Comment on Interim Rule

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July 23, 2001

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

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

Dear Sir/Madam:

The Modernization Act established economic incentives for drug companies to conduct medical research in the pediatric population. The 6 months of marketing exclusivity under the Drug Price Competition and the Patent Term Restoration Act or the Orphan Drug Act have contributed to the dramatic increase in the number of children enrolled in clinical trials. The Congress directed the FDA to adopt the HHS subpart D in order to provide additional safeguards for children participating in clinical investigations of FDA-regulated products. The Products include human drugs, medical devices, biological products, dietary supplements, food additives and food. The interim rule will contribute to a considerable decrease in the unlabeled medicines on the market for children and will establish the overdue pediatric research infrastructure. This interim rule has a great potential to provide treatment for children with rare diseases via orphan medicine and to protect them from being therapeutic orphans.

Section 50.51

Section 50.51 indicates that an IRB may approve a clinical investigation in which no greater than minimal risk presented. The condition for the approval includes adequate soliciting of the assent of the children involved and the permission of their parents or guardians. We believe that the interim rule should include a well-defined scale system for risk. The system will be able to classify procedures and would help in identifying the degree of minimal risk. For example, collecting clean-catch urine sample via the catheter has a potential to cause tissue injury and/or infection. This procedure has a higher degree of risk than testing devices involving temperature reading orally or in the ear. The interim rule should help the IRBs in granting an approval for a procedure that is based on a specific distinction of the potential risk.

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Section 50.52

Section 50.52 states that an IRB may approve a clinical investigation involving greater than minimal risk, but presenting the prospect of direct benefit to the individual subjects. We strongly believe that the interim rule should clearly state that a healthy child should not be exposed to any degree of risk. A healthy child who stands no chance to benefit from the clinical investigation has no reason to participate in one. The ethical issue is of great concern despite the fact that the clinical investigation may benefit children with the disease.

Placebo-Controlled Clinical Trials

The interim rule favors placebo-controlled trials in complicated diseases due to their potential benefits. We disagree with conducting placebo-controlled trials on healthy children. In Phase I, the medicine is tested on healthy children to ensure its safety. The child's development could be affected by such experiments and there is no evidence to the contrary. The 1998 pediatric rule is recent and studies to examine the long-term effects of clinical trials on healthy children are not available. Investigational medicines along with the potential misfortune of the placebo effects may cause healthy children a physical and a psychological harm.

We disagree with conducting placebo-controlled trials involving individuals who have the active disease. In Phase II, the medicine is tested on children with the disease that the medicine is intended to treat. The aim is to test the medicine's efficacy. Placebo-controlled clinical trial raises the ethical question on whether to give active compounds to patients who need them or to simply give them placebo. The pediatric population may develop obstacles to healthy recovery and may generate negative outcomes as they grow to become mature adults. To avoid harm, the interim rule should clearly indicate that the investigational medicine would be compared against another active medicine in the same class.

Section 50.53

Section 50.53 states that an IRB may approve a clinical investigation involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subjects' disorder. We have a great concern regarding the power that has been bestowed upon the IRBs. Protection of pediatric populations requires a high degree of competency on the part of IRBs. Upon close examination of their activities, an inappropriate set of practices has been detected in the past. As a result, horrifying incidents took place and many IRBs were ordered to halt their activities. Good science along with ethics and reasoning are needed to assess the degree of risks involved in clinical trials. The interim rule should call for educational programs and continuous training for IRB members to ensure proper and current knowledge on the related issues. We believe that a healthy child shall not participate in clinical research unless her/his personal health is at stake. The FDA should determine the adequate guidelines for the procedures and should be the only authority that makes the final decision.

Section 50.54

Section 50.54 directs an IRB to allow a clinical investigation to proceed that is not otherwise allowed by sections 50.51, 50.52, and 50.53. The FDA calls upon the Commissioner who would consult with a panel of experts to determine that the conditions of section 50.54 (b) are met. As a result, the clinical investigation can proceed. This section provides for public comments on the Commissioner's pending decision. The FDA, however, may not be able to provide for public comments if the sponsor is unwilling to disclose necessary information. We disagree with the unwillingness of the sponsor to disclose information. Ethical issues stems from the unwillingness of the sponsor to provide needed facts. The secrecy of the trial and its conduct would raise suspicion and make people uncomfortable. We strongly believe that the interim rule should emphasize on the authority of the FDA to suspend clinical investigations pending sponsor's willingness to share information.

We hope the final rule would benefit the pediatric population worldwide.

Sincerely Yours,

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