Children's Health Protection Advisory Committee

November 10, 2005

Stephen L. Johnson, Administrator
United States Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

RE: Protections for Subjects in Human Research

Dear Administrator Johnson:

The Children's Health Protection Advisory Committee reviewed the proposed rule to protect human subjects in research involving intentional dosing of pesticides. There are a number of weaknesses and ambiguities in the proposed rule that need to be corrected. As written, the proposed rule is very open to interpretation and is not sufficiently protective of pregnant women and children.

We understand that the EPA intends this proposed rule to categorically ban intentional dosing human testing for pesticides when the subjects are pregnant women, fetuses, or children. However, we do not believe that the proposed rule, as written, accomplishes this categorical ban. Below we identify several provisions in the proposed rule that undercut a categorical ban.

1. Even after a final rule is adopted a third party will be able to conduct or sponsor intentional pesticide dosing studies involving pregnant women, fetuses or children, as long as the tests are not conducted with the "intention" of submitting them to EPA for its decision-making under FIFRA or FFDCA. As such, it appears that intentional dosing studies of pesticides which are conducted for purposes of review by a foreign government or a state could be conducted and subsequently submitted to EPA for review under FIFRA or FFDCA, without running afoul of the new regulations.

2. The proposed rule does not prohibit third party intentional dosing studies conducted for some purpose other than EPA's decision-making under FIFRA or FFDCA. For example, a study could be conducted and submitted to set a maximum exposure limit for a pesticide under the Clean Water Act, and apparently could then be submitted to EPA for its use under FIFRA or FFDCA.

3. The proposed rule permits exceptions to the categorical ban through use of an exception procedure that is outlined in the proposed rule (26.603) to allow EPA consideration of research involving intentional exposure of pregnant women or children when it is deemed crucial to the protection of public health. The proposed rule does not give any indication of what those public health exigencies would be or what criteria would be used to determine whether a public health exception would be granted.

4. The EPA also appears to add additional protections for children in Subpart D. Several of these provisions, however, are ambiguous and could be taken to allow for intentional dosing studies involving children. Under proposed Sec. 26.401(a) (2), the EPA Administrator is permitted to waive any or all of the restrictions embodied in the proposed regulation. As such, the EPA can determine that any intentional dosing study of pesticides using children, who are older than neonates and up to age 18, is permissible.

5. Subpart D also allows IRBs to waive the requirement for consent of a parent or guardian for research involving children. It specifically states that such a waiver could be granted for studies involving abused or neglected children. We do not believe that this is EPA's intent and may be a matter of ambiguous wording.

The Children's Health Protection Advisory Committee could not foresee any situations in which it would be ethical to intentionally dose pregnant women, fetuses, or children. If there are such exceptional situations that EPA had in mind, these should be clearly and narrowly delineated in the proposed rule. The Committee recommends that EPA change the proposed rule in the following ways to address the ambiguities identified above.

1. EPA should extend the rule on third party intentional dosing studies of pesticides using pregnant women and children as subjects to studies submitted to EPA for decision making under any statutory authority. At a minimum, all studies submitted to EPA for any consideration should abide by the Common Rule.

2. The "public health" exception procedure proposed in 26.603 allows for wide use of the exception. Therefore, the CHPAC strongly recommends that EPA reconsider this exception, especially for pregnant women and children. This exception may inadvertently lead to the unnecessary use of intentional dosing studies in the name of public health, and needs significant clarification. At the least such exceptions, if any, should be very limited, be considered only in a public health emergency, and criteria should be developed with public input on when such an exception is justifiable.

3. The CHPAC strongly recommends that the rule not grant the EPA Administrator the sweeping authority under Sec. 26.401(a) (2) to waive any or all of the restrictions embodied in the rule when studies involving children are conducted. It is not clear when this authority would be invoked or for what purpose.

4. The EPA should never waive the requirement for consent of a parent, or a guardian when studies involve children, whether or not these children are abused or neglected.

The CHPAC understands that the details of the form, organization and function of the Human Subjects Review Board (HSRB) have yet to be developed. We recommend that the Agency give serious consideration as to how the HSRB's powers and responsibilities are defined, and how its members will be selected. We believe that the HSRB needs to be more than an advisory group and should have a degree of authority. We suggest that the HSRB have similar design and function as DHHS registered IRBs. We also recommend that the HSRB include members of constituencies such as the interested public and ethicists.

The proposed plan states that the HSRB 'should report directly to the Office of the EPA Administrator', however it does not state that the Office of the EPA Administrator has to respond to the HSRB's concerns. The plan needs to specify that the Office of the EPA Administrator will modify studies based on the HSRB evaluation of third party protocols before a study can begin. In addition, the agency needs to develop a plan for how the HSRB will deal with third party data already generated.

The CHPAC realizes that there are other significant questions raised by the proposed rule that we have not addressed. We focused our recommendations on ambiguities we see in the proposed rule, which was limited to intentional dosing studies. In the near future, EPA should consider ethical protections for observational studies of children and pregnant women. We would be happy to discuss any of these issues with you or the appropriate designee.

Sincerely,

Melanie Marty, Ph.D., Chair
Children's Health Protection Advisory Committee

cc: Susan B. Hazen
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