

Members of the General Public – Preliminary Findings from a Review of Responses to the Common Rule NPRM

Overview

This category includes 906 responses from individual members of the public that did not claim an affiliation with any organization or that indicated they were writing as a citizen. We reviewed comments related to major proposed changes specific to biospecimens, mandated use of a single institutional review board (IRB) for multi-site studies, extending the Common Rule to all clinical trials conducted by entities receiving federal funds, standard security safeguards and posting clinical trial consent forms to a public federal website. Responses in this category predominantly addressed the proposed changes to biospecimens, but did address other areas we reviewed.

In a December 30, 2015, New York Times opinion piece, Rebecca Skloot, author of the book *The Immortal Life of Henrietta Lacks*, presented her views on proposed changes to how biospecimens are regulated. The op-ed provided a link to the proposed regulations and encouraged readers to respond. Hundreds did, guided only by what some perceive to be misinformation provided in the column. The views in that op-ed were countered in other publications including an opinion piece by Michelle Meyers, Assistant Professor and Director of Bioethics Policy in the Clarkson University-Icahn School of Medicine, in [Forbes](#) which suggested that the op-ed may serve to “miseducate” the public, and the Wall Street Journal opinion piece [How Not to End Cancer in Our Lifetimes](#), by Laurie Glimcher, Dean of Weill Cornell Medicine and Provost for Medical Affairs of Cornell University. In addition to the full analysis, we reviewed the comments in two groups, pre- and post-publication of the Skloot op-ed. Approximately 215 comments were submitted prior to the publication of the op-ed and 691 following publication.

Biospecimens (55% oppose, 45% support)

We reviewed three major proposals specific to biospecimens including the proposal to expand 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. Of the 906 responses in this category, 76% (692 of 906) commented on one or more of the proposed changes. Of these, 55% (382 of 692) opposed the proposed changes and 45% (310) supported them, 15 with qualifiers. Based on the timing and content of the submissions, support appears to have been largely in response to the opinion piece by Rebecca Skloot.

Of the 215 comments submitted prior to the publication of the Skloot op-ed (submitted between September 8 and December 29), 121 commented on the proposed changes to biospecimens with 77% (93 of 121) opposed to the proposed changes, 21% (26 of 121) in favor of them and 2% (2 of 121) offering qualified support. Of the 691 comments submitted following the Skloot op-ed (between December 30 and January 8), approximately 570 commented on the proposed changes related to biospecimens. The responses were nearly evenly divided with 51% (289 of 570)

expressing opposition to the proposed changes, 47% (269 of 570) support for the changes and 2% (13 of 570) offering qualified support.

These findings provide the overarching sentiment of the responses based on content related to expanding the definition, the use of broad consent and proposed restrictions to waiver of consent. For specific categories therein, responses either concretely indicated opposition or support for a proposed change or the response was inferred based on the content of the letter (e.g., there was not explicit endorsement of broad consent or opposition to proposed changes to the waiver criteria but it could be inferred based on the content of the comments). Unlike the cohort of the general public identifying as patients and their relatives, this group focused on proposed changes to the regulations broadly and broad consent for biospecimens to a much greater extent than proposed restrictions to waiver.

Definition of “Human Subject” (61% oppose, 36% support, 3% support with qualifiers)

Sixty-three percent of responses (568 of 906) included comments on the proposal to expand the definition of “human subject” to include non-identified biospecimens. Of these, 61% (347 of 568) opposed the proposed change, 36% (206 of 568) supported it, and 3% (15 of 568) offered qualified support. Among those recommending no change, 189 suggested that if a change were made they would prefer Alternative A – expanding the definition of “human subject” to include whole genome sequencing. Many included the following comment, often verbatim:

“Due to concerns about the impact on medical care of the proposed changes regarding research on biospecimens, I would prefer that no changes be made in the current protections for residual biospecimens collected for routine care. However, if this is not possible, I support the Alternative Proposal A that would narrow the scope of the new consent requirements to only biospecimen research that generates whole-genome sequence data, rather than all biospecimen research.”

Of the 215 comments on this proposed change submitted prior to the NY Times opinion piece, approximately 80% opposed the proposed change and 20% supported it. Of the 691 comments submitted after the publication of the op-ed, approximately 57% opposed the proposed change, 40% indicated support and 3% indicated qualified support. Per those opposed:

"This will be devastating bureaucracy, and I don't see how it furthers patient privacy. It will hinder innovation and slows down research in a major way."

“This would set back human subjects research substantially and delay or prevent the acquisition of life-saving knowledge.”

“I am employed at the US Army Medical Research Institute of Infectious Diseases...but my comments and position are my own. I am concerned that the NPRM would result in a loss of the research data essential for developing medical countermeasures of tomorrow, resulting in a chilling effect on the advancement of biomedical science adding no added protections of patients. I feel strongly that the current rule exempting anonymous or de-identified specimens from human research protections is reasonable and should be

maintained. Scientific research conducted on de-identified specimens has produced major medical breakthroughs without increasing risk to the biospecimens' donors.”

“HHS needs to carefully reconsider this proposal. At a time when research is scraping along, we should not add far-reaching obstructions. Let's balance harm vs possible benefits to society.”

And those in support:

“I feel quite passionately on this matter and am bordering on outraged that I have seen nothing about this in my daily newspaper, my various doctors' offices, etc. I suspect there is a wish that the public remain ignorant about this for fear that we will demand protections that would inconvenience researchers who would rather not be bothered, and that makes me even angrier. Be assured that I will be contacting my senators and representatives to demand greater legal protection in this matter.”

“I want control over my own tissues, thank you.”

Broad Consent (53% oppose, 32% support, 15% support with qualifiers)

Sixty-two percent of responses (562 of 906) included comments on the proposal to mandate broad consent for secondary research use of biospecimens. Of these, 53% (296 of 562) opposed the proposal, 32% (183 of 296) supported it and 15% (83 of 296) offered qualified support. Thirteen comments suggested notice as an alternative to broad consent and 29 suggested opt-out as an alternative to having to opt-in to research use of biospecimens.

Of the 215 comments on this proposed change submitted prior to the NY Times opinion piece, approximately 81% opposed the proposal, 10% supported it and 9% offered qualified support. Of the 691 comments submitted after the publication of the op-ed, approximately 48% opposed the proposed requirement, 36% supported it and 16% offered qualified support. Of those offering qualified support, approximately 70 wanted specific, rather than broad, consent. Many indicated this through a prepared statement commenting on parental consent for research use of newborn DNA.

Those opposed to the proposed change cited the substantial negative impact on research and human health and the prohibitive logistics and cost and suggested that broad consent would not provide meaningful information. Some were concerned about an imbalance of the Belmont Principles, in particular autonomy versus justice and the possible exclusion of underrepresented groups, and noted the additional privacy risk associated with tracking consent.

“The harm of denying patients cancer therapy [is] more probable than the potential harms associated with unconsented use of these tissues.”

“As a citizen, I would be happy to know that some part of me I no longer needed or wanted was being used to further promote knowledge.”

“I see no problem whatsoever in the anonymous use of cells for medical research, where the cells are obtained as a byproduct of normal medical care. Instituting procedures of informed consent here would only make the medical system yet more cumbersome than it already is. The harms of not obtaining such consent are minuscule (I would say they are zero); the costs of doing so in terms of lives (and also dollars uselessly spent) are very high. There is a clear cut case for not changing the status quo on this issue.”

“The only answer I have for the rather breathless and panic-inducing question [a question asked by Rebecca Skloot in her op-ed] - "Did you know that any cells or tissues you leave behind in the process are fair game for scientists to use in their research without asking you and without getting your permission first?" - is "YES", and yes, I am okay with giving away my cells unasked, for the purpose of medical research - which potentially benefits billions of living beings, including humans, with whom I share the planet. I am all for transparency in the process of medical research and clinical trials. Current policies have already put in place important safeguards regarding health data privacy. But if further byzantine restrictions are applied to research with any and every material derived from human subjects, it will only impact medical research negatively - and that does not bode well for us or the future generations. The concerns raised about a possible re-identification of de-identified data can surely be assuaged by focal regulations prohibiting this sort of endeavor - for which it would be hard, as it is, to fathom a legitimate medical purpose.”

“I would strongly prefer that no changes be made in the current rules regarding research on tissue collected for routine care. So long as the patients are not identified in the report there is no privacy violation at all. This will impose a significant burden on people attempting to understand diseases such as cancer. Patients are harmed when our ability to make advances is impaired. The harm to these patients is real. The threat to the privacy of others is not real.”

“As a layperson, I am strongly opposed to the proposed rule. Once tissue, cells, tumors, etc. are removed from a person's body, a person no longer has any need of them or rights to them. Having read Rebecca Skloot's fascinating book "The Immortal Life of Henrietta Lacks," and having myself lost two parents to cancer, I sympathize and empathize with the plight of patients who lose loved ones, but this does not detract from the fact that tissue, cells, tumors, or any other removed parts of a person are no longer part of that person. It is more accurate to consider them medical waste. If said medical waste can be used in research to increase medical knowledge and/or improve the lives of others in any way, I am all for it.”

Some noted that the cost and infrastructure required for broad consent would be prohibitive, severely restricting future biospecimen collection and research.

“Given the enormous number of samples that are collected, and the extremely small percentage of these that ever are used in a research context, this proposed requirement is inefficient to the extreme. Table 2 in the NPRM shows that the costs just for obtaining consent to secondary use of biospecimens and identifiable private information are over

\$12 billion out of the total of \$13 billion for all NPRM-proposed changes. Using the NPRM figures, removing this one requirement from the NPRM proposals would save over 90% of implementation expense. It gets worse; however, because the NPRM Regulatory Impact Analysis asserts that broad consent would be required for only a half (15 million) of the 30 million individuals who are estimated to provide research and clinical biospecimens each year (1999 data), while in practice, broad consent would need to be obtained from most individuals, not just those identified as research participants. Thus, the cost of obtaining this documentation is underestimated and could as much as double (\$18-\$24 billion) resulting in 95-96% of the NPRM proposals' implementation expense.”

“The proposed rule would have significant detrimental impact. Many of the biologic materials impacted, such as blood, urine, and body fluids, are obtained in the course of general medical care and no specific consent is obtained for their procurement. It is unlikely that providers who collect the specimens would be willing to bear the cost of obtaining additional consent from their patients. In most systems there is no current mechanism to link the consents obtained in the patient care setting with specimens in a laboratory, nor is there any proposed funding to cover such costs. Many of the studies that would be impacted by the proposed rule will never be done if the proposal is implemented as drafted.”

“There has been a significant underestimation of the cost of including non-identified biospecimens under human subjects regulations and the consequent requirement for informed consent. The likely dramatic cost increase may substantially decrease access to specimens, particularly those from minority, rural, and underrepresented populations.”

Those in favor of the proposed change tended to cite ethical principles while some indicated concern about identifiability. Those offering qualified support generally expressed the desire for specific, not broad consent. Of those in support of the proposed changes and of broad consent, approximately 25 explicitly mention the Rebecca Skloot article, quoted the text or mentioned Henrietta Lacks.

“Please allow ME to decide if I wish to have my tissues made available for research or not. It is the polite and moral thing to do.”

“I strongly agree with these proposed changes. I feel that the old laws were put in place before modern technologies made reverse identifying of "anonymous" specimens possible. I also believe that many if not most subjects will be willing to allow their cells to be used and that it will be fairly straight forward to administer consent forms to subjects. Therefore, it should not hinder research. As a private citizen and layperson I feel that it is my right to know how the cellular material collected from me and from my young children will be used. The world is awakening to the necessity for regulation of the use of personal information in all regards and it would be wise for the United States to be current in its policies in order to protect its citizens.”

“I want people to inform me if they are using my tissues for research or other purposes. Those are MY cells.”

“I mean a written release that is signed and dated by the person in which it is clearly stated what material [is] going to be harvested and or used and describing each and every possible use therefor [of] and providing for additional notice to the individual or their designee should any permitted research result in the creation or development or [of] a for profit treatment, drug or other patentable item or procedure.”

“Until I heard about this proposed regulation, I had no idea that my "spare parts" could be used for research without my prior consent. I think it's about time that problem is fixed.”

“The current practice of using human tissue without consent is no different from the grave robbing performed on behalf of medical schools in the early 1800s (as recorded in Dickens's A Tale of Two Cities).”

“I believe that the consent document should be very specific. The consent form should indicate what research and studies the samples may be used for, how the samples will be used, the duration of the use of samples, along with where and how information derived from the samples will be published.”

“I believe consent should be obtained for all research done with human tissue, fluids, or DNA. It erodes the trust the general public has in the medical and scientific communities to perform research without a person's consent, and violates their privacy. Many people would be happy to donate their genetic material for research but they have a right to know what it's used for, as well as to find out what was learned from it, should they desire.”

Some expressed general concern over what might become of their biospecimens, including concerns about activities that are not legal such as human cloning or the very unusual circumstances surrounding the Henrietta Lacks case:

“I could not imagine how awful it would be if a clone or other unnatural thing was created with my tissue.”

Of those in support of the proposed changes, 62 expressed concern about scientists and corporations profiting from the use of their specimens and/or the desire to be compensated in the wake of any profit or to be compensated generally.

“I find the common rule appalling that scientists can profit from an individual's body without notice and without permission.”

“Yes, consent should be required. And compensation, too.”

“I support the proposed changes. If I were a patient whose tissues were donated, distributed, sold or marketed for research without my knowledge, I would mind it very

much. In the event that research on my biospecimen resulted in a commercial benefit to an individual, institution, corporation including pharmaceutical industry and academic institutions, I would like to be compensated and recognized for my contribution, and the same for my descendants if I am not alive anymore.”

Waiver of Consent (58% oppose, 42% support)

Thirteen percent of responses (115 of 906) included comments on the proposal to restrict IRB waiver of consent. Of these, 58% (67 of 115) opposed the proposed change and 42% (48 of 115) supported it. Support for the proposed restrictions resulted from use of a generic statement related to parental consent for research use of newborn bloodspots by the 48 respondents commenting on this proposal:

“Do not undo the parent consent requirement for federally-funded or any other research use or storage of newborn DNA. I also want informed written consent for every researcher access to and use of my and my family's medical records, DNA, blood and other biospecimens. No exceptions. No exclusions. No waivers. These are our rights and the federal government has no business invading our privacy.”

Those opposed expressed concern about the ability to cure cancer and other disease, in particular rare diseases. Many expressed concern about the significant loss of biospecimens going forward and the loss of archived specimens due to proposed restrictions to the current waiver criteria coupled with the consequent need to re-consent.

“The proposed changes would make a retrospective study on cancer or anything else basically impossible. This means we would lose opportunities for research and changing medicine for a better future.”

“At present, previously collected de-identified biospecimens (which are to otherwise be discarded) are considered IRB-exempt (Category 4). The proposed rule change would effectively disallow such research. Placing such research under IRB oversight is reasonable, but disallowing such research by requiring a priori informed consent would effectively abruptly halt all such research, which is often conducted for public health purposes. For example, if one wanted to retrospectively test serum samples collected by CDC among immigrating refugees to the U.S. for XYZ disease conditions of public health importance, such as the sero-status for: HIV, hepatitis A/B/C, measles, mumps, rubella, etc. this would be disallowed. This is bad public policy which would diminish improving the health of Americans.”

“I oppose. Without the ability for open tissue studies rare diseases will never be cured. The scientist[s] need better access.”

“I think this new policy will have a severe negative impact on generating new understanding of human disease. It is a reactive policy to address the concerns of a very small minority of persons, as the majority of the society agrees that it is best to increase knowledge than let valuable tissues get old in shelves with no use. As long as the

research is sound and there are adequate policies in place to protect the identity of subjects, there should be no major impediment to perform retrospective analyses in banked patient-derived samples.”

“Patients with the most intractable diseases and difficult to treat cancers would be affected the most. There are definite ways to safeguard confidentiality and achieve protection of human subjects without having to basically (that is what it amounts to) throw away archival specimens that did not have an initial consent from the patient. These safeguards can be developed and implemented easily. The Institutional Review Board can then supervise the implementation and, if necessary, with government oversight and/or random auditing. But, I strongly caution the government not to make, what I think, is a tremendous error that would be very costly to drug development, patient care, and the elimination of the disease burden in our nation.”

Single IRB (52% oppose, 48% support)

Three percent of responses (25 of 906) included comments on the proposal to mandate use of a single IRB for multisite studies, 52% of those commenting (13 of 25) opposed the proposed change, 40% (10 of 25) supported it and 8% (2 of 25) offered qualified support. Those opposed suggested that there should not be a mandate without exploration of the alternatives and that it would increase the burden on the lead PI. One commenter stated that, “there is no overriding human subject protection reason for changing the regulations; there is no mission-related need for all the Common Rule agencies to subscribe to a single model for all multi-site studies.” A comment offering qualified support suggested that a single IRB should not be mandated until the “kinks are worked out” and another that “further thought and/or guidance needs to be provided regarding the details of how this is to be accomplished, without inadvertently making the process more cumbersome instead of less.”

A comment in support of the mandate nonetheless suggested that:

“depending on the nature of the study, there may already be collaborative agreements executed as part of the administrative workflow; however, for other studies, the execution of a collaborative agreement could produce more administrative burden and delays than submitting a human subjects application to the local IRB.”

Another noted that single IRB review is a realistic option at this time but that there would be “a cost associated with this for the attorneys of the institutions involved to develop appropriate agreements.”

Extending the Common Rule to All Clinical Trials

Six responses included comments on the proposal to extend 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. Four of the six indicated support and two were opposed, with one commenting that:

“...most clinical trial sites already review all human subject research through an IRB that operates under the FDA regulations and/or Common Rule regulations. The NPRM uses surgical trials, which are not FDA regulated, as examples of studies that would be enfolded into coverage. If these studies are conducted at FWA institutions, they are already voluntarily covered and if conducted at non-FWA facilities, they most likely would not be captured by an expansion because federal funding for any research is probably absent. Thus, there seems to be a fairly limited effect and less than a strong impetus for adding this requirement to the common rule.”

Posting Consent Forms

Regarding posting clinical trial consent forms to a public federal website, seven opposed the proposed change and two responses supported it. One comment suggested that “while noble, this goal may not better inform the public.” One response opposed proposed security safeguards.

Overarching Concerns

Of the 906 comments in this category, 21 suggested that the Common Rule should be revised or rewritten in some way and should not move to a final rule. Comments suggested that there are “serious deficiencies in the proposal” and that it should be “scrapped”; that it “highlights the need for additional public discussion regarding its implications”; “may take several more iterations”; that it would be “premature to adopt a new set of regulations based on the current NPRM”; that “efforts to finalize the NPRM as currently written should not move forward”; and that “the common rule should not be changed at this point because the NPRM itself is a very risky experiment.” One response suggested that “Instead of making one, sweeping revision to the regulations and rushing it's finalization prior to the next presidential election...changes [should] be made incrementally on an ‘as needed’ basis” and “allow for consideration to be made on each issue with evidence to support the appropriate action.” It was suggested that OHRP be far more transparent in the development of the next iteration, not work in secrecy and not ignore all sources of suggestion such as those of SACHRP. One response urged HHS to develop “a second NPRM, or a series of shorter NPRMs with specifics, not questions and no undeveloped promises.” “It is important to not rush this and to get it right. Please adopt a more deliberative approach with ongoing feedback and refinement and then propose a simplified rule.”