VIEWPOINT

# Revamping the US Federal Common Rule
## Modernizing Human Participant Research Regulations

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**On January 19, 2017,** the Office for Human Research Protections (OHRP), Department of Health and Human Services, and 15 federal agencies published a final rule to modernize the Federal Policy for the Protection of Human Subjects (known as the "Common Rule").[1] Initially introduced more than a quarter century ago, the Common Rule predated modern scientific methods and findings, notably human genome research.

Research enterprises now encompass vast multicenter trials in both academia and the private sector. The volume, types, and availability of public/private data and biospecimens have increased exponentially. Federal agencies demanded more accountability, research investigators sought more flexibility, and human participants desired more control over research. Most rule changes become effective in 2018, giving institutions time for implementation.

### Genesis of the Common Rule

A sad history of failed oversight of human research participants, exemplified by the Tuskegee syphilis study and military radiation experiments, provided impetus for federal protections. The 1979 Belmont Report formed the intellectual backdrop for federal research protection, introducing ethical principles of respect for persons, beneficence, and justice. A driving purpose of the 1991 Common Rule was to create uniformity consistent with ethical standards in research conducted or funded by federal agencies.[2] The Common Rule defined human participant research, specified the role and scope of informed consent, and required research oversight and compliance through institutional review boards (IRBs) at participating research entities.

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### The Changing Research Landscape

The Common Rule, although an ethical landmark, was antiquated almost from its inception. Digitization of research data, biobanking of human tissues, and electronic health records were rapidly altering the research landscape. Informed consent forms, the bulwark of protection, ballooned to the point that many participants could not fully understand the risks and benefits—the forms became more a hedge against institutional liability than a promotion of human dignity and autonomy.

Costs escalated as investigators strived to implement complex rules and fulfill repetitive IRB requirements. The rule failed to meaningfully distinguish research from hospital oversight and public health practices. High-profile cases of unethical research heightened public mistrust.

### Modernizing Research Regulations

The OHRP last updated the Common Rule in 2005, issuing a proposed rule in 2015 that garnered more than 2000 public comments. National Research Council[3] and National Academies[4] reports also proved influential. Major changes to human subject research protections are noted in the **Table**.

The Common Rule enhances participant protections while limiting administrative burdens on research entities and investigators. It clarifies what qualifies as human subject research, exempting educational studies, behavioral assessments, public benefit program reviews, and secondary studies of stored biospecimens entailing minimal risks or conducted with "broad" consent. Researchers can examine confidential data or tissue banks for prospective participants without consent.

The Common Rule reduces IRB administrative responsibilities. Subject to exceptions, it (1) clarifies IRB procedures for research approval; (2) dispenses with onerous reviews of grant applications, contracts, and ongoing minimal-risk studies (eg, data analyses); (3) requires (in 3 years) single IRB approval and oversight of multiinstitutional research (unless tribal or state laws mandate additional IRB review); and (4) facilitates online tools to help IRBs assess an expanded array of "exempt" or "expedited" research.

The rule simplifies the informed consent process to enable participants to better understand the scope, risks, and benefits of research. Prescribed elements of consent forms include a concise, up-front explanation of information a "reasonable" person would desire, such as purposes, risks, benefits, and alternative treatments. Investigators are empowered to seek broad consent to use identifiable data or biospecimens in unspecified future research instead of requiring additional consent, IRB waivers, or data deidentification.

The OHRP's decision to not reform the Common Rule in certain areas was just as consequential. The rule still applies only to federally funded research. However, federal agencies can require enterprises receiving any federal research funds to apply Common Rule protections to all non-federally funded investigations. The rule also fails to mandate security measures such as encryption to safeguard personal data against hacking or unwarranted disclosure. In addition, it does not address compensation for research-related injuries.

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Table. The Common Rule: Major Reforms

| Preimplementation | Postimplementation |
|---|---|
| Broadly defines *human subject research* to generally apply Common Rule safeguards regardless of risk level | Establishes newly defined categories of exempt or excluded research studies based on the level of risk posed to study participants |
| Entails lengthy and complex informed consent processes and requirements | Requires consent forms to include up-front concise and focused descriptions of key information, risks, and benefits of the study<br>Requires online posting of consent forms used in applicable studies |
| Unclear as to consent requirements for secondary uses of human biospecimens | Allows investigators to obtain broad consent for use of identifiable biospecimens in future unspecified research studies<br>Does not require consent for secondary uses of nonidentifiable biospecimens |
| For multi-institutional studies, permits local IRBs approvals at each participating institution | Generally requires the use of a single IRB for multi-institutional studies within the United States<br>Federal agencies can determine that using a single IRB would not be appropriate in some multi-institutional contexts |
| Fails to adequately distinguish between human participant research and public health practice | Explicitly excludes public health surveillance from human subject research |

Abbreviation: IRB, institutional review board.

## Biospecimens and Genetic Data

The Human Genome Project opened new vistas for research, including genetic sequencing of stored or future biospecimens (eg, blood, tissues, cells). Launched in 2015, the Precision Medicine Initiative aims to collect genetic data from more than a million people, also examining lifestyle data to better target prevention and treatment.[5] The rule supports the need to obtain informed consent for such studies. Classification of "human subjects" clearly includes living persons from whom biospecimens are obtained through intervention, interaction, or mere analysis. If existing or emerging technologies can match biospecimens to individuals, the specimens are regarded as identifiable.

Public controversy has swirled around the practice of using existing biospecimens for future research without participant, parent, or family consent. In 2011, parents sued Minnesota over the health department's collection, use, storage, and dissemination of newborn screening samples.[6] A genome sequence of Henrietta Lacks' tissue (first gathered in 1951) ignited public concern in 2015 over the fair use of an individual's cell line.[7]

The question arises whether investigators have to obtain consent for all future uses of biospecimens, even if nonidentifiable. Individuals have personal and even property claims, particularly if the data can be rendered identifiable. Yet requiring future consent can prove costly and burdensome for investigators. The very process can create a sampling bias, undermining research utility. The OHRP ultimately decided that secondary research on nonidentifiable biospecimens could be conducted without additional informed consent, including newborn sample studies. Once the Common Rule is implemented on January 19, 2018, the Newborn Screening Saves Lives Reauthorization Act of 2014 limiting such research will no longer be operational.

## Distinguishing Public Health Practice and Research

Public health agencies have lamented failures to properly distinguish between human participant research and public health practice. Certainly, surveillance and other epidemiologic investigations gather personal information and can generate generalizable knowledge. Yet these activities are vital to public health, with the primary goal of safeguarding populations. Requiring IRB approval forced health departments to curtail, restructure, or discontinue important activities. Although not entirely resolved, the Common Rule clarifies the distinction between public health practice and research. In defining research, the rule explicitly exempts the newly defined classification of public health surveillance, broadly worded to include an array of public health practice activities. As a result, governmental agencies and their contracted partners can undertake routine and emergency "public health surveillance activities" without IRB review and approval.

## Advancing Research, Protecting Participants

Common Rule reforms strike a difficult balance between facilitating modern research while safeguarding privacy. Allowing secondary biospecimen research after obtaining an initial consent and without significant IRB oversight should generate new discoveries with fewer costs. In this sense, the rule recognizes important collective interests in science and health.

Yet weighing the interests of funders, investigators, and participants still poses a major challenge. In an age of big data and cybersecurity threats, and as new technologies reveal personal identities, ethics rules become even more important. Federal oversight will remain the bulwark against unethical practices. In the end, treating human research participants with respect and fairly is essential for continuing public support of vital scientific investigations.

ARTICLE INFORMATION

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