**Citizens for Responsible Care and Research, Inc. (CIRCARE)**
(A wholly independent, volunteer, non-profit, tax-exempt organization,
incorporated under the laws of the State of New York)
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Office of Science and Technology
Policy Executive Office of the President

VIA e-mail: bioeconomy@ostp.gov

In re: Office of Science and Technology Policy, Notice, Request for Information: Building A 21st Century Bioeconomy, 76 Fed. Reg. 62,869 (2011),

These comments respond to regulatory concerns raised in the Office of Science and Technology Policy's Request for Information.

INTRODUCTORY STATEMENT:

We are especially concerned that:

1. Protection of patients and of subjects of biomedical, behavioral, and social research might be perceived as hindering scientific and technical advance; and

2. These protections might therefore be cut back—to the detriment of patients, research subjects, and science itself.

Citizens for Responsible Care and Research, Inc. (CIRCARE) is the oldest human research protection organization in the United States and is entirely independent. We advocate conscionable research. We are private citizens dedicated to effective protection of human subjects in behavioral and biomedical research. Our board members and officers are from science, law, research policy, ethics, medicine, nursing, social work, education, and care-giving. Some of have been voluntary subjects of research. Experience represented in our board and officers includes governmental and academic Institutional Review Board membership and chairmanship and university faculty in national and international law and ethics of human subjects research. We serve without pay. CIRCARE receives no support from industry or government.

The National Bioeconomy Blueprint purposes include "to ... identify

regulatory reforms that will reduce unnecessary burdens on innovators while protecting health and safety ....” Protection of health and safety, including protection of patients and human subjects of behavioral and biomedical research, is not antithetical to nor does it deter well-conceived research. Science and society benefit from a credible, largely earned reputation of medical concern for the public welfare. Medicine, because of its long-established ethical tradition of clinical beneficence and fidelity to the individual patient, brings with it a presumption of trustworthiness.

But as the record shows, there continue to be rogues in research and more than occasional disdain for the dignity and rights of human subjects of biomedical, behavioral, and social research. We continue to encounter disregard for the relevant ethics and law. The most notorious of these violations continue to make it difficult to recruit research subjects even where they stand to benefit. Biotechnology and information technology, including data-mining, are combining to pose serious threats to personal privacy in the course of research, notwithstanding their potential impacts if brought to commercial fruition. Eagerness to minimize human research protections will exacerbate inability to recruit subjects for meritorious studies. Personal medical data essential to validate new medical research techniques and development of diagnostics and therapeutics will not be readily available if researchers cannot be trusted to protect their information from access for which there is no informed consent.

U.S. law on federally supported research and on research in support of Food and Drug Administration indications requires that Institutional Review Boards “review biomedical and behavioral research involving human subjects ... in order to protect the rights of the human subjects of such research,” 42 U.S.C. § 289(a), implemented in the Common Rule, 45 C.F.R. pt. 46, and by the FDA, 21 C.F.R. pts. 50 & 56.

The OSTP RFI rightly refrains from asserting that current regulation to protect research subjects arbitrarily inhibits meritorious research and development. But in a recent Advance Notice of Proposed Rulemaking, Docket HHS-OPHS-2011-0005, 76 Fed. Reg. 44,512 (2011), the Department of Health and Human Services states that existing human research protections constitute undue burden and proposes to foster research by altering dramatically what has been a generally effective, stable, predictable, mostly supportive regulatory environment. We pointed out in response the DHHS ANPRM rests on highly questionable assumptions and its proposed changes would run weaken existing protections substantially, counter to law, and would be to the detriment of science itself. http://www.regulations.gov/#!documentDetail;D=HHS-OPHS-2011-0005-0336 and http://www.circare.org/submit/circare_anprm_response_201109.pdf.

We generally endorse the stated “grand challenge” goals:... such as ‘‘smart anti-cancer therapeutics that kill cancer cells and leave their normal neighbors untouched; early detection of dozens of diseases

from a saliva sample; personalized medicine that enables the prescription of the right dose of the right drug for the right person; a universal vaccine for influenza that will protect against all future strains; and regenerative medicine that can end the agonizing wait for an organ transplant.''
Still, as we make plain in our response to the DHHS ANPRM and in our comments above, we must be very careful to ensure protection of health, safety, and the rights and dignity of patients and research subjects and that the "burdens" reduced are in fact "unnecessary." We note that reaction to the DHHS ANPRM has been mixed, with some research institutions finding the proposals impractical, and we see with dismay that many of the comments that favor the proposed changes seek only convenience and freedom from regulation.

Some of the responses to the DHHS ANPRM, especially from behavioral and social science, contend that protection of human subjects of research restricts academic freedom. These are not separable concerns, in view of increasing interest in conjoining behavioral, genetic, and neural science and technology. We remind you of the legal and ethical adage that one's freedom to swing a fist ordinarily ends where another's nose begins.

CIRCARE RESPONSE TO QUESTIONS IN OSTP RFI:

*"(13) What specific regulations are unnecessarily slowing or preventing "bioinnovation?"*

*"Please cite evidence that the identified regulation(s) are a) slowing innovation, and b) could be reformed or streamlined while protecting public health, safety, and the environment."*

We commend OSTP for insistence that evidence of regulations' having slowed "bioinnovation" be specific. Although the human subjects regulations have been termed complex and overprotective and an unnecessary "regulatory barrier" or "regulatory burden," we have seen no evidence to support those assertions. To the contrary, we see a continuing need for effective regulation to protect research subjects and patients. See Howard Brody, *The Future of Bioethics* (Oxford University Press 2009).

The project launch delays that we have seen in human subjects research were attributable largely to institutional procedures unrelated to regulatory responsibilities; to Institutional Review Board concerns that sponsor demands were insufficiently protective; and to investigator failure to meet even minimal requirements for human subjects protection.

Where we have seen delays in mounting multi-site studies, the delays have been attributable to failure of one or more IRB's to spot a critical ethical problem.

On the other hand, we have seen the necessity for pulling back newly developed FDA-regulated articles because information material to FDA decision

and patient protection had been withheld. We have seen delays in marketing of needed FDA-regulated articles because of laxity in manufacturing practices and failure to assure safety and quality of chemical feedstocks.

Delay attributable to protection of human subjects will be minimized by strengthening the legal and technical direct-hire staffing of the DHHS Office for Human Research Protections and FDA; by fostering agency willingness and capacity to issue clear regulatory guidance, to audit, and to enforce; and by making the regulatory environment more stable, predictable, and effective.

Centralizing the IRB system, as some critics urge, would destroy a relatively simple system of audited institutional self-regulation, it would minimize the role of local knowledge in ascertaining vulnerability of individuals who might be research subjects, and it would lead to a tremendously complex system of voluminous, time-consuming information exchange for which there are no foreseeable federal resources.

*(14) What specific steps can Federal agencies take to improve the predictability and transparency of the regulatory system? (Please specify the relevant agency.)*

Department of Health and Human Services:

> Retain the Common Rule and its FDA implementation without amendment, and use agency notice-and-comment guidance to deal with questions of interpretation. Changing the system would render the current, easily understood system less stable and less predictable and thereby lead to unnecessary delay, perhaps exacerbated if the Congressional Review Act comes into play.

Food and Drug Administration and
Office for Human Research Protections:

> Minimize inconsistency and increase quality and predictability of IRB outcomes and credibility and trustworthiness of IRB processes and human subject protections by requiring that IRB decisions be reasoned decisions on the record, redacted only for trade secrets, and that they be timely published—electronically and searchable.
>
> Audit the provenance of biospecimens in OHRP-overseen research, in order to ensure that (a) these materials have been obtained in compliance with the letter and spirit of human subjects protection requirements, (b) associated genomic and other donor data are credible, and (c) these materials have not moved through a black market in human tissues.

Food and Drug Administration,

Office for Human Research Protections, and
National Institutes of Health:

In order to enhance subject protection, cut unnecessary delays in worthy product development, and cut the time spent on activities apparently leading to failure: Clarify the duties of data and safety monitoring entities to emphasize that subject safety is the paramount consideration, and require these entities to report their basic reasons, not merely there conclusions, in their recommendations to stop or suspend trials or to continue trials as open-label and cross-over.

Office for Human Research Protections:

Education and training:

Reorient internal and external training programs and materials to recognize that the Common Rule itself recognizes that it is not the only applicable law and that IRB's must take into account all relevant law. The current focus is misleading and narrow, dealing almost exclusively with the Common Rule.

Reorient internal and external training programs toward the goal of legislative and regulatory intent, expressed in the Belmont Report and in statute, of protection of the rights of research subjects. The current focus is misleadingly on compliance minima irrespective of project and research population.

Train institutional officials and trustees on obligations under assurances.

Enforcement:

Strengthen OHRP direct-hire enforcement capacity, especially with qualified legal talent, to improve the agency's regulatory credibility, consistency, and predictability.

Audit compliance with U.S. and foreign institutional assurances, to improve the agency's regulatory credibility consistency, and predictability. Use direct-hire staff for this purpose.

Timely web-publish warning and enforcement actions, for easy searching, so as to foster compliance and predictability in the system.

Take seriously the applicability of international law, under which

> the United States also has obligations for its activities at home and abroad, and foreign law where U.S. researchers and research entities are involved. OHRP's website publishes a useful, if inevitably incomplete and non-authoritative, compilation in this regard. But OHRP, research institutions, and even many in the research bioethics community seem not to accord that law any significance.

Office of Information and Regulatory Affairs, and
Office of Science and Technology Policy:

> Ensure that regulatory development and interagency proceedings, including harmonization of agency guidance to the extent practicable and desireable for human subjects protection be public and on the record, with all ex parte contacts made public also in a timely and readily accessible way.

*(15) What specific improvements in the regulatory processes for drugs, diagnostics, medical devices, and agricultural biotechnology should federal agencies implement? What challenges do new or emerging technologies pose to the existing regulatory structure and what can agencies do to address those challenges?*

Office of Science and Technology Policy:

> Biomedical research and development and the biotechnology, biomedical, pharmaceutical, and research instrument industries are transnational. Whether here or abroad, medical development can be hindered or fostered by patent law and practice. Privacy law differs substantially, relevant European law being more protective generally than that of the United States. Law and practice regarding product safety differ substantially from country to country. We urge that as these issues are reviewed the rights of patients and research subjects and the safety of products and practices be considered paramount.

*Responders are free to address any or all the above items, as well as provide additional information that they think is relevant to the development of a National Bioeconomy Blueprint.*

As we state above, OHRP and FDA both need strengthened direct-hire legal and technical resources for enforcement (OHRP as to whether human subjects protection requirements are met for federally supported research, andFDA as to whether a broader array of requirements are met for research in support of applications for indications).

We will be pleased to be of further assistance.

Sincerely,

For Citizens for Responsible Care and Research:

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