Association of Clinical
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Submitted at https://www.regulations.gov

Re: **Docket No. FDA-2022-D-0738** Ethical Considerations for Clinical Investigations of Medical Products Involving Children: Guidance for Industry, Sponsors, and IRBs

To Whom It May Concern:

The Association of Clinical Research Professionals (ACRP) submits the following comments on the Food and Drug Administration's (FDA) Draft Guidance: Ethical Considerations for Clinical Investigations of Medical Products Involving Children. ACRP appreciates the opportunity to provide comments on this valuable guidance.

The Association of Clinical Research (ACRP) supports clinical research professionals through membership, training and development, and certification. Founded in 1976, ACRP is a non-profit organization with more than 12,000 members who work in clinical research.

At ACRP we are improving quality in clinical research by directly impacting the professionals conducting clinical trials. We are leading innovation in clinical research workforce development by setting standards for professional competence and building and validating competence in the workforce.

INTRODUCTION (I)

- No feedback

BACKGROUND (II)

- No feedback

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ETHICAL FRAMEWORK (III)

- Section A: the final paragraph of the section states "When it is considered scientifically necessary to conduct a clinical investigation in children, it is imperative that the clinical investigation be well-designed to collect interpretable data... Studies that are not well-designed expose children to unnecessary risks, are unlikely to yield informative study results and as a result may be considered unethical." Perhaps the sentence should be stated in the guidance that this is true of all clinical investigations, but due to children's status as a vulnerable population they are due additional considerations in terms of design. It should be clearly stated that this is scientifically necessary for all clinical investigations to be ethical.

- Section E: Additional detail on component analysis and determination of what constitutes minor increase over minimal risk could be beneficial. Is the list of factors for consideration in the middle of the section intended to be exhaustive? If not, can it be stated as such? Some examples are given of what is minor increase over minimal risk versus exceeding that level, but not necessarily a clear rubric for how that might be extended to other interventions.

- There seems to be a disconnect between parent consent and a child who does not want to assent. This is addressed to some degree in the first full paragraph of page 10, but if a child is blatantly refusing a study that a parent is consenting to, perhaps there should be an age where lack of assent should be deemed refusal to participate. In different states there are different considerations that need to be made. In some states children of a certain age have more medical autonomy. State and local considerations should be reflected in the guidance. The guidance should speak more to the intersection of consent and assent in situations where there might be disagreement, especially with respect to the age of the child (example age 5 versus age 17).

APPLICATION OF SUBPART D TO PEDIATRIC CLINICAL INVESTIGATIONS (IV)

- Statements in Section A speak to the necessity of inclusion of pediatric patients in clinical trials and product development, presumably in hopes of increasing the number of indications that might be approved in pediatric populations - absolutely true statements. On the other hand, there is limited provision for how sponsors and investigators might accomplish that in scenarios where adult studies may not be feasible or ethical. Considering FDA's threshold for evidence in support of marketing applications, what is the likelihood of approval of applications for such indications? It would be helpful to have more guidance from the agency on how one would address some of the typical requirements for early phase in the scenario where you wouldn't be able to do adult studies i.e. dose finding, PK and PD.

Additional Feedback

- It would be helpful from an IRB perspective if the FDA would include further examples in regard to minimal risk, minor increase over minimal risk and greater than minimal risk.

The Association of Clinical Research Professionals is grateful for the FDA's consideration of this feedback. Please feel free to contact Bridget Gonzales at bridget.gonzales@acrpnet.net.

Respectfully submitted on behalf of the members of ACRP,

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