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Final Rule Material:
Changes to Exempt Determination Process

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Introduction

The Final Rule (45 CFR 46, Subpart A - "Federal Policy for the Protection of Human Subjects" [the Common Rule]) revised and expanded the categories for exempt research. New categories were added, and two new processes were introduced: **limited IRB review** and **broad consent**. This material will review the exempt determination processes and the new exemption categories.

This material uses the term "pre-2018 rule" to refer to the current Common Rule and "Final Rule" or "revised Common Rule" when referring to the revised rule. For consistency and clarity, it also uses citations to the U.S. Department of Health and Human Services (HHS) regulations at 45 CFR 46, Subpart A as published in the *Federal Register* on 19 January 2017.

How is research determined to be exempt?

The Final Rule did not specify or restrict who can determine if research is exempt. The institution usually has a policy on who has the authority to determine if research is exempt, but the Final Rule, like the pre-2018 rule, did not specify. Due to the potential for conflict of interest, however, the Office for Human Research Protections (OHRP) continues to recommend that investigators not be given the authority to make an independent determination that their own human subjects research is exempt. Limited IRB review as a condition of exemption must be conducted by an IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB.

Significant Change to Common Rule

The Final Rule established new exempt categories of research based on their risk profile. Under some of the new categories, exempt research would be required to undergo limited IRB review to ensure that there are adequate privacy safeguards for identifiable private information and identifiable biospecimens (HHS 2017).

Updates to Exemption Categories

- *Category 1 – Revised*
- *Category 2 – Revised*
- *Category 3 – Replaced**
- *Category 4 – Revised*
- *Category 5 – Revised*
- *Category 6 – Unchanged*
- *Category 7 – New*
- *Category 8 – New*

** (Pre-2018 Rule Category Eliminated / New Category Added for Final Rule)*

Summary of Changes

The pre-2018 rule had six exempt categories in 46.101(b). The revised rule gave exempt categories an entire section in 46.104, and now includes eight categories in 46.104(d)(1-8).

Below is a summary of the changes to each of the exempt categories from 46.104(d). Because one of the major emphases of the Final Rule revisions was to address concerns associated with social and behavioral research, this resource will highlight the changes that are most relevant for researchers in the social and behavioral sciences.

It is important to note that "exempt" does not always mean exempt from all of the requirements of the Common Rule (HHS 2017). For example, the new Exempt Category 7 includes specific regulatory requirements of broad consent and limited IRB review as a condition of being exempt from other regulatory requirements.

Category 1: Research in Established or Commonly Accepted Educational Settings

This category has been amended from the pre-2018 rule to include a condition that the research is not likely to have adverse impacts on students learning required educational content or assessment of educators who provide instruction (HHS 2017). The exemption may only be used for studies about normal educational practices.

Category 2: Educational Tests, Surveys, Interviews, Observations of Public Behavior

During the time of the pre-2018 rule, this was the category most used by researchers in the social and behavioral sciences. Under the pre-2018 rule, research in this category may be exempt if the identity of the subjects could not be readily ascertained either directly or indirectly and if the disclosure of identifiable data would not cause harm.

The new regulation allows for exemption as long as one of the three criteria is met:

(1) Information obtained is not identifiable
(2) Disclosure outside of the research would not put subjects at risk of harm
(3) Information obtained can be identifiable but the IRB has done a limited IRB review in keeping with 46.111(a)(7), which relates to there being adequate provisions for protecting privacy and maintaining confidentiality

Importantly, the revised Common Rule eliminated the "and" – instead there is an "or." That is, research could be exempt that is any of the following:

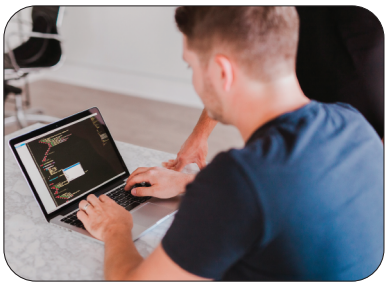
(1) Not Identifiable
(2) Does not pose any risk if there is disclosure (regardless if identifiable or not)
(3) Does not pose any risk if there is limited IRB review in keeping with the 46.111(a)(7) criteria

The Final Rule allows for the exemption of research collecting identifiable information with the potential to cause harm if disclosed, provided that the IRB has determined that "there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data" (46.117(a)(7)). This new requirement is called a limited IRB review.

Also, the Final Rule revised this category to include visual or auditory recording as research methods. Surveys also cannot include collection of biospecimens or interventions, as those additional activities would disqualify the research from this category.

When the research is subject to Subpart D and includes children, Category 2 still does not allow surveys or interviews or the observer participating with children (public behavior observation without intervention is permitted).

Category 3: Benign Behavioral Interventions in Conjunction with the Collection of Information From Adult Subjects



This is a new category. Benign behavioral interventions are defined as "brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing" (HHS 2017).

An example provided is having subjects solve puzzles under various noise conditions.

Research using deception is not eligible for exemption in this category unless the subjects prospectively agree that they will be unaware of or misled regarding the nature and purpose of the research.

As with research in Category 1, exemption is permitted if the data are recorded in such a way that the identities of the subjects cannot be readily ascertained either directly or indirectly or if the identities can be ascertained, a disclosure of the subjects' responses outside the research setting would not reasonably place the subjects at risk of harm. Alternatively, if the subjects' identities can readily be ascertained and if a disclosure of subjects' responses has potential to harm subjects, the exemption is permitted if the IRB conducts a limited review and determines that there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data.

Important Notes about Category 3	• Deception is allowed if certain criteria are met • This exemption is only for benign behavioral research with adults, and is not applicable to children

Category 4: Secondary Research for Which Consent is Not Required

This category covers secondary research uses of identifiable private information or identifiable biospecimens. The Final Rule revised and clarified the pre-2108 rule category for the use of secondary use of data. Category 4 does not require informed consent if at least one of the criteria listed below is met.

There are four available options for use of the exemption:

1. Use of publicly available identifiable private information or identifiable biospecimens.
2. Information recorded by the investigator in such a way that the identity of the subjects cannot be readily ascertained, and the investigator will neither contact the subjects nor re-identify subjects.
3. Research use of identifiable health information when that use is regulated by HIPAA as health care operations, research, or public health activities and purposes as those terms are defined in HIPAA.
4. Analysis of data on behalf of a federal agency or department – as opposed to an investigator-initiated analysis of federally supplied data – if the requirements of certain federal laws are met.

It is important to note that data do not need to be existing ("on the shelf") at the time of the research study, as was previously required by the pre-2018 rule. The data can be collected prospectively and still be used for exempt research under Category 4 in the Final Rule.

Category 5: Research and Demonstration Projects that Are Conducted or Supported by a Federal Department or Agency

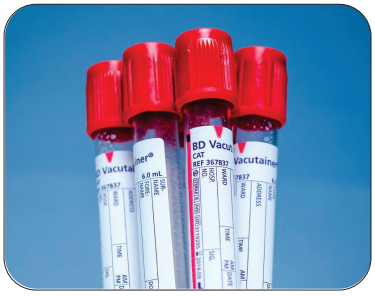
The category has been revised to: allow research supported by a federal agency (not just conducted) to qualify for this exemption; provide examples of the types of public benefit and service programs covered by the exemption; and clarify the federal components for which the exempt research is subject to approval (for example, delegated subordinate agencies).

Category 6: Taste and Food Quality Evaluation and Consumer Acceptance Studies

This is the only unchanged category.

Category 7: Storage or Maintenance for Secondary Use for Which Broad Consent is Required

This is a new category. This category is for the storage of identifiable biospecimens and identifiable private information, prior to secondary analysis. The storage and maintenance may be exempt if the IRB conducts a limited IRB review to determine that there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data, and if broad consent is obtained.



What is secondary research?

Secondary research is re-using identifiable information and identifiable biospecimens that are collected for some other "primary" or "initial" activity (HHS 2017).

For example, medical records, leftover tissue/samples from a hospital's pathology specimen repository, or excess blood drawn for clinical purposes.

Secondary research is not surveys, interviews, or collection of samples by the investigator (that would have a primary research purpose).

Institutions can create their own templates for broad consent (which may be electronic). Broad consent includes at least seven and possibly nine elements of consent. It includes five standard elements of consent such as providing information to subjects (or legally authorized representatives) in languages understandable to the research subjects (or the legally authorized representatives). Broad consent also includes elements particular to secondary analysis, such as a general description of the data and of the types of research that may be conducted. Additional elements may be needed, if for example, the research involves whole genome sequencing.

This category may be more widely used by biomedical researchers to allow them to use data gathered during the practice of research and medicine either by another researcher or through another study. However, social and behavioral researchers may also use identifiable private information for secondary analysis.

Category 8: Secondary Research for Which Broad Consent is Required

This is also a new category. Category 8 allows the secondary analysis of existing private identifiable data and identifiable biospecimens provided broad consent was secured and the documentation of consent was either secured or waived. The IRB must also conduct a limited IRB review to determine that there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data as noted in 46.111(a)(7), and that the use is within the scope of the broad consent. Category 8 also requires that the investigator does not include returning individual research results to subjects as part of the study plan; however, the exemption does not prevent investigators from returning results if required by law.

Similar to Category 7, this category may be more widely used by biomedical researchers. However, social and behavioral researchers may also use identifiable private information for secondary analysis.

Exempt Research and Subpart Applicability

Subpart B

- *The Final Rule is consistent with the pre-2018 rule.*
- *Each of the exemptions can be applied to research subject to Subpart B.*

Subpart C

- *The Final Rule changes the pre-2018 rule to allow the exemptions to apply to Subpart C for research involving a broader subject population if the research only incidentally includes prisoners.*
- *The Final Rule permits the exempt secondary research of information or biospecimens from subjects who are prisoners, if that research is not seeking to examine prisoners as a subpopulation.*
- *The Final Rule allows subjects to continue in exempt research if they become prisoners during a study.*

Subpart D

- *The Final Rule allows research with children to be exempt for categories 1, 4, 5, 6, 7, and 8.*
- *TheFinal Rule does not permit the exemption of research with children that includes identifiable information and is reviewed under a limited IRB review.*
- *Consistent with pre-2018 rule, observation of thepublic behavior of children under Category 2 is allowed only if the researcher does not participate in theactivities being observed.*
- *Consistent with pre-2018 rule, surveying and interview procedures with children may not be exempt.*

Broad Consent for Exempt Research

Broad consent will be an optional alternative that an investigator may choose instead of, for example, conducting the research on nonidentified information and nonidentified biospecimens, having an Institutional Review Board (IRB) waive the requirement for informed consent, or obtaining consent for a specific study.

(Final Rule Preamble, HHS 2017)

The Final Rule allows the use of broad consent from subjects for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens. As noted above, it is an alternative informed consent process with required elements. Broad consent was developed to balance public concerns about the use of information or biospecimens for research without consent. Broad consent aims to respect subjects' autonomy and provide appropriate privacy safeguards, and reduce burden on investigators that would result from requiring specific consent for each secondary research study.

It remains to be seen how broad consent will be used by researchers in the social and behavioral sciences, humanities, or education; however, it will be an available option for consent.

Where does data come from?

Researchers in the social and behavioral sciences, humanities, and education may collect:

- De-identified data
- Data with informed consent
- Data from research approved without informed consent
- Data for secondary analysis when informed consent was secured by the original data collector

Can broad consent be altered or waived?

The IRB cannot omit or alter any of the elements of broad consent. However, the IRB can waive the requirement of documentation (signature). The IRB must determine that broad consent is appropriately documented or that the requirement of documentation has been waived in accordance with 46.117.

Further, if a subject refused to provide broad consent, the IRB cannot waive consent for the storage, maintenance, or secondary research use of the subject's identifiable private information or identifiable biospecimens. This is meant to respect a subject's autonomy.

Limited IRB Review as a Condition of Certain Exempt Research

The Final Rule introduced a new concept of limited IRB review as a condition of exemption for four of the exempt categories listed above.

When is limited IRB review required?

For Categories 2 and 3, it is only sometimes an option.

- A limited IRB review is only required if the research involves identifiable information (the regulation states "information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects" [HHS 2017]). Then, the IRB must conduct a limited IRB review to determine if there are adequate provisions in place to protect privacy and confidentiality as defined under 46.111(a)(8).

For Categories 7 and 8, it is always required. These are the broad consent exempt categories.

- Category 7 requires limited IRB review for secondary research involving storage or maintenance of identifiable private information or identifiable biospecimens to determine if conditions of 46.111(a)(8) are met. This includes if broad consent was obtained and documented (or waiver of documentation was obtained) in accordance with the requirements for broad consent, and if there are any changes made for research purposes to the way information or biospecimens are stored or maintained, there are adequate protections for privacy and confidentiality.

> "Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information" (46.102(e)(5)).

> "An identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen" (46.102(e)(6)).

- Category 8 is also for secondary research, and requires a limited IRB review to determine if broad consent was obtained and documented (or waiver of documentation was obtained) in accordance with the relevant regulatory requirements, and there are adequate provisions in place to protect privacy and confidentiality. Category 8 also stipulates that the researcher does not include returning individual research results to subjects as part of the study plan (except where legally required).

How is limited IRB review applicable to research in the social and behavioral sciences, education, and the humanities?

For research in these areas, a limited review may be required when the research involves benign behavioral interventions in conjunction with the collection of information from adult subjects (Category 3) and when it involves educational tests, surveys, interviews, or observations of public behavior (Category 2). A limited review must be conducted for exempt research in these categories when information is recorded in a manner in which the identity of the subjects can be readily ascertained and a disclosure of the data could pose a risk of harm (limited review does not need to be conducted if the identifiable data would not reasonably place the subjects at risk).

Who may be a limited IRB reviewer?

An IRB may use the expedited review procedure to review research for which limited IRB review is a condition of exemption.

"Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB" (HHS 2017).

There is only one criterion for limited review for these categories: "When appropriate, there are adequate provisions to protect the privacy of the subjects and to maintain the confidentiality of the data" (46.111(a)(7)).

The regulation does not provide guidance on what are adequate provisions to protect privacy and maintain confidentiality. The Final Rule's preamble listed some considerations for IRBs.

IRB Considerations for Privacy and Confidentiality Safeguards (Final Rule Preamble)

- Extent to which identifiable private information is or has been de-identified and the risk that such de-identified information can be re-identified
- Use of the information
- Extent to which the information will be shared or transferred to a third party or otherwise disclosed or released
- Likely retention period or life of the information
- Security controls that are in place to protect the confidentiality and integrity of the information
- Potential risk of harm to individuals should the information be lost, stolen, compromised, or otherwise used in a way contrary to the contours of the research under the exemption

References

- *U.S. Department of Health and Human Services (HHS). 2017. "Federal Policy for the Protection of Human Subjects." Federal Register 82(12):7149-274.*

- *U.S. Department of Health and Human Services (HHS). 2018. "Federal Policy for the Protection of Human Subjects: Six Month Delay of the General Compliance Date of Revisions While Allowing the Use of Three Burden-Reducing Provisions During the Delay Period." Federal Register 83(118):28497-520.*