

Exemption 4 applies to the secondary research use of identifiable private information or identifiable biospecimens. One change in the revised Common Rule is that the private information and biospecimens no longer have to be in existence prior to the start of the research. Under the revised rule, for example, a research study that proposes to analyze samples or information that will be collected for clinical purposes in the future could qualify for this exemption if it meets at least one of the applicability provisions.

Another change is that if an investigator records information about individuals in a nonidentifiable manner, the investigator must not attempt to re-identify or contact the research subjects.

Also, some new provisions have been added to Exemption 4 so that more research can be exempt. In the pre-2018 Common Rule, there are two provisions for when Exemption 4 can be used: (1) when the identifiable materials are publicly available, or (2) when the information is recorded by the investigator in a nonidentifiable manner. The revised Common Rule retains these two provisions, and it also adds two new ones:

When the investigator's secondary use of the identifiable private information is regulated under HIPAA as "healthcare operations," "research," or "public health." Note that HIPAA does not apply to biospecimens, so this provision applies only to the secondary use of identifiable private health information (which can include information obtained from biospecimens).

When the secondary research is conducted by or on behalf of a federal department or agency, using data collected or generated by the government for nonresearch purposes, and the information is subject to federal privacy standards and other requirements specified in the exemption.

[Refer to 45 CFR 46.104(d)(4) of the revised Common Rule.]

Exemption 7 is a new exemption in the revised Common Rule that covers the storage or maintenance of identifiable private information or identifiable biospecimens for secondary research. Secondary research refers to research with materials originally obtained for nonresearch purposes or for research other than the current research proposal. The exemption can only be used when there is broad consent from the subjects for the storage, maintenance, and secondary research use of their identifiable materials.

The use of exemption 7 in the revised Common Rule requires the IRB to conduct a limited review of specific requirements that pertain to the use of the exemption. The IRB is not asked to conduct a standard IRB review using all the criteria at 46.111. For Exemption 7, the IRB review is limited to the determinations described in 46.111(a)(8), which pertain to protections for privacy and confidentiality and broad consent.

[Refer to sections 45 CFR 46.104(d)(7), 111(a)(8), and 116(d) of the revised Common Rule.]

Exemption 8 is a new exemption in the revised Common Rule that covers the secondary research use of identifiable private information or identifiable biospecimens originally obtained for nonresearch purposes or for research other than the current proposal. There are four requirements that must be satisfied to use exemption 8: broad consent must be obtained from the subjects for the secondary research use of their identifiable materials, documentation or waiver of documentation of informed consent must be obtained, an IRB must conduct a limited review to make certain determinations relating to privacy and confidentiality protections and broad consent, and investigators cannot include the return of individual research results to subjects in the study plan. Note that this requirement does not limit an investigator's ability to abide by any other legal requirement to return individual research results.

[Refer to sections 45 CFR 46.104(d)(8), 111(a)(7) and 46.116(d) of the revised Common Rule.]

The use of Exemption 8 in the revised Common Rule requires the IRB to conduct a limited review of specific requirements that pertain to the use of the exemption. The IRB is not asked to conduct a standard IRB review using all the criteria at 46.111. For Exemption 8, the IRB conducts a limited review to determine whether the following criteria are met:

There are adequate privacy and confidentiality protections as required under 46.111(a)(7), and

The research to be conducted is within the scope of the broad consent.

[Refer to sections 46.104(d)(8) and 46.111(a)(7) of the revised Common Rule.]

Limited IRB review is a process that is required only for certain exemptions, and does not require an IRB to consider all of the IRB approval criteria in §46.111. In limited IRB review, the IRB must determine that certain conditions, which are specified in the regulations, are met. Limited IRB review may be done via the expedited review mechanism, that is, by the Chair or an experienced IRB member designated by the Chair (although it can also be conducted by the full IRB). Continuing review is not required.

[Refer to sections 45 CFR 46.109(a) and 46.109(f)(1)(ii) of the revised Common Rule.]

There are four exemptions that may require limited IRB review: Exemptions 2, 3, 7, and 8.

Exemption 2 is for research that only includes interactions involving educational tests, survey or interview procedures, or observation of public behavior if at least one of the three provisions included in this exemption is met. Limited IRB review is required only if the third provision of the exemption is being used—that the information obtained is recorded by the investigator such that the identity of the subjects can readily be ascertained either directly or through identifiers. For this provision of Exemption 2, the limited IRB review serves to determine that adequate provisions are in place to protect the privacy of subjects and maintain confidentiality of the data.

Exemption 3 is for research involving benign behavioral interventions in conjunction with specified data collection methods if the criteria listed in one of three possible provisions are met. Limited IRB review is required only if the third provision of the exemption is being used—that the information obtained is recorded by the investigator such that the identity of the subject can readily be ascertained either directly or through identifiers. For this provision of Exemption 3, the limited IRB review serves to determine that adequate provisions are in place to protect the privacy of subjects and maintain confidentiality of the data.

Exemption 7 is for the storage and maintenance of identifiable private information or identifiable biospecimens for potential secondary research use, for which broad consent is required. This exemption requires limited IRB review to determine that the requirements for broad consent are met; that broad consent is appropriately documented or documentation of broad consent is appropriately waived; and that there are adequate provisions in place to protect the privacy of subjects and maintain confidentiality of the data, if there will be a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained.

Exemption 8 is for secondary research involving identifiable private information or identifiable biospecimens, for which broad consent is required. This exemption requires an IRB to determine through limited review that there are adequate provisions in place to protect the privacy of subjects and maintain confidentiality of the data, and that the research to be conducted is within the scope of the obtained broad consent.

[Refer to sections 45 CFR 46.104(d)(2)(iii), 46.104(d)(3)(i)(C), 46.104(d)(7), and 46.104(d)(8)(iii) of the revised Common Rule.]

The limited IRB review process may be done either via the expedited review mechanism, that is, by the Chair or an experienced IRB member designated by the Chair, or by the convened IRB.

[Refer to sections 45 CFR 46.109(a), 46.110(b)(1)(iii), and 46.110(b)(2) of the revised Common Rule.]

There is one new element that has been added to the basic elements of informed consent at §116(b). This new element requires a notice about whether participants' information or biospecimens collected as part of the current research might be stripped of identifiers and used for other research in the future. The purpose of this is to increase transparency by letting participants know that it might happen. If potential participants find it objectionable, they may not want to participate in the study.

Consent forms will need to say either that information or biospecimens collected for the research might be stripped of identifiers and used in other research in the future, or that this will not happen. Note that this is only about future research use of information and biospecimens that will be stripped of identifiers. Consent for the future use of identifiable private information and identifiable biospecimens for future unspecified research is covered under the section for “broad consent,” or could also occur under conditions where an IRB determines that a waiver of informed consent is appropriate.

There are three new additional elements of informed consent at section 116(c). Note that these are additional elements; they may not be relevant to all studies, in which case, they wouldn’t need to be included. These new additional elements are all notices. One is a notice about possible commercial profit, the second is a notice about whether clinically relevant research results will be returned to the subjects, and the third is a notice about whether research activities will or might include whole genome sequencing.

[Refer to 45 CFR 46.116(c)(7), (8) and (9) of the revised Common Rule.]

There is a change regarding the waiver and alteration of informed consent in the revised Common Rule. There is one new waiver criterion, which applies to research with identifiable private information or identifiable biospecimens. This new criterion is that the IRB must determine that the research could not practicably be carried out without using the information or biospecimens in an identifiable form. The purpose of this additional criterion is that if the research could be done using non-identifiable information, then that is what should be done. In these cases, researchers shouldn’t be using identifiable information because it increases the risk of breaches of privacy or confidentiality.

[Refer to 45 CFR 46.116(e) and 45 CFR 46.116(f) of the revised Common Rule.]

Only the Common Rule (45 CFR 46, Subpart A) has been revised. The other HHS subparts have not been revised at this time. However, the revised Common Rule includes some changes to the applicability of exemptions to research that falls under the other subparts.

The exemptions are applicable to subpart B research (research with pregnant women, fetuses, and neonates) as long as the conditions of the exemptions are met.

The exemptions do not apply to research subject to subpart C (research with prisoners), except for research aimed at involving a broader subject population that only incidentally includes prisoners.

Exemptions 1, 4, 5, 6, 7, and 8 can apply to subpart D research (research with children) as long as the conditions of the exemptions are met. The first two provisions of exemption 2 (§46.104(d)(2)(i) and (ii)), are applicable to subpart D research involving educational tests or the observation of public behavior

when the investigator(s) do not participate in the activities being observed. The third provision of exemption 2 (§46.104(d)(2)(iii)) may not be applied to research with children. Exemption 3 does not apply to research with children.

[Refer to section 45 CFR 46.104(b) of the revised Common Rule.]