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November 7, 2011

The Honorable Kathleen Sebelius
Secretary
Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

**RE: Draft Guidance on Exculpatory Language in Informed Consent Issued by the Office for Human Research Protections and the Food and Drug Administration (Docket Number HHS-OPHS-2011-0014)**

Dear Secretary Sebelius:

Public Citizen, representing more than 225,000 members and supporters nationwide, strongly opposes the proposed draft guidance on exculpatory language in informed consent because, contrary to the *Federal Register* notice announcing the availability of this draft guidance document for comment (76 FR 55390) – which states that the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) are seeking to "enhance human subjects protection" by "actively working to harmonize the agencies' regulatory requirements and guidance for human subjects research" – the proposed guidance would weaken protections for human subjects.

In particular, the draft guidance proposes to reverse both the OHRP's and the FDA's decades-long policy positions prohibiting investigators from asking prospective subjects to waive **any** rights when seeking informed consent. The revised guidance would unnecessarily narrow this prohibition to only those waivers of rights that would result in freeing or appearing to free an entity or individual from liability for negligence. Furthermore, we are not aware of, nor has the OHRP or the FDA provided, any justification for the proposed policy reversal.
This proposal, like the proposals described in the Department of Health and Human Services' (HHS) advance notice of proposed rulemaking on human subjects research protections (76 FR 44512), reflects a troubling trend by HHS toward the weakening, rather than strengthening, of the protections for human subjects.

## A. Current Regulations and Policy

The HHS human subjects protection regulations at 45 C.F.R. 46.116 state the following:

> No informed consent, whether oral or written, may include any exculpatory language through which the subject … is made to waive or appear to waive any

> of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

The FDA human subjects protection regulations at 21 C.F.R. 50.20 have an identical provision.

Since at least the early 1990s, the OHRP and the FDA have interpreted the above regulatory provision as prohibiting informed consent from including waivers of any legal rights, not just rights related to liability claims for negligence.

For example, the OHRP's November 15, 1996 guidance entitled, "'Exculpatory Language' in Informed Consent," states that the HHS regulations at 45 C.F.R. 46.116 prohibits the following statements from being included in informed consent for research:[1]

- I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all right, title, and interest to said items.
- By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.
- I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.

Since the 1990s, during compliance oversight evaluations the OHRP has repeatedly cited institutions for noncompliance with the HHS human subjects protection regulations when the agency found language, such as the above statements, in informed consent documents approved by institutional review boards (IRBs).

Likewise, the FDA's 1998 guidance entitled, "Institutional Review Boards Frequently Asked Questions – Information Sheet Guidance for Institutional Review Boards and Clinical Investigators," states the following:[2]

> **52. Is it acceptable for the consent document to say specimens are "donated"?**
>
> What about a separate donation statement? It would be acceptable for the consent to say that specimens are to be used for research purposes. However, the word "donation" implies abandonment of rights to the "property." **21 CFR 50.20 prohibits requiring subjects to waive or appear to waive any rights as a condition for participation in the study.** Whether or not the wording is contained in "the actual consent form" is immaterial. All study-related documents must be submitted to the IRB for review. Any separate "donation" agreement is regarded to be part of the informed consent documentation, and must be in compliance with 21 CFR 50. [Emphasis added]

On multiple occasions during the past two decades, the FDA also has cited institutions for noncompliance with the FDA human subjects protection regulations when the

agency during its inspections of IRBs found language waiving subjects' rights related to tissue specimens in IRB-approved informed consent documents.

Therefore, the OHRP and the FDA currently have policies regarding the prohibition against exculpatory language in informed consent that are completely harmonized and are most protective of the rights and welfare of human subjects. Furthermore, both agencies presumably have considered their long-standing policy interpretations of 45 C.F.R. 46.116 and 21 C.F.R. 50.20 to be legally defensible.

**B. The Proposed Guidance**

The August 19, 2011 draft guidance entitled, "Guidance on Exculpatory Language in Informed Consent,"[3] would greatly narrow the scope of what language is prohibited under the HHS and FDA human subjects protection regulations. Only waivers for rights related to claims of malpractice or negligence would be prohibited.

As a result of this new interpretation of the regulatory provisions regarding exculpatory language in informed consent at 45 C.F.R. 46.116 and 21 C.F.R. 50.20, the OHRP and the FDA now explicitly declare in the proposed guidance that informed consent for research may include the following types of statements:

- By agreeing to this use, you are giving up all claims to any money obtained by the researchers from commercial or other use of these specimens.
- I voluntarily and freely donate any and all blood, urine, and tissue samples to the [name of research institution] and hereby relinquish all property rights, title, and interest I may have in those samples.
- By consenting to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples collected during this research.
- Although the results of research, including your donated materials, may be patentable or have commercial value, you will have no legal or financial interest in any commercial development resulting from the research.

Of note, both the draft guidance itself and the notice in the *Federal Register* announcing the availability of the draft guidance fail to offer any explanation for this complete reversal of the OHRP's and FDA's long-standing policy interpretations regarding the types of language prohibited from being included in informed consent under the exculpatory language provision under 45 C.F.R. 46.116 and 21 C.F.R. 50.20.

Clearly, such a change in the OHRP and FDA policies would adversely impact the rights and welfare of human subjects. Therefore, the agencies should provide the public with a sound and compelling ethical justification for this dramatic policy change before implementing the change. Perhaps the current policies of the OHRP and the FDA regarding the prohibition against using exculpatory language in informed consent are a major impediment to the conduct of important research offering significant benefits to society. If this is the case, the agencies should provide specific examples documenting such circumstances. However, we are not aware of any data indicating that the current

OHRP and FDA policies have interfered with the conduct of any human subjects research or placed undue burdens on any researchers.

In closing, since we are not aware of, nor has the OHRP or the FDA provided, any justification for the proposed change in the agencies' policies, Public Citizen strongly opposes the proposed draft guidance on exculpatory language in informed consent because it would weaken protections for human subjects. If there is a compelling justification for the proposed changes, the OHRP and the FDA should articulate that justification in writing and provide an opportunity for the public to consider whether such justification is valid. Absent such justification, the current OHRP and FDA guidance should be retained.

Furthermore, we urge you to investigate why OHRP, which should be working to protect the interests of human subjects, seems more predisposed to taking actions that diminish the protections for human subjects.

Thank you for the opportunity to comment and for taking our comments into consideration.

Sincerely,

Sidney M. Wolfe, M.D.
Director
Public Citizen's Health Research Group

cc: Dr. Jerry Menikoff, Director, OHRP
Dr. Irene Stith-Coleman, Director, Division of Policy and Assurances, OHRP

[1] Office for Protection from Research Risks. "Exculpatory Language" in Informed Consent. November 15, 1996. Available at http://www.hhs.gov/ohrp/policy/exculp.html. Accessed November 4, 2011.
[2] Food and Drug Administration. Institutional Review Boards Frequently Asked Questions - Information Sheet: Information Sheet - Guidance for Institutional Review Boards and Clinical Investigators. January 1998. Available at http://www.fda.gov/RegulatoryInformation/Guidances/ucm126420.htm#Informed%20Consent%20Process. Accessed on November 4, 2011.
[3] Office for Human Research Protections and the Food and Drug Administration. Guidance on Exculpatory Language in Informed Consent. August 19, 2011. Available at http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM271036.pdf. Accessed November 4, 2011.