



## **Comments on Proposed Rulemaking Regarding Federal Policy for Protection of Human Subjects**

**HHS–OPHS–2015–0008**

*Submitted by the International Pharmaceutical Privacy Consortium*

**January 6, 2015**

These comments are submitted on behalf of the International Pharmaceutical Privacy Consortium (the “IPPC”). The IPPC was formed in 2002, and is comprised of chief privacy officers and other data privacy and security professionals from a number of research-based, global pharmaceutical companies. The IPPC seeks to advance innovative privacy solutions to protect patients, enhance healthcare, and support business enablement. Additional information about the IPPC, including a list of its members, can be found at the conclusion of these comments or at [www.pharmaprivacy.org](http://www.pharmaprivacy.org). The IPPC thanks HHS for the opportunity to comment on the proposed changes to the federal regulations governing studies with human subjects found in the Notice of Proposed Rulemaking published at 60 Fed. Reg. 53933 on September 8, 2015 (“the NPRM”). The IPPC previously submitted comments on the Advanced Notice of Proposed Rulemaking on this subject released in 2011.

IPPC members sponsor clinical research to support applications to market new drugs. This research is subject to the Food and Drug Administration regulations governing protection of human subjects. Although such research is not directly within the Common Rule’s scope, the IPPC understands that the FDA intends to harmonize its requirements with those included in the Common Rule. IPPC members also regularly sponsor research at institutions that receive federal funding for research, which, under the standard proposed in the NPRM, would bring all research at that institution within the scope of the Common Rule. Accordingly, much of the research sponsored by IPPC members is or will become subject to the revised Common Rule, or to FDA regulations which may be harmonized with the Common Rule.

In our 2011 comments on the ANPRM, we indicated that the IPPC supports continuing efforts to align FDA requirements and the Common Rule. Consistent standards allow for greater efficiency in planning multi-site research studies and help ensure that patient data and information will be protected in the same fashion, regardless of whether the research activity falls within the scope of the FDA’s regulations or the Common Rule. The IPPC also applauds HHS’s proposed exclusion of “research” activities undertaken by a covered entity from the scope of the Common Rule. As the NPRM correctly notes, such research is already subject to “independent controls provided by HIPAA.” The IPPC also wishes to express its support for the NPRM’s categorization of secondary research with identified private information and identified biospecimens as an “exempt” category of research and the NPRM’s recognition that “broad” consent to future research with identified private information and identified biospecimens provides appropriate protections and safeguards for research subjects.



However, the IPPC notes that HHS has not standardized the treatment of “non-identified” or “de-identified” information and specimens across the Common Rule and HIPAA. We believe that the HIPAA Privacy Rule correctly recognizes that use of appropriately de-identified information or specimens poses little risk to patients and data subjects, and permits this data to be transferred or disclosed without additional restriction. This facilitates epidemiological and health outcomes research vital to monitoring the safety and efficacy of medicines, improving treatment regimes, and understanding emerging public health challenges. Although the Common Rule would treat most research with de-identified information as falling outside the scope of the Common Rule, it takes the opposite position with respect to biological specimens.

Accordingly, the IPPC wishes to focus its comments on this important issue and the question posed in the Common Rule: “Which of the three proposals regarding the definition of human subject achieves the most reasonable tradeoff between the principles of autonomy (including transparency and level of trust) versus beneficence (as measured by facilitating valuable research)?”.<sup>1</sup> The IPPC believes that none of the proposals in the Common Rule strike this balance appropriately, and urges HHS to conduct a more rigorous evaluation of the public’s attitudes on research with de-identified biospecimens than it has done. The four studies cited in the Common Rule and HHS’s sense of the wishes of the majority of individual commenters on the ANPRM do not form an adequate basis for such a sweeping change in the research and development process that produces cures and treatments for the diseases that affect US citizens.

1) *HHS has not established that patient “autonomy” would be well served by requiring broad consent for research with de-identified biospecimens.*

HHS begins its exploration of the “autonomy” interests of patients by noting that allowing “secondary research with biospecimens collected without consent for research . . . is not consistent with the majority of the public’s wishes, which reflect legitimate autonomy interests.”<sup>2</sup> This remarkable statement has no citation, and can be understood only by reference to an earlier portion of the NPRM, which cites four studies on patient attitudes towards research with biospecimens.<sup>3</sup> At best, however, these studies provide limited support for HHS’s position. None of the studies purport to have captured a nation-wide snapshot of the public’s attitudes on research with de-identified biospecimens (one study, in fact, measured only attitudes of patients at one hospital in the Netherlands). If anything, the studies emphasize the need for further research in this area. All four studies contain some version of the statement that there are “very few published studies comparing the effects of informed consent procedures.”<sup>4</sup>

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<sup>1</sup> The NPRM, 80 Fed. Reg. at 53946.

<sup>2</sup> The NPRM, 80 Fed. Reg. at 53944.

<sup>3</sup> The NPRM, 80 Fed. Reg. at 53938, fn 5-8.

<sup>4</sup> Vermeulen E. et al. A trial of consent procedures for future research with clinically derived biological samples. *British Journal of Cancer*, 2009 Nov 3;101 (9): 1505-1512;1505; *See also* Simon CM et. al. Active choice but not too active: Public perspectives on biobank consent models. *Genetics in Medicine*. 2011 Sep; 13(9): 821-831; 825 (“Several key studies of US and Canadian public attitudes and preferences toward bio-bank consent models have been conducted; however no clear consent choice is evident in most of these studies”); Trinidad SB et al. Research practice and participant preferences: The growing gulf. *Science* 2011 Jan 21; 331(6015):287-288; 288 (“For example, over 90% of respondents in a national US survey would be willing to have their samples and health data



To the extent these studies support any conclusions about the public's attitudes towards biomedical research, however, they uniformly indicate that the vast majority of patients and people would be happy to participate in biomedical research. In studies that looked at *actual* consent rates, the studies found overwhelmingly that patients were happy to have their samples used for future research or stored in a biobank: 99% of participants in the Vermeulen E. et al. study consented; 86% of the individuals surveyed in Trinidad SB et al. study consented.<sup>5</sup> To be sure, the studies at issue all indicate a preference for some information about possible future research, and a stated preference for the opportunity to provide consent. But across all four cited studies, a clear theme emerges: few patients actually object to the use of their biospecimens for medical research, even when given the chance.

The reasons given by members of the public for seeking the opportunity to provide consent further illuminate the shortcomings in HHS's research into public attitudes around de-identified biospecimens. Across all four studies, the most commonly expressed concern about research related to the privacy protections in place to safeguard participant data. However, it is not clear that all studies asked participants to differentiate their concerns between identified biospecimens and de- or non-identified biospecimens. Where the distinction was made clear, it seems that participants favored broad participation in the study and wide access to data. In the Vermeulen E. et al. study, where the anonymous nature of the biobank was clearly explained, 99% of participants consented to use of their information.<sup>6</sup> And in the Kaufman DJ et al. study, 53% of men and 45% of women suggested that, if de-identified, their information could be made "available on the internet to anyone."<sup>7</sup> Neither of remaining studies appear to have directly asked patients to express their preferences regarding consent to use de-identified biospecimens in future research.

The IPPC feels that these studies indicate, at most, a preference among some members of the public to understand how their medical information could be used in future research and a real concern about privacy. However, they do not indicate that the public, as a whole, *actually* objects to the use of biospecimens, as HHS suggests, or that the privacy concerns expressed by patients cannot be mitigated through other appropriate measures.

*2) The HHS's informed, broad consent requirement for use of de-identified biospecimens does not address the actual concerns of patients or create a substantive increase in patient privacy.*

Although patient privacy concerns are real, HHS has long recognized that the risks to patients stemming from the use of de-identified data are low and outweighed by the benefits

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placed in a biobank for research. However, views on consent were mixed: 48% preferred one-time, "blanket" consent, while 42% wanted the opportunity to re-consent for each use of their data."); Kaufman DJ. et al. Public opinion about the importance of privacy in biobank research. *American Journal of Human Genetics* 2009 Nov; 85(5); 643-654, 644 ("A small number of studies have examined privacy concerns related to participation in genetic research that would collect, analyze, and store participant's DNA samples.")

<sup>5</sup> The remaining studies (Kaufman DJ et al., and Simon CM et. al.) dealt only with the attitudes of focus group participants.

<sup>6</sup> Vermeulen E. et al., at 1509.

<sup>7</sup> Kaufman DJ, et al., at 648.



associated with research and development of new treatments and cures. Indeed, even in the NPRM, HHS continues to treat de-identified information as outside the scope of the Common Rule. This creates an illogical dichotomy between the treatment of biospecimens and data. If de-identified data poses limited risks to data subjects, such that consent to its use is not required, why does research with de-identified biospecimens, the result of which would be the creation of de-identified data, merit separate treatment?

HHS does not clearly address this question in the NPRM, and instead refers vaguely to unresolved debates around whether “certain analytic results (e.g. decoding the whole genome) should be considered to yield identifiable data.”<sup>8</sup> Although the NPRM purports not to resolve those debates, the only logical basis for the divergent treatment of biospecimens and data would be a belief that all biospecimens are, by the nature of the genetic or other material contained therein, inherently (rather than potentially) identifiable – a belief for which HHS provides no evidentiary or experiential support, and one it characterizes as the subject of unresolved debate.

However, the NPRM points to no evidence suggesting that the re-identification of appropriately de-identified biospecimens through genomic sequencing or other analysis is either a current possibility or a likely future one. Notably, if the subject’s name and other information is not associated with the biospecimen, the only way to re-identify a de-identified or discarded biospecimen would be to compare an analytical result derived from testing on that biospecimen to an identified database of analytical results. In other words, to harm any human subject via the re-identification of a biospecimen, a would-be wrongdoer would *already* need to be in possession of that subject’s identified medical information or genomic data. Then, to inflict harm on the data subject (above and beyond any harm that could be inflicted by merely possessing identified medical and genomic information), the would-be wrongdoer would then need to (1) conduct or locate an analysis of the tissue sample that produced a result, (2) match that result to a result already in the wrongdoer’s possession and (3) run an additional analysis on the biospecimen to learn new information not already in the wrongdoer’s possession. HHS presents no evidence indicating that such a complicated and resource-intensive process poses a real risk to patients. To be sure, the threat to identified patients and research participants from illegal cyberattack, while small, is not wholly illusory. The IPPC would contend, however, that this risk is addressed appropriately in other portions of the NPRM, like Section \_\_\_\_ .105, where proposed security standards for information and specimen storage are described. More to the point, however, requiring informed consent before permitting research with de-identified biospecimens does little to protect patients from this risk.

Nor does HHS satisfactorily explain why the NPRM’s proposed exemption for research and development of “certain tests and assays (such as research to develop a diagnostic test for a condition using specimens from individuals known to have the condition and those known not to have the condition), quality assurance and control activities, and proficiency testing,” complies with “the underlying ethical principles” that have caused HHS to single out de-identified biospecimens for new consent requirements. These exempted tests still require manipulation of biospecimens, the extraction of information from those specimens, and the storage of the same. HHS points to nothing in the limited studies underlying its proposed rule for biospecimens that

<sup>8</sup> The NPRM, 80 Fed. Reg. at 53944.



suggests that the public views these activities differently than it views research and development activities designed to extract “new” information from biospecimens. None of the studies cited by HHS even clearly differentiate between the category of activities HHS believes require the patient’s awareness and consent, and the categories of biospecimen research that HHS believes can be done without the patient’s knowledge. Although the IPPC supports the exemption for these activities and urges HHS to retain it, the IPPC’s position is grounded in its general support for privacy regulations that enable appropriate research, rather than in support for HHS’s artificially drawn distinction.

Last, the IPPC notes that HHS appears to have ignored the impact of other laws and regulations in the United States on the concerns voiced by patients in the few studies it cites. As one of the studies cited by HHS notes, its results were obtained:

“before the passage of the Genetic Information Nondiscrimination Act of 2008 (GINA), which prevents health insurers and employers from denying coverage, adjusting premiums, or otherwise discriminating on the basis of genetic information. With the passage and implementation of GINA, the risks and potential harms of misuse of genetic research will decrease.”<sup>9</sup>

It is not clear that HHS has considered the impact of GINA, HIPAA, or other state laws prohibiting the misuse of medical information in reaching its determination that patient consent to the future use of de-identified biospecimens is required to advance “legitimate” patient autonomy interests. At least some of HHS’s evidence for the existence of these autonomy interests is based on a historic patient concern about a now illegal practice.

### Conclusion

The practical burden of additional consent requirements should be clear to HHS. Implementing record collection and retention systems to document consent and verify that an appropriate consent exists for each sample will cost time and money. Ultimately, small health systems, including those serving rural or low income populations, may elect to avoid this expense. The potential loss of these biospecimens will have a negative impact on research into new cures and treatments.

The IPPC urges HHS to reconsider its approach to consent and research with de-identified biospecimens. The IPPC recommends that HHS specifically study attitudes on research with de-identified biospecimens among patients who have been informed about the legal framework that protects their genetic data from misuse. Existing and robust frameworks for protecting patient privacy already address the concerns voiced by patients in the few studies that HHS cites in support of its position. Rather than requiring a broad consent, which has little practical impact on the privacy concerns of patients, HHS should instead focus on facilitating the public’s clear support for, and desire to participate in, biomedical research.

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<sup>9</sup> Kaufman DJ et al. at 651.



## APPENDIX: INTERNATIONAL PHARMACEUTICAL PRIVACY CONSORTIUM

<b>MEMBERS</b>	Members of the IPPC include: <ul style="list-style-type: none"><li>◆ AbbVie</li><li>◆ Amgen</li><li>◆ Astellas Pharma</li><li>◆ Bristol-Myers Squibb</li><li>◆ Celgene</li><li>◆ Eli Lilly and Company</li><li>◆ GlaxoSmithKline</li><li>◆ Johnson &amp; Johnson</li><li>◆ Merck &amp; Co., Inc.</li><li>◆ Novartis</li><li>◆ Novo Nordisk</li><li>◆ Otsuka</li><li>◆ Pfizer Inc.</li><li>◆ Roche</li><li>◆ Sanofi</li><li>◆ Shire</li><li>◆ Takeda Pharmaceuticals</li></ul>
<b>VISION</b>	The vision of the International Pharmaceutical Privacy Consortium is to be the leading voice in the global bio-pharmaceutical industry to advance innovative privacy solutions to protect patients, enhance healthcare, and support business enablement.
<b>MISSION</b>	As an organization of pharmaceutical companies, the IPPC advances the protection of individual privacy, anticipates and responds to new challenges affecting the protection of health information, augments member companies' data protection capabilities through the development and sharing of industry best practices, educates internal and external stakeholders on data protection in the pharmaceutical industry and the importance of data to pharmaceutical innovation, and provides a forum to ensure that the global pharmaceutical industry speaks with one, coherent voice on data privacy issues.