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SACHRP Releases Guidance on Broad Consent Under Revised Common Rule

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Background

On Jan. 19, 2017, the U.S. Department of Health and Human Services (''HHS''), along with 15 other federal departments and agencies, promulgated regulations (the ''Final Rule'') to update the Federal Policy for the Protection of Human Subjects in Research (the ''Common Rule''). (82 Fed. Reg. 7149 (Jan. 19, 2017).) The Common Rule is the set of federal regulations setting forth the ethical framework for the conduct of research involving human subjects conducted or supported by most agencies of the federal government, including the National Institutes of Health. Most provisions of the Final Rule are set to take effect on Jan. 19, 2018, and for purposes of this article, we use the Final Rule's terminology of the ''Pre-2018 Rule'' to reference the Common Rule provisions that were changed by the Final Rule. (*See id.* at 7149.)

Among other important changes, the Final Rule establishes a framework for ''broad consent'' under the Common Rule. The Pre-2018 Rule permits research institutions to seek study-specific consent to collect and store identifiable data or identifiable biospecimens and to seek institutional review board (''IRB'') waiver of consent to use such data or biospecimens for a later, specific project. Additionally, under the Pre-2018 Rule, institutions are able to define in an informed consent form specific future uses of the data or biospecimens that may proceed without additional consent or waiver of consent. However, the Final Rule (i) specifically introduces ''broad consent'' into the Common Rule framework, describing it as ''seeking prospective consent to unspecified future research,'' (ii) creates a pathway for broad consent to serve as a substitute for study-specific informed consent, and (iii) allows a wide latitude for investigators and research institutions to re-use identifiable data and identifiable biospecimens for other research activities. (82 Fed. Reg. at 7150.) Importantly for industry sponsors of clinical research, ''broad consent'' would allow investigators to conduct industry-funded studies without additional IRB approval or subject consent. Further, as the Food and Drug Administration (''FDA'') has indicated that it will revise its own regulations to be consistent with the Final Rule, to the extent permissible under existing statutory law and the FDA's regulatory mission, it may well be that the FDA also adopts similar ''broad consent'' provisions in its own regulations. (*See* Section 3023 of the 21st Century Cures Act, which requires HHS to harmonize differences between the Common Rule and FDA regulations, to the extent practicable.)

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The preamble to the Final Rule charged the HHS Secretary with developing guidance to provide recommendations for the interpretation of the broad consent provisions of the Final Rule. (*See* 82 Fed. Reg. at 7222.) The HHS Secretary's Advisory Committee on Human Research Protections (''SACHRP'') was subsequently asked to formulate guidance and an associated template broad consent form for the HHS Secretary to consider. On July 26, 2017, SACHRP approved a lengthy guidance regarding broad consent, as well as a template broad consent form intended to guide implementation of the broad consent provisions of the Final Rule. (SACHRP, *Draft Guidance on Broad Consent under the Revised Common Rule* (July 26, 2017) (hereinafter, the ''Broad Consent Guidance''.) HHS will consider the SACHRP recommendations, but is not bound to adopt them in full or in part. Nevertheless, SACHRP recommendations and work products have often been viewed by the research community as representing consensus, mainstream position statements that can be of significant assistance in navigating complex human subjects research issues.

The key issues addressed in the Broad Consent Guidance, described in further detail below, will affect a variety of clinical research stakeholders, including life sciences companies, academic medical centers, and hospitals. Specifically, institutions will need to assess whether the benefits of using broad consent outweigh the potential drawbacks of such use for any proposed research activity, and reconsider (and potentially re-

vise) their procedures for obtaining informed consent accordingly.

Broad Consent Framework Under the Final Rule

Under the Pre-2018 Rule framework, if researchers had not secured study-specific consent, then they had two alternatives to use identifiable data or identifiable biospecimens for secondary research: (1) securing IRB waiver of consent or (2) removing personal identifiers from data and biospecimens, rendering research on such de-identified data outside the jurisdiction of the Common Rule. The Final Rule explicitly permits researchers to obtain broad consent for the storage, maintenance, and secondary research uses of identifiable biospecimens and identifiable data. (*See* Barth et al., *HHS Finalizes Comprehensive Revisions to the Common Rule*, 11 LSLR 03 at 6-7 (Feb. 3, 2017).)

Specifically, the Final Rule creates two new categories of research that may be exempted from compliance with the Common Rule if certain conditions, including broad consent, are met. These categories of exemptions are:

(1) storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use, if an IRB conducts a limited IRB review and makes certain determinations (§ _ .104(d)(7)); and

(2) research involving use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

> (i) documentation of informed consent or waiver of documentation of consent is obtained;
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> (ii) an IRB conducts a limited IRB review and makes certain determinations; and
>
> (iii) the investigator does not include returning individual research results to subjects as part of the study plan (although the investigator is not prevented from abiding by any legal requirements to return individual research results). (§ _.104(d)(8).)
>
> Once a researcher obtains broad consent, then any subsequent storage, maintenance, or secondary research use of the individual's identifiable biospecimens or identifiable data consistent with the terms of the broad consent would not require additional consent from the individual, provided certain conditions are met, including limited review by an IRB.

However, although the Final Rule establishes the new framework for obtaining broad consent, it remained intentionally silent as to most of the nuance and details attendant to implementing a broad consent program. The recently released Broad Consent Guidance therefore provides helpful recommendations to guide the interpretation and implementation of the broad consent provisions in the Final Rule.

I. Refusal to Consent

One such area in need of further clarification has been the implications of an individual's refusal to give broad consent when offered by a researcher. The Final Rule eliminates an IRB's ability to waive consent for future research uses of identifiable data and identifiable biospecimens if an individual has been offered to provide, yet refused to give, broad consent. (§ __.116(f)(1).) Specifically, when an individual is offered but ''refuses'' to grant broad consent, the IRB cannot waive consent for the storage, maintenance, or secondary research use of that individual's identifiable data or identifiable biospecimens. (*Id.*) However, the Final Rule does not define ''refusal'' to consent or offer insight into whether researchers should view an individual's silence or nonresponsiveness as constituting a ''refusal'' to grant broad consent under the Common Rule.

The Broad Consent Guidance addresses this ambiguity by suggesting 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.'' (Broad Consent Guidance, at 7.) This does not suggest, of course, that a failure to respond be treated as granting of broad consent; rather, SACHRP recommends that an individual's lack of response be viewed as neither a refusal nor grant of broad consent. The Broad Consent Guidance states that in order to communicate effectively to individuals the distinct implications stemming from their decision to respond to the offer for a broad consent, broad consent forms used by researchers should ''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.'' (*Id.* at 8.) In addition, SACHRP recommends that a broad consent form clearly set forth an individual's three options in responding, namely (i) express agreement, (ii) express refusal, and (iii) nonresponsiveness.

This guidance brings clarity for research institutions seeking to obtain broad consent for research activities subject to the Common Rule, and eliminates possible problematic situations such as if an individual would be offered a broad consent but simply forgets to respond, leaving the institution then unable to seek IRB waiver for the storage, maintenance, or secondary research use of that individual's identifiable data or identifiable biospecimens. The recommendations eliminate an unnecessary incentive to prefer waiver of consent over seeking broad consent directly from subjects, which would have existed if the failure to respond were or could be treated as a refusal to consent. In terms of patient autonomy, this recommendation acknowledges that, in all likelihood, if someone has strong objections to providing broad consent, he or she would affirmatively express as much to researchers.

II. Parties Bound by a Person's Refusal to Give Broad Consent

Although the Final Rule sets forth a limitation regarding future use of identifiable data or identifiable biospecimens if the subject refuses to grant broad consent, it is silent as to the parties bound by such a refusal to consent. The language of the Final Rule instead simply prevents ''an IRB'' from waiving consent as a result of an individual's refusal to provide broad consent. (§ __ .116(f)(1).) As noted in the Broad Consent Guidance, this provision, without further explanation or guidance, is silent as to the application of the provision to situations in which an individual refuses to grant broad consent to one institution, yet, for many possible reasons, may be amenable to granting broad consent to one or more other institutions.

The Broad Consent Guidance therefore recommends that broad consent forms should clearly delineate

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which parties would be able under a broad consent to use the identifiable data and identifiable biospecimens for secondary research purposes. However, the Guidance further notes that refusal of an individual to provide broad consent should in any case:

> (i) not prevent those researchers or their institution from recontacting the individual at a future time to re-request broad consent (as defined by relevant institutional policies), so long as the re-contacting is neither insistent nor abusive;
>
> (ii) not prevent other institutions and researchers not identified in the initial broad consent form from requesting the individual's broad consent provided that they agree not to share identifiable data and identifiable biospecimens secured under such broad consent with the institutions and researchers initially denied broad consent unless the individual expressly consents to the sharing; and
>
> (iii) not prevent an IRB from waiving informed consent for future research uses of that person's identifiable data and identifiable biospecimens, based on a waiver application from a research team unaffiliated with, and not acting on behalf of, those researchers whose previous request for broad consent from the individual had been refused.

This more specific framework for treatment of a refusal to consent is intended to ease implementation of broad consent programs, and provide institutions that have already requested an individual's broad consent the option later to recontact individuals and request broad consent again, if not abusive and if consistent with relevant institutional policies. The Guidance further advises academic medical centers and other health care systems with decentralized research operations to implement systems ''to assure that an individual who refused to provide broad consent at one organizational unit not be approached shortly thereafter to provide broad consent by staff at other organizational units under the same leadership or governance.'' (Broad Consent Guidance, at 10.) Therefore, health care institutions implementing a broad consent program will need to develop extensive broad consent and refusal-tracking systems. Although this type of tracking is probably unavoidable, it likely will serve as a key limitation on the types of institutions and number of situations in which broad consent is used.

III. Specificity of Description of Future Uses

In its Guidance, SACHRP explains that researchers availing themselves of this new broad consent pathway will need to describe in their broad consent forms, even if generally, the range of future research uses to which the person is giving his or her broad consent. In their broad consent forms, researchers should specifically include helpful examples demonstrating the potential research uses, particularly in situations in which those uses may be ethically, religiously, or politically contentious or otherwise controversial. For example, some persons considering whether to give a broad consent may want to know – because they care deeply about – possible uses of their identifiable biospecimens for whole genome sequencing, stem cell research, research about induced termination of pregnancy, or human geography studies whose results may challenge deeply-held religious or cultural beliefs.

Multiple state laws govern testing and data disclosure for such conditions as tuberculosis, HIV infection, and mental retardation/developmental disabilities. State laws also often govern genetic testing and the use and disclosure of genetic test results. Specific federal law governs use and disclosure of identifiable information about drug and alcoholism treatment. (*See* 42 U.S.C. § 290dd-2; 42 C.F.R. Part 2.) In all of these cases, specific mention of these categories of research activities may be required in the broad consent form, in order for researchers to use and disclose identifiable data or identifiable biospecimens from those protected categories. This is reflected in the SACHRP broad consent template.

IV. Continuing Research After Withdrawal of Broad Consent

Another area of ambiguity in the Final Rule is a researcher's ability to continue research following an individual's withdrawal of initially granted broad consent. Commentary on this issue in the Final Rule suggests that investigators may continue to use a person's collected and stored data and biospecimens, even if the individual later withdraws broad consent, provided the data have been stripped of identifiers, rendering research on such de-identified data outside of the scope of the Common Rule. However, that commentary also suggests that if an investigator commits in the informed consent form to discontinue any further use following withdrawal of broad consent, then that commitment should be honored, disallowing any future use of such data or biospecimens, even if de-identified. (82 Fed. Reg. at 7221.)

In the Broad Consent Guidance, SACHRP recommends that broad consent forms should expressly provide that withdrawal of broad consent will not prevent the completion of use of the subject's data and biospecimens in a study already commenced when the request to withdraw was received, and would not prevent the continued storage and use, for research integrity purposes, of identifiable data and identifiable biospecimens already used for research purposes. SACHRP also recommends that the broad consent make clear that when identifiable data or identifiable biospecimens are distributed to third parties pursuant to the broad consent form, consequently it will be difficult for the institution to recall such data or biospecimens.

V. IRB's Responsibilities in Performing Limited Review

As stated above, under § ___.104(d)(7) of the Final Rule, storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use shall be exempt from the requirements of the Common Rule, if, *inter alia*, an IRB conducts a limited review. The Final Rule does not describe, however, the extent of diligence required by an IRB to certify that broad consent was obtained and documented appropriately.

In its guidance, SACHRP recommends that a ''limited review'' by the IRB should entail an evaluation of the broad consent form used and a review of the process used to secure such consent, in order to assess whether the consent contains the necessary elements. More specifically, the Broad Consent Guidance recommends that IRB review should include review of a certification from an investigator describing the process by which broad consent was secured and affirming that the broad con-

sent was obtained from each subject and will be available for IRB review during the entire period of the study. The Guidance notes that this limited IRB review process can be conducted through either a full IRB or expedited review process.

In addition, in order for a study to be exempt from the Common Rule, under § ___.104(d)(8)(iii), an IRB must determine that the secondary research use of identifiable private information and identifiable biospecimens falls within the scope of the broad consent. Recognizing that the Final Rule does not further explain what is ''within the scope of the broad consent,'' SACHRP recommends that the IRB should review the actual template broad consent form(s) used or relied upon, in order to assess whether the proposed secondary research use falls within the scope of the broad consent that was secured.

VI. Return of Research Results

The Final Rule states that secondary research use of identifiable biospecimens and identifiable private information is exempt from the Common Rule, if, among other things, ''[t]he investigator does not include returning individual research results to subjects as part of the study plan.'' (§ ___.104(d)(8)(iv).) The Final Rule once again is silent, however, 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.

The Broad Consent Guidance offers recommendations on this provision. According to the Guidance, the return of individual research results need not actually occur for the research to be excluded from the exemption, but rather if the intention to return individual research results is part of the study plan, then the research would not qualify for exemption. However, the Guidance specifically notes that a study plan would nevertheless fall under the exemption if it allows for disclosure to subjects only of incidental findings, meaning clinically meaningful results that are unrelated to the study's design.

Importantly, SACHRP also notes the public benefits of returning results in certain situations, and therefore in developing the study plan, the Broad Consent Guidance urges sponsors and investigators to balance carefully the utility of returning individual research results against the increased potentially burdensome regulatory requirements resulting from not meeting the exemption criteria.

VII. Effect of Non-Regulatory Broad Consent

While the Final Rule creates a new regulatory scheme for ''broad consent,'' the research community has in a sense long relied on non-specific consent for future uses to allow institutions to collect, store, and even use subject data and leftover biospecimens for future research, as long as those future uses have been defined adequately under Pre-2018 Rule standards. In recognition of this historic practice, the Guidance recommends that future research consent forms containing a ''non-regulatory broad consent'' should continue to be effective, even in light of the newly established regulatory ''broad consent.'' In addition, after the effective date of the Final Rule, a consent for future research using identifiable data and/or identifiable biospecimens should be analyzed as before, to assure that the consent has sufficiently detailed the proposed future research use, even if the non-regulatory ''broad consent'' would not meet the regulatory criteria for ''broad consent'' under the Final Rule.

VIII. Use of a Single Combined Form for Primary Study Consent and Broad Consent

The Broad Consent Guidance addresses the permissibility of using a single combined form for the primary study consent and the broad consent. The Final Rule does not require that broad consent be obtained on a form separate from that of a primary study-specific consent, so long as the content and other requirements for broad consent are satisfied.

In its Guidance, SACHRP recommends that broad consent may be combined with a consent form for a primary research study in certain circumstances; however, a non-research clinical consent form may *not be combined* with a broad consent form. If a broad consent is offered for a primary study, the Guidance clarifies that it should be so offered as an optional adjunct to the primary study consent, allowing the participant to partake in the primary study without having to agree to the broad consent.

The Guidance acknowledges, however, that there are circumstances in which it is logical and appropriate for a broad consent to be required in order to participate in the primary study, specifically certain registry or biobanking studies, given that as a threshold matter it is generally understood that the biospecimens and data to be gathered are essential to future studies related to the purposes of the registry or biobanking study. SACHRP therefore has recommended that a broad consent be able to be combined with a consent form for a primary study such that the prospective individual can consent only to both the primary and future studies, or to neither, in appropriate, carefully defined, necessary circumstances. In those circumstances, SACHRP has recommended that the IRB carefully review such combined consents and determine that the purpose of the broad consent is in fact critical and integral to the aims of the primary research. The Guidance recommends that for any primary study consent that also requires the individual to provide broad consent, similar to the Health Insurance Portability and Accountability Act (''HIPAA'') Privacy Rule, that the purpose(s) of the broad consent be integral to the primary study aims.

In addition, SACHRP recommends that when broad consent is not an integral part of the primary study design, the single combined consent form should include an option for an individual to affirm or decline expressly whether to provide broad consent, whether through a signature line or initials box. This would allow the subject to communicate clearly and effectively that he or she refuses to grant broad consent, which, as previously discussed, would then prohibit IRB waiver of consent for the secondary research use of that subject's identifiable biospecimens and identifiable data. The Guidance further notes that this ability to refuse to grant broad consent is consistent with HIPAA, ''which permits a researcher within a HIPAA-covered entity to seek authorization for the use or disclosure of protected health information for a 'conditioned' research-related treatment activity (i.e., the primary study) and other 'unconditioned' research activities (e.g., future, unspecified research) in a single, combined authorization form.'' (Broad Consent Guidance, at 15-16.)

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IX. Conclusion

Under the Final Rule, researchers are afforded more options to secure permission to use identifiable data and identifiable biospecimens for secondary studies. The panoply of options now includes the following: (i) study specific-consent and full or expedited IRB review; (ii) broad consent and limited IRB review (under the exemptions that rely on broad consent); (iii) waiver of consent and full or expedited IRB review; (iv) other exemptions; or (v) de-identification to remove the research activity from the scope of the Common Rule, which would not require informed consent or IRB review.

The recommendations set forth in the Broad Consent Guidance, including the interpretation of a non-response to an offer of broad consent and the ability to combine a broad consent and primary study consent form, are intended to provide researchers helpful flexibility and clarify the regulatory pathway for securing broad consent. Practically speaking, given that health care institutions implementing a broad consent program will need to develop extensive broad consent and refusal-tracking systems, these provisions will likely be most relevant to those involved with biorepository or databank studies, where the use of broad consent would be specifically targeted to well-defined subject groups. Researchers in other settings may be less likely to view broad consent as their preferred mechanism for securing effective consent for unspecified future uses of data and biospecimens; other methods, such as IRB waiver of consent or ''non-regulatory broad consent,'' will likely be more common methods of seeking downstream consent in other research settings.

The broad consent guidance is at http://src.bna.com/rJc.

The template broad consent form is at http://src.bna.com/rJd.