“Broad Consent” under the New Common Rule and Survival of the Old “Broad Consent”

Mark Barnes, JD, LLM
Partner, Ropes & Gray LLP
Co-Chair, Multi-Regional Clinical Trials Center of Harvard and Brigham and Women’s Hospital
Disclosures

- I am a partner and Ropes & Gray, LLP
- I do not plan on discussing unlabeled/investigational uses of a commercial product
Background

- New Regulatory “Broad Consent”
- Survival of Old Non-Regulatory “Broad Consent”
- Challenges of Regulatory Broad Consent
- Conclusion

The Final Rule establishes a framework for “broad consent,” a new type of regulatory consent under the Common Rule for non-exempt storage, maintenance, and research use involving identifiable information and biospecimens.

- Broad consent is intended to serve as a substitute for traditional informed consent in a range of defined circumstances.

Final Rule effective date was set as January 19, 2018, but has been delayed to July 19, 2018. See 83 Fed. Reg. 2885 (Jan. 22, 2018).
Background

- The research community has **relied on a theory of broad consent in a general sense** for many years.
  - Permits institutions to collect, store, and use subjects’ data and identified biospecimens for unspecified future research.

- Prior to the Final Rule, if researchers had not secured consent adequate for a specific research use, the Common Rule contemplated only two alternatives for using identifiable data or biospecimens in a research study:
  - Obtaining an IRB waiver of consent, or
  - Removing personal identifiers so that the research would not involve identifiable private information (and therefore fall outside the Common Rule’s jurisdiction).
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Under revised Common Rule, if regulatory broad consent is obtained, any subsequent storage, maintenance, and secondary research uses of the individual’s identifiable biospecimens and data consistent with the broad consent would not require additional consent.

Regulatory broad consent under Common Rule has multiple mandated elements, including:

- General description of types of research that may be conducted.
- Description of identifiable private information or identifiable biospecimens that might be used in research.
- Whether sharing of identifiable private information or identifiable biospecimens might occur.
- Types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens.
Elements of Regulatory Broad Consent

- Description of period of time that the identifiable private information or identifiable biospecimens may be stored and maintained and description of period of time that they may be used for research (both can be indefinite).

- Description of any reasonably foreseeable risks or discomforts to the subject.

- Description of any benefits to the subject or to others that may reasonably be expected.

- Statement describing extent, if any, to which confidentiality of records identifying the subject will be maintained.

- Statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
Elements of Regulatory Broad Consent

- Statement that the subject’s biospecimens may be used for commercial profit and whether subject will share in profit (if applicable).

- Statement as to whether research will (if known) or might include whole genome sequencing (if research involves biospecimens).

- Statement that subject or legally authorized representative will not be informed of details of specific research studies, including purposes, and that they might have chosen not to consent to some of the specific studies (unless such details to be provided).

- Statement that clinically relevant research results, including individual research results, may not be disclosed to the subject (unless it is known that such results will be disclosed in all circumstances).

- Explanation of whom to contact for answers to questions about subject’s rights and storage and use of identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.  See §___.116(d).
Refused to Consent” under Regulatory Broad Consent

- If an individual is asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens, and the individual “refused to consent,” an IRB cannot waive consent for the storage, maintenance, or secondary research use of that person’s identifiable private information or identifiable biospecimens. See 82 Fed. Reg. 7267 (Jan. 19, 2017).

- However, researchers could simply choose to de-identify the subject’s data and biospecimens and then conduct further research with them.

  - A person’s refusal to give broad consent also does not prevent the unconsented uses of their identifiable data and biospecimens for purposes that are not considered “research” under the revised Common Rule – such as quality assurance.
“We agree with the public comments that favored allowing institutions to create their own broad consent forms that could be tailored to a variety of circumstances. Therefore, under the Final Rule, investigators and institutions may develop broad consent forms, which, provided specified conditions are satisfied, would meet the exemption for the storage and maintenance for secondary research use of identifiable biospecimens or identifiable private information. . . . *At a later time, the Secretary of HHS expects to develop guidance on broad consent, which could include broad consent templates.*”

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Survival of Non-Regulatory Broad Consents

- Prior to the Final Rule’s adoption of an express regulatory broad consent, it has been **longstanding practice in research institutions to obtain broad consent** to future research uses of data and biospecimens.

- The adoption of an express regulatory broad consent should **not be construed to invalidate these non-regulatory broad consents**, which have provided, and continue to provide, a basis for research activities.
  - Recognition that non-regulatory broad consent survives the introduction of the new regulatory broad consent is detailed on the following slides.
Survival of Non-Regulatory Broad Consents

“While the Final Rule creates a new regulatory scheme for “broad consent,” the research community has long relied on consent for future uses in the general sense to allow institutions to collect, store, and use subject data and leftover biospecimens for future research. SACHRP believes that future research consent forms signed before and after the effective date of the Final Rule . . . will continue to be effective. After the effective date of the Final Rule, a consent for future research using identifiable data and/or biospecimens must be analyzed as before, to assure that the consent has sufficiently detailed the future research uses, even if that consent would not be sufficient to meet “broad consent” as used in the Final Rule for purposes of the exemptions at §§104(d)(7) and (d)(8) or the broad consent framework under §116(d).” Secretary’s Advisory Committee on Human Research Protections (“SACHRP”), Guidance on Broad Consent under the Revised Common Rule (Jul. 26, 2017) (emphasis added).
Survival of Non-Regulatory Broad Consents: the HITECH Precedent

- Under Final Rule implementing the Health Information Technology for Economic and Clinical Health ("HITECH") Act, the Health Insurance Portability and Accountability Act of 1996 ("HIPAA") was interpreted to permit broad authorizations for future uses of Protected Health Information, in order to align HIPAA with the Common Rule, which was understood to permit broad consent to future uses of identifiable or identified data and biospecimens.
“[M]any commenters noted that the Department’s interpretation limiting the scope of a HIPAA authorization for research appeared to diverge from the current practice under the Common Rule with respect to the ability of a researcher to seek subjects’ informed consent to future research so long as the future research uses are described in sufficient detail to allow an informed consent. These commenters, as well as [SACHRP] . . . had urged the Department to allow the HIPAA authorization to permit future research use and disclosure of protected health information. . . . We modify the prior Departmental interpretation that research authorizations must be study specific. . . . We also agree with commenters that this approach best harmonizes with practice under the Common Rule regarding informed consent to future research, and allows covered entities, researchers and Institutional Review Boards to have flexibility in determining what adequately describes a future research purpose depending on the circumstances.” 78 Fed. Reg. 5566, 5612 (Jan. 25, 2013) (emphasis added).
Revised Common Rule offers insights into what information might be required in an original consent form’s description of purpose so that additional consent would not be required for future use. The below table, based on SACHRP FAQ Guidance updated March 2018, shows application of Common Rule informed consent requirements to future research.

This analysis of the effect of primary consent, however, is not dependent on regulatory broad consent, and would be the same for non-regulatory broad consent under the pre-2018 Common Rule.

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<th>Common Rule Informed Consent Requirements</th>
<th>Application to Future Research</th>
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<td>45 C.F.R. § 46.116(a)(1). A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject’s participation, a description of the procedures to be followed, and identification of any procedures which are experimental.</td>
<td>Consent form should be sufficiently clear that the study involves research. No additional duration of personal involvement is expected, and typically subjects will undergo no additional procedures beyond those described for the primary study. Duration of biospecimen/data storage and use may need to be described. The primary aspect of this element that may be unclear at the time the primary consent is presented is the purpose of the future research.</td>
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### Application of Common Rule Requirements to Future Research

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<td><strong>45 C.F.R. § 46.116(a)(2).</strong> A description of any reasonably foreseeable risks or discomforts to the subject.</td>
<td>Risks of future research are primarily related to maintenance of privacy and confidentiality, and there are no additional discomforts.</td>
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<td><strong>45 C.F.R. § 46.116(a)(3).</strong> A description of any benefits to the subject or to others which may reasonably be expected from the research.</td>
<td>Benefits of future research are almost always indirect. It can be disclosed that participants should expect no personal benefit in advance of a specific description of the research.</td>
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<td><strong>45 C.F.R. § 46.116(a)(4).</strong> A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.</td>
<td>Given the nature of future research, there would be no alternative procedures or courses of treatment.</td>
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<td><strong>45 C.F.R. § 46.116(a)(5).</strong> A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.</td>
<td>This element is particularly applicable to future research, as biospecimens and data will necessarily be maintained, often for an uncertain duration.</td>
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<td>45 C.F.R. § 46.116(a)(6). For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.</td>
<td>Future use typically would not involve greater than minimal risk.</td>
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<td>45 C.F.R. § 46.116(a)(7). An explanation of whom to contact for answers to pertinent questions about the research and research subjects’ rights, and whom to contact in the event of a research-related injury to the subject.</td>
<td>In most cases, the contact information should be the same as that for the original protocol, and research-related injury is likely not relevant.</td>
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<tr>
<td>45 C.F.R. § 46.116(a)(8). A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.</td>
<td>Discontinuation raises particular problems in storage and maintenance of biospecimens and data for future research.</td>
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Background

New Regulatory “Broad Consent”

Survival of Old Non-Regulatory “Broad Consent”

Challenges of Regulatory Broad Consent

Conclusion
Challenges of Regulatory Broad Consent

- There are a number of practical reasons why the research community may prefer to continue using non-regulatory broad consent – even after the advent of regulatory broad consent.

- Further, there are interpretation ambiguities that exist under the provisions of the new regulatory broad consent, which may complicate reliance upon the regulatory broad consent in certain circumstances.
Daunting Logistics of Regulatory Broad Consent

- Extensive and seamless IT system capacity will be necessary for any institution to implement fully a regulatory broad consent tracking system.
  - Both broad consents as well as refusals to consent (unless the materials are destroyed) must be tracked over the lifetimes of persons who give broad consent and persons who refuse to give such consent.
  - Note that HIPAA’s requirements apply to protected health information for life plus 50 years.
Daunting Logistics of Regulatory Broad Consent

- Given the complexity of electronic tracking processes, practically speaking, only large research institutions with interconnected, interfacing and fully interoperable medical records systems will be able to implement and benefit from the broad consent regime established in the Final Rule.
  - A “confederated,” non-IT-unified health system will simply not be able, without significant error, to track these consents and refusals to consent.

- These logistical barriers will greatly limit the utility of the regulatory broad consent option.
Interpreting Regulatory Broad Consent

- IRB must determine **whether a proposed secondary research use is compatible with the original consent.**
  - If the original consent form **specifically prohibited** the proposed research activity, it is presumed the research is not allowable.
  - If the consent does **not specifically prohibit the proposed use**, IRBs should consider several questions to determine compatibility:
    - What is the nature of the proposed secondary research?
    - Could it **reasonably be understood to fall within the scope of research** described in the original consent form?
    - Does the secondary research use impose **new or significantly greater risks (including privacy risks)** not described in the initial consent form?
    - Are there **known concerns of the study population(s)** about the proposed secondary use?
On July 26, 2017, the Secretary’s Advisory Committee on Human Research Protections ("SACHRP") approved draft guidance on broad consent under the Final Rule.

Guidance provides recommendations regarding the interpretation of several ambiguous areas under the Final Rule.

- Areas requiring clarification, and SACHRP’s proposed interpretations, are set forth in this section.
Defining “Refusal to Consent”

- Final Rule does not delineate whether an individual’s silence, non-responsiveness, and/or express declination to give broad consent would constitute “refusal to consent” for purposes of determining whether an IRB can later waive consent for the storage, maintenance, or secondary research use of an individual’s identifiable private information or identifiable biospecimens.

- While express declination to give broad consent is plainly “refusal to consent” under the Final Rule, the meaning and legal import of a person’s silence or non-responsiveness to a request to provide broad consent is less clear.
Defining “Refusal to Consent”

- Both pre- and post-Final Rule, if a person is approached about participating in a registry, databanking or biobanking study, and refuses to consent or does not respond at all, this does not prevent future waivers of consent granted by an IRB for secondary research uses.
SACHRP Recommendations on “Refusal to Consent”

- SACHRP has recommended that HHS interpret “refusal to consent” to include only a person’s express declination to give broad consent, as demonstrated by an individual’s unambiguous written or oral communication to that effect.
  
  - SACHRP recommended that the broad consent form expressly state that failure to respond (i) will not be treated as a refusal to consent, (ii) will not prevent researchers from seeking a waiver of consent or pursuing an exemption, and (iii) will not act as affirmative broad consent.

  - SACHRP also recommended, as a best practice, that for persons who were offered broad consent through a medium other than face-to-face contact – e.g., by internet or mail – researchers attempt to provide participants who have not responded within a reasonable timeframe with a second offer of broad consent.
SACHRP Recommendations on “Refusal to Consent”

- SACHRP has recommended that an IRB continue to be able to waive consent under §___116(f) for the future research uses of the identifiable data or biospecimens of a person who neither expressly provides consent nor expressly declines consent.
Parties Bound by a Person’s Refusal to Give Broad Consent

- Final Rule does **not** identify the party(ies) bound by an individual’s refusal to consent. Instead, the Final Rule prevents “an IRB” from waiving consent based on an individual’s refusal to provide broad consent.
  
  - Without more limitation or explanation, the **prohibition could apply to all U.S. IRBs, investigators, and institutions** with respect to the refusing individual’s identifiable biospecimens and identifiable private information.
  
  - This approach would ignore the possibility that an individual may:
    
    - Refuse broad consent at one institution or for one investigator, and
    
    - Provide broad consent or decline to respond to a request for broad consent at another institution or when asked by a different investigator.
SACHRP Recommendation on Parties Bound by a Person’s Refusal

- SACHRP has recommended that the broad consent form clearly delineate which party(ies) would be able to use the data and biospecimens for secondary research purposes.
SACHRP Recommendation on Parties Bound by a Person’s Refusal

- However, refusal to provide broad consent should **not**:
  - Prevent those researchers or their institution from **recontacting the individual to re-request broad consent** after a reasonable interval or after a material change in the participant’s circumstances that could affect his or her willingness to provide broad consent.
  - Prevent other institutions and researchers not identified in the initial broad consent from **requesting the individual’s broad consent provided that they agree not to share the information and biospecimens with the institutions and researchers initially denied broad consent** unless the individual expressly consents to the sharing.
  - Prevent an IRB from waiving informed consent for future research uses of that person’s identifiable data and biospecimens, based on **a waiver application from a research team unaffiliated with, and not acting on behalf of, those who sought the broad consent.**
Describing Scope of Future Uses

- Broad consent forms must contain a general description of types of research that may be conducted with identifiable private information or identifiable biospecimens. See §____.116(d)(2)).

- At what level of generality should the description be given?

- Should examples be provided?
SACHRP Recommendation on Describing Scope of Future Uses

- Purposes may be described generally, but should also contain some illustrative examples, especially listing any controversial areas of potential research uses (e.g., creation of cell lines, abortion/induced termination of pregnancy) and the areas for which specific mention is required by applicable laws (e.g., genetic testing, drug abuse/alcoholism, HIV/STDs, mental health).

- Attempts should not be made to present an exhaustive list of research areas or issues, as such a list cannot be comprehensive and could, in fact, mislead the individual considering the broad consent.
Continuing Research after Withdrawal of Broad Consent

- If an individual gives broad consent but later withdraws it, investigators may continue to use that person’s collected and stored data and biospecimens so long as they have been subsequently stripped of identifiers so as to not be subject to the Common Rule. See 82 Fed. Reg. 7217 (Jan. 19, 2017).

- However, guidance also indicates that if an investigator promises that withdrawal of a broad consent would mean that there would be no future research use of that person’s information and biospecimens, then the promise should be honored, precluding future use of that information and those biospecimens even in de-identified form. See id.
SACHRP recommended that, if an individual gives broad consent but later withdraws it, investigators may continue to use that person’s collected and stored data and biospecimens so long as they have been subsequently stripped of identifiers so as to not be subject to the Common Rule.

Broad consent forms should describe that withdrawal of broad consent:

- Would not prevent the completion of use of that person’s data and biospecimens in a study already commenced at the time of the withdrawal request.
- Would not prevent the continued storage and use, for research integrity purposes, of information already generated from that person’s data and biospecimens.
IRB’s Responsibilities

- Final Rule does **not describe the extent of diligence required by an IRB** to certify that broad consent has been obtained and documented appropriately.
SACHRP Recommendation on IRB’s Responsibilities

- SACHRP recommended a limited IRB review to assess whether broad consent is obtained in accordance with the applicable requirements.
  - Would require **an evaluation by the IRB of the broad consent form used and a review of the process used to secure such consent.**

- To satisfy the requirement that the IRB ensure that broad consent is appropriately documented, **SACHRP has recommended that the investigator:**
  - Certify that he or she has obtained such a consent from the subjects, or otherwise has assured that those subjects have in fact given such broad consent;
  - Certify that the broad consent is documented and available and will remain available for IRB review, if the IRB determines that such review is appropriate; and
  - Provide a summary of the process used to seek broad consent, including the use of requests made in-person and by mail, telephone, and/or email.
Return of Research Results

- In the Final Rule under § 104(d)(8)(iv), secondary research use of identifiable biospecimens and identifiable private information is exempt from the Common Rule, if, *inter alia*, “[t]he investigator does not include returning individual research results to subjects as part of the study plan.”

- Final Rule is silent as to whether the plan to return individual research results must be intended to apply to each and every subject, or only to at least one subject, for the research to be excluded from the exemption.
  - But return of *general or aggregate research findings* would not preclude use of this exemption, which applies only to return of *individual* research results.
  - Further, this provision does not prevent an investigator from abiding by any legal requirements to return individual research results.
SACHRP has recommended that, if a study plan were to provide for the return of individual research results (i) only to a single subject, (ii) to a subset of subjects (who may, for example, be discovered to have a significant finding) or (iii) to all subjects, then the study plan should be considered to include the anticipated return of individual research results to subjects under §104(d)(8)(iv), and thus not be eligible for an exemption from the Common Rule.

Under this proposed interpretation, however, a study plan would continue to meet the exemption criterion if it allows for reporting or disclosure to subjects of incidental findings, which are clinically meaningful risks unrelated to the study’s design or endpoints.
Use of a Combined Form for Primary Study Consent and Broad Consent

- Final Rule does **not require** that broad consent be obtained on a form separate from that of a primary study-specific consent.
  - Content and other requirements for broad consent must be satisfied.
  - Broad consent form must be offered to a prospective subject only under circumstances that provide the prospective subject sufficient opportunity to discuss and consider whether or not to participate, and that minimize the possibility of coercion or undue influence.
SACHRP recommended that a broad consent be able to be combined with a consent form for a primary study.

- But SACHRP recommended that a clinical consent form not be combined with a broad consent form.

- Clarifies the difference between research and medical treatment.

- Clarifies that receiving the clinical procedure does not depend on providing broad consent.
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- Pre-Final Rule broad consent is still valid, but must be judged carefully regarding the specificity of the consent vis-à-vis the proposed research use.

- Regulatory “broad consent” under the Final Rule is logistically complex to implement, especially due to the need to track “refusals to consent.”
Conclusion

- Regulatory “broad consent” under the Final Rule will be most useful:
  - Integrated with consent for a biobanking or databanking study, for which “refusals to consent” are unimportant.
  - Integrated with a consent for a primary interventional study, to allow downstream uses of data and/or biospecimens collected in the study.
  - In “command and control” institutions with fully integrated electronic patient or client records, so that refusals to consent can be readily and accurately tracked.