children infected with the HIV virus who had not yet developed the AIDS disease.

The vast majority of HIV positive children contracted the virus perinatally. Of the 131,498 babies born in New York City in 1990, 1,644, or 1.25 percent, tested positive for HIV.

Nationally, according to the Centers for Disease Control, some 14,000 children under age 13 had been diagnosed as HIV positive or had developed AIDS between the time of the emergence of the illness in the mid 1980's and 1993. During the same period in New York City, 3,634 children under 13 were diagnosed as HIV positive or as having developed AIDS.

In 1989, the NIH AIDS Program Advisory Committee recommended "cutting through" bureaucracies that prevent children from receiving potentially beneficial treatment through involvement in research. The NIH sponsored clinical trials in seven states: Colorado, Illinois, Louisiana, Maryland, New York, North Carolina and Texas. Also, in 1989, the Secretary for Health and Human Services' Workgroup on Pediatric HIV Infection and Disease, supported by the AmericanAcademy of Pediatrics, recommended that guidelines be developed governing the participation of foster care children in HIV clinical trials.

The City of New York's Previous Procedures

In 1988, at the urging of local hospitals, health care workers, and advocacy groups, the New York City Human Resources Administration (HRA) and its Child Welfare Administration (CWA), first began to develop its policy to allow children in foster care to participate in HIV clinical trials. This decision was made in the face of the rising number of HIV positive children in the New York City foster care system with high rates of illness and death.

Those urging HRA to develop such a policy argued that foster children with HIV/AIDS should not be categorically denied access to promising treatments that were available to children not in foster care who were already being enrolled in these trials by their parents. At the time, AZT had just been approved for use in adults and was about to begin trials in children; it was the first medication demonstrated to slow the progression of AIDS. The only way to receive the medication or medication regimen was to participate in a clinical trial. These medications were not available to children outside of the trials, even though in many cases adults were receiving the medications with prescriptions.

Before making the policy decision that HRA would consider the enrollment of children in foster care in HIV clinical trials when appropriate, HRA conducted an exhaustive review of the ethical, medical, and legal implications of foster child participation in clinical trials. The decision to go forward was also made after meeting with representatives from the NIH and with several of the New York City investigating physicians who were conducting clinical trials. A series of discussions with NIH were held in order to clarify the process for its scientific approval of protocols. Consultations were also held with representatives from the New York City Department of Health, the New York State AIDS Institute, and the National Medical Association.

On January 24, 1989, HRA approved the first HIV clinical trial for participation by children in its care. HRA made an initial decision that because certain clinical trials offered children a therapeutic benefit they fell under the umbrella of "medical treatment" and outside the definition of human research. The essential criterion for permitting such participation was a determination by HRA that the trial offered each participating foster child a significant potential treatment benefit, along with concomitant minimal risk of injury or harm.

The early approach to assessing a clinical trial and then agreeing to enroll a child from foster care was so cautious and the review process in place was so cumbersome that the medical community and advocacy groups excoriated HRA for delaying critical medical care for terminally ill children, and urged HRA to speed up its clinical trial approval process. Otherwise, these groups argued, children would miss the opportunity to enroll, or their disease would progress to a point where they could no longer benefit from the new treatments.

In response, HRA developed a new procedure, which provided comparable safeguards for children, while addressing the need for timely response. Beginning in 1991, the NIH agreed to forward approved clinical trial protocols to HRA while local hospital Institutional Review Boards were conducting their own reviews. HRA then convened a panel of two to four physicians specializing in pediatric HIV/AIDS, as

well as program staff from the HRA/CWA Pediatric AIDS Unit (PAU) and HRA legal staff. The physicians on the panel would conduct a scientific and medical analysis, including whether there was a significant potential medical benefit for the participants, and a discussion of the risks associated with the trial. CWA program staff would weigh in, offering opinions on the protocol based on the agency's policy.

Next, the legal staff would synthesize this material, write a description and analysis of the protocol for the HRA Commissioner and state a legal opinion regarding whether enrollment in the protocol was allowable under state law. The final determination for permitting children to enroll in the HIV clinical trial was made by the Commissioner. For approved trials, a letter of agreement was signed between the investigating physician at the hospital and the HRA Commissioner.

When the Commissioner of HRA agreed to permit the enrollment of children in foster care in particular clinical trials, it was because, after a multi-level review that included the participation of medical professionals, the Commissioner had determined that those trials provided significant potential medical treatment not available outside of the clinical trial. The determination as to whether it was appropriate for a particular child to participate in a particular trial would follow the approval of the trial itself for potential enrollment by children in care. That determined, the consent from the parent would then be sought and obtained, unless the parents' whereabouts were unknown or the child was freed for adoption, in which case the Commissioner or his/her designee would consent.

Those HIV protocols that had been approved for foster children all had a treatment arm that offered a promising drug or therapy that would otherwise be unavailable to foster children and were being provided to children not in foster care who were enrolled in the clinical trials. While it was recognized that there were some risks involved in the use of these treatments, such risks were deemed minimal compared to the contemplated benefits for these children.

As the number of pediatric AIDS cases increased across the United States, the National Institutes of Health (NIH) AIDS Program Advisory Committee (as reported in a 1992 U.S. Surgeon General report entitled "*Points to Consider: Involving HIV Positive Foster Children Who Are Wards Of The State in HIV/AIDS Research*") raised issues concerning foster children in clinical trials. "*Committee members recommended "cutting through" bureaucracies that prevent children from receiving potentially beneficial treatment through involvement in research. The American Academy of Pediatrics (AAP) Committee on Drugs endorsed the inclusion of children in state care/custody in clinical trials in certain circumstances. The AAP also raised concern about the lack of participation of children in clinical research and reported that only a small fraction of all drugs marketed in the U.S. had clinical trials performed in pediatric patients. The AAP has continually supported the inclusion of children in clinical trials as a way of protecting children not only from the harms of life threatening diseases, but because clinical trials are a controlled setting, they also protect children from harms which might result from children taking medications whose dosages have only been tested in adult populations.*"

In 1996, the New York City Administration for Children's Services was established. The policies and procedures from CWA were continued under Children's Services unless specifically changed. In 1998, Children's Services revised its HIV testing and assessment procedure and included in the new procedure a section on clinical trial enrollment, modifying the existing HRA procedure.

Through this new procedure, the threshold question when a foster child's participation in a clinical trial was being considered continued to be whether the clinical trial offered a significant potential benefit to the child, with a concomitant minimal risk of injury or harm. Children's Services continued to convene its panel of experts in pediatric HIV disease to advise the agency of the risks and benefits of proposed studies or trials for children in foster care suffering with HIV/AIDS. This panel of experts, together with Children's Services professional staff, then heard a presentation given by the lead physician at the hospital conducting the trial.

The Commissioner, after reviewing the recommendations made by Children's Services legal and medical staff, as well as the written scientific evaluation and the protocol from the physicians on the panel, then decided whether that trial was appropriate for children in foster care. Also, for a foster child to be enrolled in the trial, the child's mother or legally acknowledged father had to consent to the child's participation if her or his whereabouts were known to Children's Services. The child's foster parent could not provide consent. If the child's birth parent could not be located after written and documented reasonable efforts, Children's Services would make the decision.

One key addition was included in the policy enacted in 1998: once all of the appropriate actions were taken leading up to an executed agreement for the trial, it then

required that an independent physician would review each child's case to confirm that the study enrollment would provide the best available treatment for that child.

In most of the clinical trials that Children's Services has reviewed to date, the medications had already been FDA approved for adults and the clinical trials were intended to determine what dosage of the medication would be advantageous for children. In other trials, the medications had been individually FDA approved and these clinical trials were to evaluate the effects of combination treatments and dosage involving those medications. In fact, Children's Services only approved clinical trials where risks and discomforts to children were minimized and the therapeutic value outweighed the risks.

The vast majority of clinical trials were conducted very early on in the HIV/AIDS epidemic and only half the clinical trials reviewed were accepted for participation. Between 1996, when Children's Services was established as an independent agency, and 2001, only four trials were approved and one of these was approved for one child only. No clinical trials have been approved since 2001.

In the late 1990's, there was a dramatic shift in the field of pediatric AIDS, as effective treatments were at last available outside of clinical trials, treatments which had been developed as a result of the information learned from earlier clinical trials. At the same time, fewer infants were born HIV positive due to medical interventions that dramatically reduced the rate of perinatal transmission. As noted in a New York Times article dated January 30, 2005, "AIDS among infants . . . may be on the verge of being eliminated in the United States. . . ." As a result, there was no longer a pressing need for children to have access to clinical trials, except in isolated instances, where HIV infected children had developed resistance to existing medications.

Recent Events

Beginning in March 2004, Children's Services initiated an extensive review of the agency's PAU hard copy files on HIV children who participated in clinical trials. This review garnered a list of 89 children who appeared to have participated in clinical trials at some point between 1989 and 2001.

To have a more complete understanding of the clinical trial enrollment process, 24 cases were selected for a detailed medical record review. The sample included 11 children currently in foster care; 7 children who, at the time, had been discharged from foster care within the past 2 years, either through adoption or reunification; and 6 children who died while in foster care. All of the six children who were deceased had died between 1992 and 1998. There was nothing in the records to suggest that clinical trial medications contributed in any way to the children's deaths. On the contrary, it appears that the medications extended the lives of many children. Five of the children died of AIDS-related illnesses and one died of unrelated causes.

I decided to conduct an internal query of agency records to be sure that Children's Services had identified and reviewed all information pertaining to the enrollment of foster children in clinical trials. It was determined through that review that more children had been enrolled in clinical trials than were identified in the initial review. At this time, Children's Services believes that approximately 465 children were enrolled in clinical trials.

Development of New Policy

We are now near finalization of a new policy governing the enrollment of children in clinical trials. Beginning last summer, this policy was developed after a series of meetings with focus groups and interviews with a multidisciplinary group of experts in pediatric HIV/AIDS. It will add additional protections for children in care including clarification regarding the importance of parental consent and child assent. This proposed policy would further protect children, by guarding against any potential conflicts of interest or appearances thereof on the part of physicians who review clinical trials and make recommendations regarding enrollment of children in foster care.

It is important to note that this policy is being revised to provide further protections as an additional safeguard; not because any information suggests children were inappropriately enrolled in clinical trials was uncovered. We will be glad to share this new policy upon completion of its revision.

Vera Institute of Justice Review

I have asked the Vera Institute of Justice, to research Children's Services' policies and procedures to ensure that HIV-positive children and children with AIDS who were in our care were appropriately enrolled in clinical trials. The Vera Institute is particularly well qualified to carry out this kind of investigation. Over more than four decades, Vera has developed an international reputation as an independent,

nonprofit organization that provides the highest quality research on a wide range of justice-related issues. The analysis organized by the Vera Institute will also examine whether:

- all necessary consents by parents and other guardians were obtained,
- the individual children's enrollments in clinical trials were reasonable and appropriate, given the scientific knowledge and medical options available at the time,
- NIH protocols were followed, and
- HRA and Children's Services properly monitored children after they were enrolled.

The Vera Institute will also seek to locate the children who participated in these trials while in foster care to ascertain their current medical condition and solicit their feedback regarding the medical care they received.

We have asked Vera to conduct this study in order to address ongoing questions from the public and the press about the history of clinical trials. Vera is committed to developing this comprehensive and transparent understanding of Children's Services' policies and practices during this period. Although we believe that the policies in place at the time reflected good practice, and while we have seen no evidence that would cast doubt on the intentions of those in decision-making authority at the time, we are committed to providing transparent and accurate information in our dealings with the public.

In order for us to be effective in our mission to protect New York City's children, it is my firm belief that we must have a sense of mutual trust with those families we seek to serve. I have only been the Commissioner of ACS since August of 2004 but I have worked in the field of child welfare for most of my professional life, and I certainly understand why this is a subject that causes great concern. It involves the well being of children, sick children, and vulnerable children who were in the care of Children's Services and not in the care of their own parents. We will do all we can to ensure that Vera's review fully answers all public concerns about the participation of New York City foster children in HIV clinical trials, in the late 1980's and 1990's.

Vera will organize a review of case records and medical records for all of the children identified as clinical trial participants, and will prepare a public report regarding its findings. Vera's work will be reviewed by an independent Medical Oversight Committee (Committee), consisting of nationally known experts in pediatric AIDS, medical ethics, and taxonomy of clinical trials. These independent experts—whose work will be funded by private foundations—will provide oversight for Children's Services' current policies and comment on the Vera review. This Committee will provide additional expertise and accountability for all of the City's actions as part of the Vera Institute's review. The Committee's findings will include recommendations for future Children's Services policy regarding clinical trial participation, as well as an analysis of the procedures and protocols that were used in the past. Dr. Robert L. Johnson, an expert on HIV/AIDS, will chair the Committee. As with the Vera Institute's report, the Committee's comments will be public.

Concurrent with the Vera Institute's review, Children's Services will conduct additional case record reviews to ensure that every child in foster care who participated in clinical trials has been identified, and will continue to interview Children's Services staff members who played a role in developing and implementing the HIV clinical trial policy over the last eighteen years.

Conclusion

Faced with an AIDS epidemic in the late 1980's and early 1990's, left without effective treatment for children, and at the urging of medical professionals, HRA developed its policy in an effort to allow children in foster care to have access to medication that was being made available to children not in foster care. The essential criterion for permitting the participation of children in foster care was a determination by HRA that the trial offered each participating child a significant potential treatment benefit, along with concomitant minimal risk of injury or harm.

Statement of Stephen A. Spector, M.D., Pediatric Aids Clinical Trials Group, and University of California, San Diego, La Jolla, California

My name is Stephen A. Spector, M.D. I am a Professor of Pediatrics at the University of California, San Diego, and Principal Investigator and Chair of the Executive Committee of the Pediatric AIDS Clinical Trials Group (PACTG). Over the past

15 years the PACTG, funded by the National Institute of Allergy and Infectious Diseases and National Institute of Child Health and Development, has been the world leader in the development of therapies to prevent the HIV mother-to-child-transmission and to treat children infected with HIV. It is the organization that is most responsible for changing pediatric HIV/AIDS from a once invariably fatal disease to a chronic illness. I believe my comments, in large part, reflect the opinions of all PACTG investigators and the American Academy of Pediatrics.

I am pleased to have an opportunity to respond to the unfounded suggestions by some that HIV-infected foster children were inappropriately enrolled in clinical trials. In the 1980s and for much of the 1990s, HIV/AIDS was a fatal disease with many children not surviving beyond their first few years of life. Limited treatments were available and the only access for children to potentially life saving medications was through clinical trials. These experimental therapies were unproven, but offered hope for HIV-infected children and their families. Investigators of the PACTG offered children the opportunity to participate in clinical trials regardless of race, ethnicity, creed or financial status. As pediatricians and child advocates, every effort was made to make these potentially life saving treatments available to children who were HIV infected and in foster care. At no time were clinical trials targeted for foster children and foster children comprised only a small proportion children who participated in any study. The suggestion that foster children were specifically singled out for participation in studies of new treatments is not only false, but undermines the heroic efforts of many dedicated health professionals who worked tirelessly to help save the lives of all children with HIV/AIDS. In fact, many foster children are alive today because they able to receive "experimental" drugs that were only available, at that time, as part of clinical trials. To have left foster children out of these clinical trials would have deprived them of benefits provided to other children.

All children, including those in foster care, are perhaps the most vulnerable group of the general population with regard to possible exploitation in clinical research protocols, and yet they are the group that can often have the most significant and prolonged benefit from such studies. Every effort must be made to retain the dignity and well-being of children in every step of the clinical protocol process. This includes the request for study participation, explanation of risks and benefits of a study, obtaining consent from parents (and in the case of foster children, a court appointed advocate) and assent from children of appropriate age, monitoring for treatment side effects, and presentation and publication of research findings. The success of treatments for children with HIV/AIDS demonstrates the benefits that studies of new drugs can provide not only for HIV-infected children but also for children with other potentially fatal diseases. To deny children in foster care an opportunity to benefit from such treatments would be medically unacceptable and morally reprehensible.

Despite the many advances that have been made in the treatment of children with HIV/AIDS, much research remains to be done before there is a cure. HIV-infected children must continue to have access to new treatments. The differences of biological and chemical handling of drugs in children is well known, and the assumption that drug processing will be similar to that in adults and will require a simple dose reduction for children, has proven time and again to be flawed. Thus, therapeutic and preventive interventions must be studied in children and not extrapolated from studies in adults. Investigators, sponsors, research review boards, regulators, and others engaged in pediatric research are rightly held to a higher standard of concern because of the fragile nature of children and their rights to a life as free as possible from pain and suffering. However, the zeal to protect children from any harm in entering into clinical trials must be transformed into a passion to provide children with scientific information on drugs that might vastly improve the quality of their lives.

Although we can celebrate the great strides that have been made in treating children infected with HIV, many improvements are still required to optimize and hopefully one day cure HIV/AIDS. All HIV-infected children, including those in foster care, should continue to have an opportunity to receive treatment with these new potentially beneficial drugs as they become available.

Statement of Patricia Sabato, Sandy Hook, Connecticut

My name is Patricia Sabato. I'm from Newtown, CT and am writing to you regarding the hearings on clinical drug trials in children. My son Stephen was put on Dexedrine Spansule by Dr. Irivin Jennings of Family and Children's Aid in Danbury. CT. He was seven years old and he ended up hospitalized at Elmcrest Hos-

pital in Portland, CT and was kept on the same medication. In 1998 Stephen was, once again hospitalized. He went to Four Wind's Hospital in Katonah, NY. He was put on Prozac and Clonadine and received at least one injection of Thorazine. From here he went to Hallbrooke Hospital in Westport, CT and remained on these drugs. When he returned home, the Dr. at the Danbury Hospital CCATS program changed him to Wellbutrin. Dr. Jennings kept Stephen on this medication until 1999. Despite my efforts not to medicate my son because of the negative side effects and the behaviors he was demonstrating, and knowing some of these drugs were not FDA approved for children, I was ordered to continue him on these drugs. July 1999 he was placed in a Residential Treatment Center called Green Chimney's in Brewster, NY for one year. I was assured I would be included in his full treatment plan, I was not. Stephen remembers having his blood taken frequently and was not sure why. He was discharged June of 2000.I have had a hard time obtaining any record's of Stephen's. There were no safeguards for the right to refuse drugs administered to my child during our involvement with The Department Of Children And Families of CT or his placement at Green Chimney's in NY. I have no idea if any information was derived from the forced drugging of FDA unapproved medications and wonder if my son was any part of a clinical drug study.

Rockford, IL 61103
May 31, 2005

Subcommittee on Human Resources
Committee on Ways and Means
United States House of Representatives

Chairman Herger:

The testimony of Donald Young, M.D., of U.S. Department of Health and Human Services referred to as Protections of Children Enrolled in Clinical Trials raises questions and concerns, as does the statement of Elizabeth Monk, of the Illinois Department of Children and Family Services.

Dr. Young testifies on page 3, that, "HHS continues to believe strongly that clinical trials to test new treatments in children are essential and that the framework established by the existing regulation offers adequate protection for individuals participating in trials." I am appalled that any children are used as subjects in any clinical trials and that it is sanctioned and aggressively pursued by a U.S. department! There can be no justification for this kind of conduct! The existence of "framework established by the existing regulation" does not protect and does not remove the sting of offering up children for medical experiments! The young and old of our society, the innocent, the weak, the defenseless and vulnerable need protection, yes, not from a regulation of appointing an advocate, but protection from being in a class of humans upon which researchers can gain access.

Apparently, at least one of the states do not insist on appointing an advocate unless there is significant risk. Ms Monk of Illinois DCFS testifies that, "If DCFS ever decided to approve a research study that has more risk with the prospect of direct benefit, these clinic IRBs are prepared to assign an independent advocate for our wards in compliance with federal regulations." There can be risk in taking an aspirin! A clinical trial involving any drugs could cause serious adverse effects or even aggravate an existing condition, cause pain and suffering and even cause death. That is a risk! Experimenting with dosage levels causes risk and even death, all of which I understand is a concern for this hearing.

Dr. Young, on pages 5 and 6 refers to the lack of a "standard medical treatment" for HIV for children in foster care and that a report prepared by HHS recommended that State and local child welfare agencies should create systems to manage the participation of children in foster care in special medical treatment and experimental trials." Again, no children should be subjected to medical experiments! Further, if there is no standard medical treatment, THEN A STANDARD SHOULD BE DEVELOPED using the best known treatment! Just because there is a lack of a standard that does not justify or give leave for this Government to subject children to experimental trials, let alone children who are most vulnerable, who cannot give informed consent, and whose biological parents may be under distress and duress and cannot give informed consent.

Refer to the testimony of Deputy Secretary Roberta Harris of Wisconsin Department of Health and Family Services of May 18, 2005, at page 2 refers to World Medical Association Declaration of Helsinki's position on the voluntary nature of participation in research. Ms Harris states that the children in their welfare system are

vulnerable because of conditions in the homes they come from. There is the stress and trauma of being removed from their homes and an economic disadvantage may cause consent under duress. Her comments and quotes indicate how difficult it is to reach a status of informed consent for all parties involved.

How well can one be informed in order to give INFORMED consent? Some adult clinical trials have had tragic results, some of which have been halted before completed. Even though the subjects in those studies were adults were they truly able to get enough information? Are there protections in place even for the adult to be adequately informed of risks?

Dr. Young's statement refers to "Efforts in the early 1990's to increase the enrollment of foster children in clinical trials affected state policies. Today, child welfare agencies continue to differ in their policies regarding whether or under what circumstances children in foster care may be enrolled in clinical trials." It is disturbing that HHS was conduction "Efforts" to get children in clinical trials. What were these "Efforts"? And how aggressively were they pursued? Who and what department or what group(s) were behind the efforts? I would urge this Committee to determine what was done to get the states to turn over their wards to the researchers. It appears, and to their credit, some states resisted.

The Associated Press articles refer to some children having serious adverse effects from these medical experiments and even death may have resulted from experimenting with dosage levels. I trust this committee will investigate these matters fully and demand accountability.

I emphasize again that no children should become subjects of medical experiments or clinical trials. Just because a procedure was put in place to give each child an independent advocate to monitor a child subjected to clinical trials does not justify or make more acceptable giving access to the most vulnerable of our society to medical researchers.

I refer to page 2 of Ms Monk's (of Illinois) statement. "If DCFS ever decided to approve a research study that has more risk without the prospect of direct benefit, these clinic IRBs are prepared to assign an independent advocate for our wards in compliance with federal regulations." What? It appears that NO independent advocate has been assigned and further it appears someone preordained the experiments to be without risk!

Also, note Ms Monk says "one drug protects them from the flu." Isn't there a standard medical treatment in place for the flu? If there is a standard medical treatment in place for flu, how and why would Illinois give access to their wards for research on flu vaccines?

I would hope that all of the Illinois cases be studied carefully. It might not be as rosy of a picture as she paints. How many died? Were the deaths attributed to the clinical trials? Ms Monk says 20 kids presently are on 5 research studies. That's twenty children too many. What are these studies for? Children as well as foster children should not be subjected to medical experiments. The foster children in most cases lack a loving, caring and attentive parent to protect them and cannot really give informed consent.

There was horrific disregard for humanity that took place in World War II Germany, some of which started out being directed toward the weak and vulnerable, in orphanages and hospitals, but then was directed to millions who lost their lives in the concentration camps. A society does not just lose their regard for human life overnight. It is a step at a time downward and soon that society slips further and faster downward. Many vowed, "Never Again." We in the U.S. cannot and should not be allowing access to our children for medical research. There is no argument that justifies it! Perhaps we need to review the transcripts of the Nuremberg trials. There were many, including doctors who were held accountable.

An immediate halt should be called to medical experiments on children. Further, any unused grant money should be returned to the U.S. Treasury and any grants used for clinical studies on children who did not get an independent advocate should be repaid. That money won't compensate for loss society experiences from such conduct, but our tax money should not be used in this manner. It's a disgrace! If the weak and vulnerable continue to be treated in this manner, Lord help us, it becomes a slippery slope.

Respectfully submitted,

Sharon Schuldt

William Glasser, Inc.
Chatsworth, California 91311
May 20, 2005

Congressman Wally Herger
Rayburn House Office Building
Washington, D.C. 20515

I am very interested in the Congressional Hearing focused on protecting children from being involved in experimental psychiatric drugs or drugs of any kind. Most of the children enrolled are foster children or children who aren't really looked after by any protective agency. I believe the government should become the protective agency.

I am a Board Certified Psychiatrist who has been working in mental health for over forty years. I've worked not only with children and adults, but also extensively in the schools. In the schools that are following my ideas, no children are given any kind of psychiatric drugs at the instigation of the schools. We can't stop parents from giving their children these drugs, but we can certainly advise parents that these drugs are really not necessary. These *Glasser Quality Schools* are highly successful and are perhaps the most successful schools in the country where students are not taking any psychiatric drugs.

Your legislation can certainly close a big gap to the practice of using children who have no way of protecting themselves and no parents who are really that interested in them. That should not be allowed. There should be some sort of protection for the children and that protective operation should swing into operation if any children are asked to participate in any kind of medical experimentation at all.

As a Board Member of an organization called Ablechild, I am working with Gloria Wright and other members to reduce the drugging of all children and the practice of advising parents to put their children on drugs. No one knows what the long-term effects are from these drugs. The short-term effects, in many cases, are somewhat disastrous and include violent activity and suicide.

I am the President of The William Glasser Institute. We teach and train people to deal with mental health all over the world with adults and children. I am very well known and have been spending most of the latter part of my professional life warning people about the dangers of psychiatric drugs. There is no evidence that the drugs are in any way helpful, but there is a great deal of evidence that they may be harmful. If the purpose of our government is to protect people against unwarranted intrusions into their privacy from the people who are making money off of these intrusions and paying little or no attention to the children, then this is a wrong you should certainly right.

If you would like to learn more about my work, my website address is www.wglasser.com. You will see that there is a lot of information on the website that supports what I am saying here.

I also appreciate being on the Ablechild Board of Directors and I am doing everything I can to help them.

Cordially,

William Glasser, M.D.
Board Certified Psychiatrist

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