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Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

COMMENTS ON
IRB WAIVER OR ALTERATION OF INFORMED CONSENT FOR CLINICAL INVESTIGATIONS INVOLVING NO MORE THAN MINIMAL RISK TO HUMAN SUBJECTS - GUIDANCE FOR SPONSORS, INVESTIGATORS, AND INSTITUTIONAL REVIEW BOARDS
Docket No. FDA-2017-D-3235

Public Citizen, a consumer advocacy organization with more than 400,000 members and supporters nationwide, submits these comments with regard to the guidance "IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects," the availability of which was announced by the Food and Drug Administration (FDA) in the *Federal Register* on July 25, 2017.

The guidance states that the FDA intends to revise the informed consent provisions of its regulations governing the protection of human subjects (21 C.F.R. Parts 50 and 56) to comport with Title III, section 3024, of the 21st Century Cures Act but that until the agency promulgates revised regulations, it does not intend to object to an institutional review board (IRB) approving a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth in 21 C.F.R. 50.25, or waiving the requirements to obtain informed consent when the IRB finds and documents that:

(1) The clinical investigation involves no more than minimal risk (as defined in 21 C.F.R. 50.3(k) or 56.102(i)) to the subjects;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The clinical investigation could not practicably be carried out without the waiver or alteration; and

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Public Citizen offers the following comments regarding (a) the FDA's decision to issue the guidance without first seeking public comment on a draft guidance document and (b) the content of the guidance document.

Issuing final guidance without soliciting public comment

In the *Federal Register* notice announcing the availability of the guidance,[1] the FDA asserted that the agency was implementing the guidance without prior public comment because it had determined that prior public participation was not feasible or appropriate given that the "guidance presents a less burdensome policy that is consistent with public health."

We find the FDA's justification for not seeking prior public comment to be insufficient. In particular, the FDA offers no examples of significant public health needs that were going unmet in the absence of final guidance on this topic. We are not aware of any urgent public health needs that have gone unaddressed because IRBs could not waive the requirements to obtain informed consent. It also would have been feasible for the FDA to solicit public comment on a draft guidance document before issuing final guidance.

The content of the guidance

The guidance, like the *Federal Register* notice announcing its availability, emphasizes that the waiver of informed consent requirements is "a less burdensome policy." Implicit in this statement is that the policy for waiving informed consent will lessen burdens for investigators conducting FDA-regulated clinical investigations. We are troubled by the absence of any discussion in the guidance of the ethical underpinnings of informed consent for human subjects research. As the FDA is aware, federal regulatory requirements for obtaining the informed consent of human subjects of research are founded upon the bedrock ethical principle of respect for persons, which was articulated in the *Belmont Report*.[2] The fact that obtaining informed consent of human subjects may be burdensome for investigators does not outweigh the rights of research subjects to voluntarily agree to be enrolled in research, even research that involves no more than minimal risk. We recommend that the guidance be revised to include a discussion of these ethical considerations.

The FDA guidance states that "[w]aiver of informed consent for certain FDA-regulated minimal risk clinical investigations will facilitate investigators' ability to conduct studies that may contribute substantially to the development of products to diagnose or treat diseases or conditions, or address unmet medical needs." We are concerned that the guidance document fails to describe the types of clinical investigations for which the agency might consider an IRB's waiver of informed consent to be appropriate. For example, does the agency believe that the waiver of informed consent would be appropriate from both an ethical and regulatory perspective for clinical trials testing investigational new drugs or medical devices, and if so, under what circumstances would that be the case?

[1] 82 FR 34535-34536.
[2] National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. April 18, 1979. https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html. Accessed September 17, 2017.

The guidance document references a recommendation from the Secretary's Advisory Committee on Human Research Protections (SACHRP) to the Secretary of Health and Human Services that the FDA adopt the provisions for waiver of informed consent that exist under the Common Rule at 45 C.R.F. 46.116(d). We note from the references provided in footnote 7 of the guidance document that the pertinent SACHRP recommendation was presented within the context of a series of recommendations related to cluster randomized trials, but the discussion section of the guidance does not mention such trials. Does the FDA believe that clinical investigations designed with cluster randomization would be the typical type of research for which waiver of informed consent would be appropriate?

We urge the FDA to issue expanded guidance that includes a discussion of the types of clinical investigations — such as cluster randomized trials — for which the agency might consider an IRB's waiver of informed consent to be appropriate from both an ethical and regulatory perspective. Ideally, this discussion would provide specific examples of actual or hypothetical clinical investigations with an analysis of the four findings that need to be made and documented by the IRB. This discussion should highlight the types of clinical investigations that the agency might consider to reasonably involve no more than minimal risk to human subjects and to be impracticable to carry out without the waiver of informed consent.

Thank you for the opportunity to comment on these important public health matters.

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