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Scott Gottlieb, MD
FDA Commissioner
c/o Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Docket No. FDA-2018-D-1540, “Considerations for Inclusion of Adolescents in Adult Clinical Trials” (83 Federal Register 25675)

Dear Commissioner Gottlieb:

Public Responsibility in Medicine and Research (PRIM&R) appreciates the opportunity to comment on the Food and Drug Administration (FDA)’s draft guidance for industry on Considerations for the Inclusion of Adolescent Patients in Adult Oncology Clinical Trials published June 4, 2018.

PRIM&R is a nonprofit organization dedicated to advancing the highest ethical standards in the conduct of research. Since 1974, PRIM&R has served as a professional home and trusted thought leader for the research protections community, including members and staff of human research protection programs and institutional review boards (IRBs), investigators, and their institutions. Through educational programming, professional development opportunities, and public policy initiatives, PRIM&R seeks to ensure that all stakeholders in the research enterprise understand the central importance of ethics to the advancement of science.

PRIM&R applauds the draft guidance, and believes it represents the right direction for institutions and organizations that conduct oncology research, provided that careful attention is paid to the processes of obtaining consent or assent from adolescent patients and their parents or guardians.

We agree with the FDA that, unless there is compelling scientific reason to exclude adolescents from adult oncology trials, they should be offered access to such trials. Currently, adolescent subjects must wait until pediatric trials are begun after completion of late-phase adult trials. The proposed approach will enable researchers to provide data about safe and effective treatments for adolescent cancer patients
sooner than is currently the case. The guidance is a welcome further indication of the FDA’s commitment to enhancing clinical trial access to demographic groups historically excluded from important research and its benefits.

One area of the guidance could benefit from further clarification. In Part III, with respect to first-in-human or dose-escalation trials, the draft guidance states that adolescents may not be enrolled in adult trials prior to the availability of initial adult pharmacokinetic and toxicity data. After such data are available, adolescents may be enrolled, and sponsors should “consult with the responsible FDA review divisions to determine the amount and type of adult data needed before enrolling adolescent patients.”

We suggest that the guidance should remind its intended audience that, even after the FDA has determined that adequate adult toxicity and pharmacokinetic data exist to safely enroll adolescent patients in a particular oncology trial, the determination by an investigator and an IRB that it is appropriate to offer adolescents the opportunity to enroll in an adult trial still depends on a number of additional considerations. The purpose of moving to adolescents is not simply to generate pharmacokinetic data on adolescents, so as to confirm appropriate dosing. Rather, the justification for including adolescents in an adult trial must lie in a reasonable belief—based on pre-clinical and/or clinical data—that the investigational drug may benefit the population with the condition and that the risks to adolescents are acceptable in light of the alternative treatments available for that population. Thus, the guidance should clarify that the sponsor’s evaluation of the safety data will be provided in a format that the investigator can share with an IRB to inform its determination regarding whether offering adolescents the opportunity to enroll in the trial is ethical, a decision as to which the safety data are an essential component, but by themselves are insufficient.

Finally, we urge the guidance to emphasize that it is written specifically to address inclusion of adolescents in adult oncology trials; though the guidance may be helpful to sponsors of studies on other diseases, there should be no assumption that the same considerations will hold in all cases. Sponsors considering including adolescents in adult trials related to other diseases thus should be reminded to consult with the FDA.

Thank you again for the opportunity to comment on this important guidance. My PRIM&R colleagues and I are available to discuss our comments further, should that be of interest. Please feel free to contact me at 617.303.1872 or ehurley@primr.org.

Respectfully submitted,

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Executive Director

cc: PRIM&R Public Policy Committee, PRIM&R Board of Directors