Defining the ‘human subject’

Part 2 of MESM’s series on proposed federal research regulation amendments and the impacts on commericial sponsors and research organisations

Photography by Isy & Leigh Anderson

Introduction

In part one of this series, we gave a broad overview of the proposals and proposed timelines for changes to the Common Rule of HHS Regulation (45 CFR 46, Subpart A) and the Notice of Proposed Rule Making (NPRM).

This 519 page proposed rule is a complex and detailed document, and this series of articles seeks to examine the most important proposed changes and examine how the NPRM could affect organisations carrying out clinical trials if it progresses to 'Final Rule' in its current form.

In this article we examine the rationale behind the NPRM proposals and the detail of the proposed reclassification of biospecimens as a 'human subject', irrespective of whether the sample is identifiable or not.

Any industry sponsored research taking place at an institution that also carries out federally funded research will have to comply with the NPRM.

Why do these changes matter?

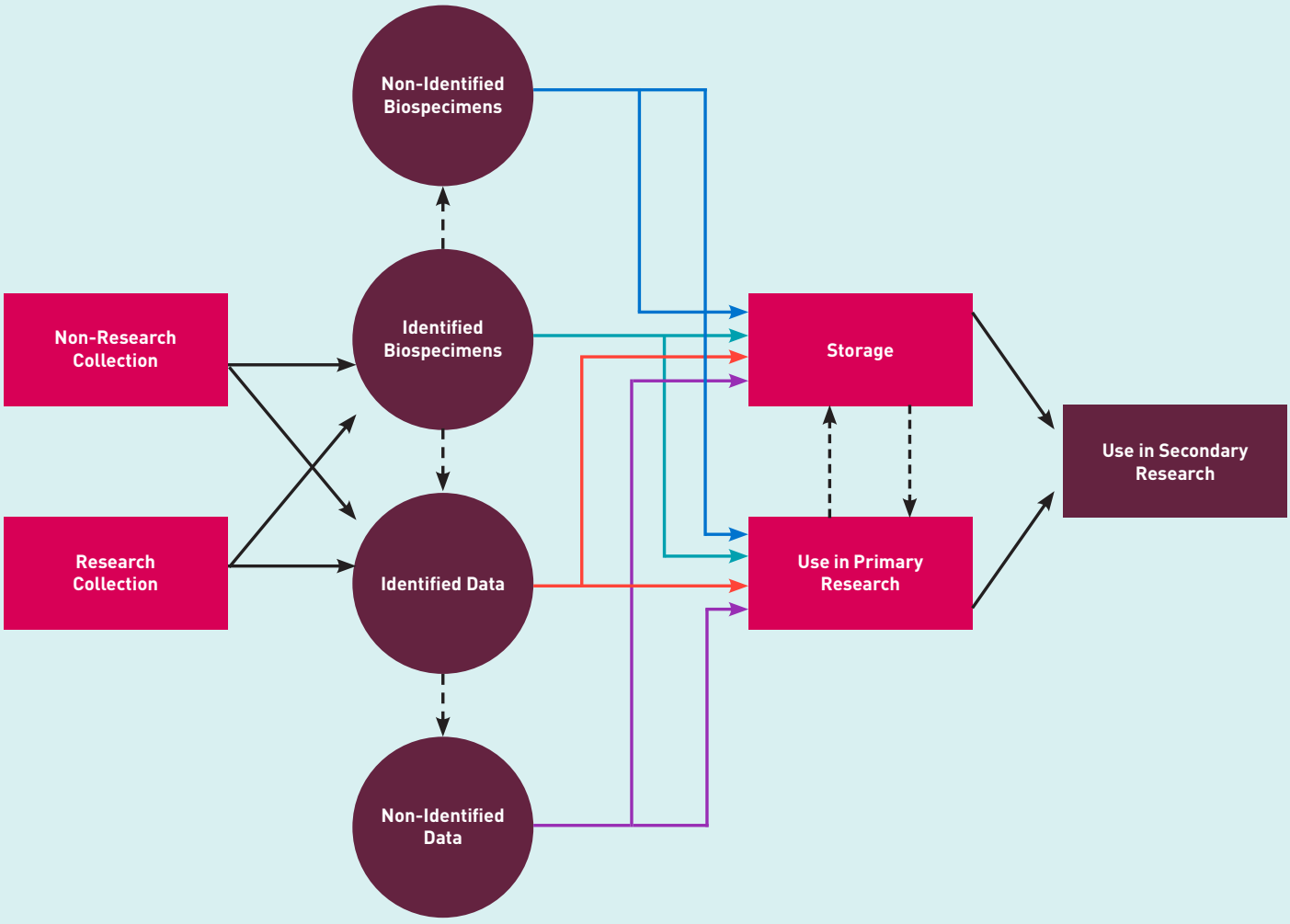
Although the NPRM only directly applies to federally funded research, several proposals within the NPRM will impact the way industry sponsored research is carried out. Any industry sponsored research that is carried out at an institution that also carries out federally sponsored research will have to comply with the NPRM.

Moreover, according the NPRM, the FDA has already stated its intention to modify its regulations in light of any Final Rule, and therefore the NPRM has considerable implications for a wide range of stakeholders across the life sciences industry.

Why have the NPRM changes been proposed?

With modern collaborative practices and widespread use of new data storage and collaboration tools, the risk of researchers losing control of biospecimens and data has increased considerably. At the same time, the risk to study participants has increased. For example, identification of genetic variations associated with lethal or chronic health conditions could have considerable consequences for both research subjects and their families. It is foreseeable that in the future genetic data could become used to qualify or disqualify individuals for loans, mortgages, health and other insurances, or even jobs.

The NPRM proposals represent many years of deliberation and are designed to bring the Common Rule up to date, improving protection for research subjects and reflecting substantial changes to modern research practices; specifically, the use of biospecimens in both primary and secondary research.



Flow of data and biospecimens from collection to research use.
Adapted from CJ Guerini et al. Journal of Law & Biosciences 1-24. June 2016

What changes to biospecimen research are being proposed?

The Common Rule NPRM proposes a very fundamental shift in the definition of 'human subjects' and extends the Human Subjects Protection Framework to non-identified biospecimens research, with impacts on biobanking, secondary research and genomic research.

The Human Subjects Protection Framework could now include non-identified biospecimens, impacting biobanking, secondary research and genomic research.

Expanding the definition of 'human subject' to cover all biospecimens

At present, the Common Rule does not apply to the research use of de-identified biospecimens, and a 'human subject' is defined as "a living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual, or identifiable private information."

The NPRM expresses particular concern that technological advances in research and data storage, along with whole-genome sequencing, could result in the re-identification at a later date of biospecimens or data that had been stripped of identifiers.

To address this concern, the NPRM proposes to expand the definition of 'human subject' to any cover living individual whose biospecimen has been collected for research and all research uses of biospecimens, irrespective of whether those biospecimens are identifiable or not, if those biospecimens have been collected or used in federally funded research.

Under the NPRM the definition of a 'human subject' will include:

§__102(e)(1) Human subject means a living individual about whom an investigator (whether professional or student) conducting research:

(i) Obtains data through intervention or interaction with the individual, and uses, studies, or analyzes the data;

(ii) Obtains, uses, studies, analyzes, or generates identifiable private information; or

(iii) Obtains, uses, studies, or analyzes biospecimens

This definition specifically covers:

1. Genome sequencing data, in whole or in part, regardless of the individual identifiability of the biospecimens used to generate the data.

2. Research use of information produced using a technology applied to a biospecimen that generates information unique to an individual such that it is foreseeable that, when used in combination with publicly available information, the individual could be identified ('bio-unique information').

The proposals would remove the controversial exercise of trying to determine whether a biospecimen may be identifiable now or at any time in the future. As a result of this modification, most future uses of biospecimens will require at least a broad informed consent for future use that is obtained either at the point of collection or prior to the subsequent use.

The intent behind this proposed modification in the NPRM is to increase the public's trust and sense of partnership in research, knowing that this research is intended to lead to improved treatment plans and new breakthrough therapies for the treatment of disease.

The proposed changes will not be applied retrospectively to biospecimens collected prior to the publication of the Final Rule, and compliance will not be required until three years after the Final Rule is published.

What does the revised definition mean for research?

This NPRM proposal means that any research using non-identified biospecimens will now be brought under the protection of the Common Rule, and as a result, will require independent review board (IRB) approval and informed consent unless subject to exclusions or exemptions, or if informed consent has been waived.

Under the NPRM, biospecimens will only be exempt from the Common Rule if research satisfies broad consent requirements, data security protection requirements and IRB review. However, if the research investigator anticipates that individual results will be returned to a research subject then no exemption is possible and informed consent must be obtained, along with a full IRB review.

How will these changes affect life sciences companies?

Under the current Common Rule, a life sciences company can obtain stored and identifiable biospecimens from an academic research institution for research purposes, provided that the original informed consent permits storage and does not limit secondary use or transfer. Even identifiable biospecimens collected as part of federally funded research would not be subject to the Common Rule.

The new NPRM proposals would subject life science companies to federal requirements for IRB review and data security measures on receipt of biospecimens that were collected during federally funded research.

Unless specific consent for the transfer and secondary research use of an individual's biospecimens has been obtained, life sciences companies could not obtain that individual's biospecimens unless the company implements NPRM data security safeguards and IRB review requirements. Whilst robust data security safeguards may currently exist within life science companies, internal non-federally funded research is not usually subjected to IRB review.

Therefore, it will be essential that provisions are made within consent forms to permit future secondary research and transfer to life science companies, and that this informed consent is gained at the time of initial specimen provision. However, companies will have no control over consent forms used for biospecimens collected during research that the company does not fund or sponsor. If the Final Rule does not provide a solution to this issue, it could lead to a reduction in the number of qualifying biospecimens available for future research, including corporate research.

These issues have been raised by life science companies during the commenting period for the NPRM, and it remains to be seen whether this problem can be addressed by changes to the wording of the Final Rule.

Additionally, the NPRM would only permit onward transfer of these biospecimens to a research centre carrying out research that is subject to the Common Rule, which implies that companies will have to implement data security measures at overseas facilities that receive transferred biospecimens. This could have major implications for international multi-centre studies, especially where facilities outside of the US have inadequate tracking and data protection systems to enable compliance with the NPRM and/or national rules for the use and storage of biospecimens that are incompatible with its provisions.

It will be essential that consent forms permit secondary research and transfer to life science companies. Informed consent must be gained at the time of initial specimen provision.

Summary

The most important points to take away from this article are:

- If the proposed regulation change proceeds to Final Rule in its current form, any biospecimen collected during research will be defined as a human subject, even non-identifiable samples.

- The reason for this new definition of a human subject is that new technologies and advances in genome sequencing present the risk that anonymised samples could be become identifiable in the future when combined with other data sources.

- For this reason, updated regulations are being proposed to protect the privacy of research subjects and to ensure a greater level of informed consent is obtained at the outset of a study.

- Biospecimens used in secondary research could be particularly impacted, as these samples will not be available for secondary use if the correct level of informed consent was not obtained when the sample was originally taken.

Part three of this article series examines the proposed changes to informed consent, and what will be required of companies carry out research.

Part four discusses which research will be subject to the Common Rule, and the potential for exclusions and exemptions.

Part Five considers the next steps for life science companies, as we wait to find out exactly how the regulations will be changed.

Sources

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