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May 15, 2001

5382 '01 MAY 18 P1:50

Dockets Management Branch
Food & Drug Administration (HFA-305)
5630 Fisher's Lane, Room 1061
Rockville, MD 20857

Re: Docket No. 00N-0074: Additional Safeguards for Children in Clinical Investigations of FDA Regulated Products- Interim Rule

Dear Sirs:

We are delighted that FDA is issuing additional safeguards for children who participate in pediatric clinical trials. Since enactment of the pediatric exclusivity provision of the *FDA Modernization Act* (FDAMA), a large number of children have been participating in medical research without adequate safeguards for this particularly vulnerable group of research subjects. While federally funded research must comply with the safeguards of the *Common Rule*, privately-funded research does not. This is why FDA's new rules for pediatric research are so important, especially in light of the fact that recent reports of corporate recruitment efforts for pediatric trials have raised ethical questions.

We deeply regret that it has taken 22 years for FDA to apply the pediatric HHS regulations to FDA regulated products that do not involve federal funds (from April 24, 1979 to 2001). The recent upsurge of privately funded pediatric trials lends a sense of urgency to FDA's new rules. FDA will now adopt HHS Subpart D, as directed by Congress, and will regulate pediatric research conducted by private sponsors. The new regulations will cover testing of drugs, medical devices, foods, etc., in children.

Section 50.52

We are particularly concerned about the proposed section 50.52, which addresses clinical studies with **more than minimal risk** to children, but that present the prospect of direct benefit to a child. The *Federal Register* notice states that these "investigations **generally** are performed in children with the disease or condition for which the product is intended".

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We suggest that when a product (drug, device, etc.) presents more than minimal risk to children, it should NEVER be tested in children who do not have the disease or condition for which the product is intended. Our primary concern is the fact that healthy children are being recruited to participate in clinical trials, and healthy children should not be exposed to risk unless their health is at stake. World-wide bioethical standards require that healthy children should not participate in clinical trials involving risk. We believe that if a healthy child stands no chance of directly benefiting from the product being tested, their participation in such trials should be prohibited.

Placebo controlled trials in children

We believe in some circumstances placebo-controlled trials may be appropriate in children. However, placebos should not be used in serious diseases where the absence of an active substance might put a child at undue risk. Placebos should be used only in benign diseases such as the common cold, mild to moderate allergies, etc. For example, testing an antibiotic for ear infections should not be compared to placebos because it might lead to permanent deafness in a child who takes the placebo. But placebos could be appropriate in tests of antihistamines or decongestants because the absence of an active drug would not lead to permanent handicaps. We believe strongly that in a controlled clinical trial, the active substance should be compared to the **best standard therapy** for that disease. Therefore, children with a disease in a control group should be given the best standard therapy and not a placebo.

Section 50.53

This section addresses trials with more than minimal risk to children which are likely to yield generalizable knowledge that is of importance for the understanding or amelioration of a disorder. We would like to see stringent requirements for this section, which do not put healthy children at risk. No healthy children should participate in this type of trial because testing a drug or device might cause harm, rather than prevent harm. IRBs should not make these decisions, and FDA should be empowered to overrule IRBs. FDA should have a bioethicist on staff to investigate such trials and determine whether they should go forward.

Section 50.54

This section addresses trials that do not fit into other categories, and allows for individual decisions by the Commissioner that conform to sound ethical principles. The Commissioner is authorized to consult with a panel of experts. Section 50.54(b) describes members of the panel of consultants who should come from various scientific and medical disciplines. We believe these panels should be required to include several pediatric health care workers, and at least one consumer advocate.

However, the proposed rule states that public review and comment will not be allowed if the sponsor is unwilling to publicly disclose necessary information. We suggest if a sponsor is unwilling to waive their confidentiality privilege the trial should NOT be approved by the FDA. The public's suspicion of medical research done behind closed doors is based on sound historic precedent, and we believe that public review of such protocols should be mandatory if children will be exposed to more than minimal risks. Surely the Willowbrook experiment would not have gone forward if the public knew the risks it posed to mentally retarded individuals.

Documentation of Assent

We suggest that consent or assent of a child or family member should be witnessed by an independent person at the research facility, and/or videotaped to assure that proper and truthful information has been provided in an understandable fashion to parents and children. We agree that FDA should not adopt waivers or exceptions to informed consent by parents or guardians.

Omissions

The proposed regulations do not include standards for conflict of interest, nor do they require that such conflicts by investigators or institutions be revealed on informed consent documents to parents or guardians. Nor do they mention rules for recruitment practices. There should be prohibitions against bribing parents with high payments to offer their children for research. Compensation should cover direct expenses such as travel, meals and lodging costs, day care for other children, etc. The regulations should also prohibit participation by healthy children in any protocol that involves more than minimal risk.

We hope the above comments are helpful.

Sincerely,

Abbey S. Meyers
President

ASM:aa

cc: Diane Dorman, Senior Director for Public Policy

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