

**Academic Researchers; Medical/Clinical Practitioners; Researchers/Practitioners –
Preliminary Findings from a Review of Responses to the Common Rule NPRM**

Overview

Approximately 400 researchers and practitioners responded. The majority of those commenting were engaged in research. We reviewed responses to a number of key proposals including proposals specific to biospecimens, mandated use of a single IRB for multisite studies, extending the Common Rule to all clinical trials, proposed data security safeguards and the proposal to post clinical trial consent forms to a federal website. Most comments focused entirely on the issue of biospecimens. However, a number of pathologists responding using a form letter provided by a professional association also addressed the areas of mandated single IRB and security safeguards.

Biospecimens (94% oppose, 6% support)

We reviewed three major proposals specific to biospecimens including the proposal to change the definition of “human subject” to include non-identified biospecimens, to mandate broad consent for secondary research use of biospecimens and to restrict IRB waiver of consent for secondary research use of biospecimens. Sixty-nine percent (276 of 401) of responses included comments on biospecimens. Of those, 94% (260 of 276) of researchers and practitioners commenting opposed one or more of the proposed changes and 6% (16 of 276) supported the changes, one response with qualifiers. Those opposed to the proposed changes to the treatment of biospecimens were researchers and physicians who conduct research. This group cited the substantial negative impact on research and human health that would result from the change, the prohibitive logistics and cost, and an imbalance of the Belmont Principles.

“We are at a time in history when we have the technology to begin to answer some of the fundamental questions regarding human disease, and when we can start to truly trial targeted disease-specific therapies. Unfortunately, the current anti-scientific atmosphere, and the near pathologic need for privacy, is stifling medical research. Recently, medical researchers started relying on unidentified clinical samples to generate data. Samples that otherwise would just go into an incinerator are being used to test hypotheses and answer clinical and scientific questions. The stated change in the Federal Policy for the Protection of Human Subjects would put a halt to innovation, and would benefit no one. Please make it easier, not harder, for physician scientists such as myself to understand, diagnose and treat disease.”

“I have been studying the ethical and legal issues surrounding the use of biospecimens and data for research for many years, combining an array of empirical and normative approaches. While I endorse your recommendation that IRB oversight be required for return of individual research results, I believe that many aspects of the proposed rule regarding biospecimens are fundamentally flawed in ways that disserve individuals, society, and research.”

Definition of “Human Subject” (94% oppose, 5% support, 1% supports with qualifiers)

Sixty-two percent (248 of 401) of responses included comments on the proposal to expand the definition of “human subject” to include non-identified biospecimens. Ninety-four percent (234 of 248) opposed the proposed change, 5% (12 of 248) supported it, and 1% (2 of 248) offered qualified support. Those opposed recommended no change to the definition, but 48 (12%) suggested that if a change were made they would prefer Alternative A – expanding the definition of “human subject” to include whole genome sequencing. Three expressed support for Alternative B if a change were made – classifying certain biospecimens used in particular technologies as meeting the criteria for “human subject.”

“I strongly urge reconsideration of the proposed inclusion of biospecimens as human subjects. In my research and in the vast majority of research undertaken by Pathologists, deidentified specimens are essential to furthering scientific knowledge that can be applied to advancing diagnostic accuracy, contributing to basic science principles and even to defining disease entities. These proposed regulations will grind Pathology research on clinical specimens to a halt. The wealth of personnel and IT resources that would be needed to comply with the proposed regulations would be prohibitive in virtually all academic medical institutions in today's economic climate. However, financial concerns should not be the major driver in this decision. I feel passionately that human subjects should be protected, even if there is a great financial or logistic cost. That being said, the emerging concept of every biospecimen being inherently identifiable, although accurate from the angle that biospecimens can be genetically sequenced, is in my opinion as a physician and a scientist, is inaccurate currently from the angle of what research is actually being done with the deidentified biospecimens and the feasibility of identifying individuals from any potential genetic information obtained.”

“The end result of this proposed change (in addition to a marked reduction in the number of samples available for research use) is that billions of dollars would no longer be available for conducting research. While not increasing the protection of human subjects (which we all agree is important), the proposed rule changes will slow research, slow medical diagnosis, and kill people because of significant and unnecessary delays it will impose on discovery.”

Broad Consent (67% oppose, 6% support, 27% support with qualifiers)

Forty-nine percent (196 of 401) of responses included comments on the proposal to require broad consent for future unspecified research use of biospecimens. Of these, 67% (131 of 196) opposed the proposed change, 6% (12 of 196) supported it and 27% (53 of 196) offered qualified support. Qualified support was offered by pathologists using a form letter provided by the American Society for Investigative Pathology (ASIP):

“If non-identified biospecimens are redefined as human subjects, we urge consideration of opt-out broad consent models for non-identified biospecimens collected in both research and non-research settings.”

Notice and opt-out were supported in 58 (14%) and 66 (16%) of responses respectively. Those opposed to the proposed changes suggested the changes would have a significant negative impact on science and public health and also highlighted the impracticability and cost.

“I would like to express my concerns with the proposed changes for biospecimens lacking identifiers. The changes proposed would require informed consent for the use of all biospecimens, even those that lack identifiers. De-identified specimens constitute an extremely valuable source of human specimens for our research community. The changes proposed will make clinical research much more difficult, and will excessively increase the regulatory and administrative burdens associated with research on biospecimens. There is a significant potential to inhibit discovery in these proposed changes, and to therefore adversely affect human health. The subjects who participate in our trials are not asking for this excessive regulation, and it does not provide meaningful protections, given that the specimens are already de-identified and that we are all already held to high ethical standards in the use of specimens for medical research. I anticipate that if enacted, this change will continue the decline in American leadership of cutting-edge clinical research, and force more meaningful studies to be done outside of the U.S.”

“In our laboratory we study aortic dissection, a devastating but rare sudden cardiovascular condition with a very high mortality. In research on less common disease, access to research samples from as many individuals as possible is needed. If informed consent as described in the NPRM is required the quality and timeliness of this research will be negatively affected, preventing some of this research from being conducted.”

Those in support of the changes were typically practitioners, some of whom may have submitted comments on the NPRM in response to an op-ed in the New York Times by Rebecca Skloot, author of the book *The Immortal Life of Henrietta Lacks*, but a small number identified as researchers. Ethical principles and patients’ rights were typically cited as well as identifiability and commercial gain or compensation.

“The proposed changes would justly require that left over biospecimens need to have been obtained with research informed consent before being used for research (to avoid for example repeating the problems with obtaining Henrietta Lacks' tumor cells known as HeLa) and broad consent would have to be given for unspecified future uses.”

“I am a physician and a potential patient and I strongly support the new regulations proposed to require consent of the donor before testing and research. I believe this will ultimately benefit the health science research community as well as protecting the rights of patients.”

“I am a medical researcher and feel obliged to comment on this. This proposed rule seems such a backward step in terms of humanity and medical research. This is lazy medical research. ‘Grab a bunch of cells removed without consent’ versus a well thought out project with ethics approval and consent of the cells' owner. Most people will consent to research, so why not ask? It is immoral to use someone's body parts (however small

and unwanted) without consent and it is not good science to work in and opportunistic and unplanned manner.”

Waiver of Consent (100% oppose)

Thirty-one percent (126 of 401) of responses addressed proposed restrictions to waiver of informed consent by an institutional review board, with 100% (126 of 126) opposed to the restrictions and no comments in support of the proposed changes.

“In the proposal, the NPRM retains four criteria used to justify a waiver of consent however, on close reading suggests that waivers should be issued in only rare circumstances. The logic of why only rare approvals should be made is not clear and the NPRM does not address this in the proposal. The NPRM suggests that these changes are in keeping with wishes of the American public. On the contrary, I would respectfully submit that the public would be upset if they know that this policy if enforced will eliminate key research that will benefit them and their families, by use of residual samples that would normally be discarded. This issues needs to be viewed under the right context-- in the setting where obtaining informed consent is not practicable-- we believe that patients would be willing to consent to use of residual sample when consent is impractical.”

Single IRB (14% oppose, 86% support)

Regarding the proposal to mandate use of a single IRB for all multi-site studies, of those providing comments (14% or 56 of 401), 14% (8 of 56) opposed the proposed mandate and 86% (48 of 56) supported it. Support was expressed primarily through form letters developed by ASIP with a handful of researchers independently expressing support – “I support mandatory single IRB review of all cooperative research and recommend that the single IRB of record also be charged with approving the protocol and the consent.”

Extending the Common Rule to All Clinical Trials (50% oppose, 50% support)

Two percent (8 of 401) of responses included comments on extending the Common Rule to all clinical trials **regardless of funding source at institutions that receive federal funding for non-exempt and non-excluded human subjects research.** Of these, four (50%) opposed the proposal and four offered support.

Security Safeguards (100% support)

Twelve percent (48 of 401) of responses included comments on proposed security safeguards, of which 100% (48 of 48) supported the proposal, support was again expressed primarily through an ASIP form letter – “I endorse the following proposals: Proposal to develop standards deemed sufficient to safeguard privacy in addition to those set forth in HIPAA.”

Posting Consent Forms (50% oppose, 50% support)

Regarding posting clinical trial consent forms to a public website (1% of responses), two of four opposed the proposed change and two supported it.

Overarching Concerns

Beyond analyzing responses to the particular NPRM elements elaborated above, we also looked at more general assessments of the status of the NPRM. Two percent (8 of 401) of comments indicated that the NPRM should not move to a final rule.

“The goals are not met, the rationale is poor, and the NPRM should be withdrawn.”

“I propose that there should be more thought put into this proposal that respects the comments from the research community before any changes are made.”

Additional Areas of Concern

A number of researchers commented on proposals not included in our review. In particular, researchers strongly opposed the proposal to remove research involving public officials from the exempt category and strongly supported the proposal to exclude oral history, journalism, biography and historical scholarship activities from the Common Rule.