

Revised Common Rule Consideration for Use of State-Mandated Central Cancer Registry Data: Guidance, Examples, and Q&A

Background

The protection of study participants (officially referred to in regulations as human subjects) in federally-funded research is governed by the U.S. Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP)¹. OHRP has developed federal policy including the Common Rule^a regarding biomedical and behavioral research involving participants in the US.² This rule provides guidance to Institutional Review Boards for oversight of human research.

Since the Common Rule was initially promulgated in 1991, the volume and landscape of research involving study participants have grown in scale and become more diverse. Revisions to the Common Rule took effect in 2018^b that address this changing landscape. This 2018 version of the Common Rule is “intended to better protect human subjects involved in research, while facilitating valuable research and reducing burden, delay, and ambiguity for investigators. These revisions are an effort to modernize, simplify, and enhance the previous system of oversight.”^c

In the case of population-based cancer registries, the 2018 version of the Common Rule’s clarification regarding public health surveillance activities, as well as new requirements for downstream use of identifiable information, are particularly relevant for use in minimal risk studies. The purpose of this document is to discuss how the 2018 version of the Common Rule applies to a cancer registry activities connected to human subject research.

What is Minimal Risk Research?

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.⁴ Research using central cancer registry data has generally been considered minimal risk. Collection of data by the state-mandated cancer registries does not constitute human subjects research and is not subject to the Common Rule from the perspective of DHHS. The 2018 version of the Common Rule has instituted new standards to reduce burden, delay and cost associated with additional and unnecessary paperwork, review, and approvals. Under the 2018 version of the Common Rule, many typical cancer cohort/cancer registry linkage studies are now considered exempt from IRB review. Importantly, the role of cancer registries releasing registry data for secondary research and data analysis (a.k.a. downstream research) will usually not be considered human subjects research under the 2018 Common Rule.

^a The Common Rule is the baseline standard of ethics to which any government-funded research in the U.S. is held; nearly all U.S. academic institutions hold their researchers to these statements of rights regardless of funding. The Common Rule Applies to non-exempt human subjects research supported or funded by a Common Rule Agency. Twenty federal agencies have adopted the 2018 version of the Common Rule.

^b The revised Common Rule was published in the Federal Register on January 19, 2017 and went into effect on January 21, 2018. For research subject to pre-2018 requirements, the pre-2018 requirements shall apply unless the research is transitioning to comply with the 2018 requirements. [§46.101(l)(3)]

^c <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html>

Do Registry Activities Require IRB Approval?

While the creation and operation of state-mandated cancer registries is public health surveillance, and not human subjects research, a registry may allow use of its data for human subjects research, referred to as “downstream research”. In order to determine whether a downstream study is non-exempt human subjects research, one must ask the following three questions about the study/research project in this specific order (see flowchart, Appendix 1):

- 1) Does the activity involve research?
- 2) Does the research involve human subjects?
- 3) Is the research with human subjects exempt?

Examples of various types of studies including cancer registry data and the OHRP interpretation regarding the need for IRB review are included below. Additional information is included in the Q&A section at the end of this document and can also be found in the list of resources.

Examples of Central Cancer Registry Downstream Research

The Office for Human Research Protection provided a webinar entitled “Considerations for Registries and Data Centers under the Revised Common Rule”⁵ on August 14, 2020. The webinar was geared toward central cancer registries and their affiliated IRBs. The webinar provided information on the Common Rule requirements for IRB oversight, which activities require IRB approval, how to determine if activities involve research, and whether IRB continuing review is required. A significant portion of the webinar focused on various examples of downstream research involving registry data and whether IRB review is required. Some of these examples are provided below.

EXAMPLE 1.0

Researchers in an NCI-funded study will administer surveys to study participants once they agree to participate in the study. Researchers will then send the participants’ PII to state cancer registries to check if they have been diagnosed with cancer. Registries will only link this information to their data and, if there is a match, release those full identifiable records to the researchers.

Does the researcher’s downstream protocol require IRB approval under the Common Rule?

More information needed. This is likely research with primary and secondary research components but it could be a public health surveillance activity. It is likely human subjects research, possibly exempt.

Do registry activities require IRB approval under the Common Rule?

No. Even if the protocol is non-exempt human subjects research, the registry is only linking to respond to a request for releasing information to researchers. Registry release should occur according to the terms and standard operating procedures (SOPs) of the state cancer registry.

Example 1.1

Researchers in an NCI-funded study will administer surveys to study participants once they agree to participate in the study. Researchers will then send the participants’ PII to state cancer registries to check if they have been diagnosed with cancer. Registries will only link this information to their data and, if there is a match, release those full identifiable records to the researchers, who will collect blood samples from the matching participants.

Does the researcher’s downstream protocol require IRB approval under the Common Rule?

Likely yes. This is likely research involving human subjects, and no exemption seems relevant.

Do registry activities require IRB approval under the Common Rule?

No. Even if protocol is non-exempt human subjects research, registry is only linking to respond to a request for releasing information to researchers. Registry release should occur according to the terms and SOPs of the cancer registry.

EXAMPLE 1.2

Researchers in an NCI-funded study will administer surveys to participants once they agree to participate in the study. Researchers will then send the participants' PII to state cancer registries to check if they have been diagnosed with cancer. Registries will only link this information to their data and, if there is a match, release those full identifiable records to the researchers. Researchers will contact participants for consent to collect tumor samples from their healthcare providers.

Does the researcher's downstream protocol require IRB approval under the Common Rule?

More information needed: This is likely secondary research, but it could be a public health surveillance activity. It is likely human subjects, but could be exempt.

Do registry activities require IRB approval under the Common Rule?

No. Even if protocol is non-exempt human subjects research, registry is only linking to respond to a request for releasing information to researchers. Registry release should occur according to the terms and SOPs of the cancer registry

EXAMPLE 1.3

Researchers in an NCI-funded study will administer surveys to participants once they agree to participate and obtain their consent to obtain tumor samples if they develop cancer. Researchers will then send the participants' PII to state cancer registries to check if they have been diagnosed with cancer. Registries will link this information to their data and, if there is a match, registry will reach out to participants' healthcare providers to obtain tumor samples and then release the full identifiable records to the researchers.

Does the researcher's downstream protocol require IRB approval under the Common Rule?

More information needed: This is likely secondary research, but it could be a public health surveillance activity. It is likely human subjects research, but could be exempt.

Do registry activities require IRB approval under the Common Rule?

If downstream protocol is not exempt, then registry activities require IRB approval. The registry's employees are obtaining identifiable private information for the purpose of the downstream protocol.

EXAMPLE 2.0

Researchers in an NCI-funded research study ask the registry to provide contact information for breast cancer patients in the registry. The registry will only release the patients' contact information to the researchers. Researchers will ask the patients to join the study and obtain blood samples from those who agree.

Does the researcher's downstream protocol require IRB approval under the Common Rule?

Likely yes. This is likely research involving human subjects, and no exemption seems relevant.

Do registry activities require IRB approval under the Common Rule?

No. Only releasing materials to investigators is not considered involved in the downstream research. Registry release should occur according to the terms and SOPs of the cancer registry.

EXAMPLE 2.1

Researchers in an NCI-funded research study ask the registry to provide contact information for breast cancer patients in the registry. The registry will contact patients to ask them for permission to be contacted by these researchers. Researchers will then ask patients to join the study and obtain blood samples from those who agree.

Does the researcher's downstream protocol require IRB approval under the Common Rule?

Likely yes. This is likely research involving human subjects, and no exemption seems relevant.

Do registry activities require IRB approval under the Common Rule?

No. Only asking subjects for permission to be contacted by downstream investigators is not considered involved in the downstream research. Registry release should occur according to the terms and SOPs of the cancer registry.

Questions & Answers

1. What are Public Health Surveillance activities that are deemed not to be research?

- Activities conducted, supported, requested, ordered, required, or authorized by a public health authority (a person or authority responsible for public health matters as part of its official mandate, or a person, or entity under a grant of authority or contracted by such agency).
- Activities limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance.

2. When does the activity involve research?

Research refers to a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge. There are 4 types of activities deemed **NOT** to be research:

- Scholarly and journalistic activities;
- Public health surveillance activities;
- Information collection for criminal justice purposes; and
- Operational activities for national security purposes.

3. When does the research involve human subjects?

A human subject, or participant, is a living individual about whom an investigator conducting research either obtains information or biospecimens through intervention or interaction with the individual, or obtains, uses, studies, analyzes, or generates identifiable information or identifiable biospecimens.

4. What is secondary research?

Secondary research involves use of information/biospecimens originally collected for a purpose other than the proposed research. Secondary research that only uses non-identifiable materials/data is not human subjects research.

5. Which registry activities do not require IRB approval for the purpose of downstream research?

- Only releasing data is not considered involvement in the downstream research (even if identifiable).

- Other regulations beyond the Common Rule and institutional policies may apply (e.g., HIPAA, state law).
- Registry release of data should occur according to its terms and policies/procedures.

6. Which registry activities may require IRB approval for the purpose of downstream research?

Whether registry activities for a downstream protocol require IRB approval depends on:

- Whether the downstream protocol is non-exempt, human subjects research (if not, regulations do not apply, IRB review not required).
- Whether registry's employees or agents are involved in human-subjects research activities for the downstream protocol. Simply releasing identifiable materials to investigators is not considered human subjects research activity.
- For more information visit:
<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-engagement-of-institutions/index.html>.

7. When are registries' employees or agents involved in the human subjects research for the purpose of downstream research?

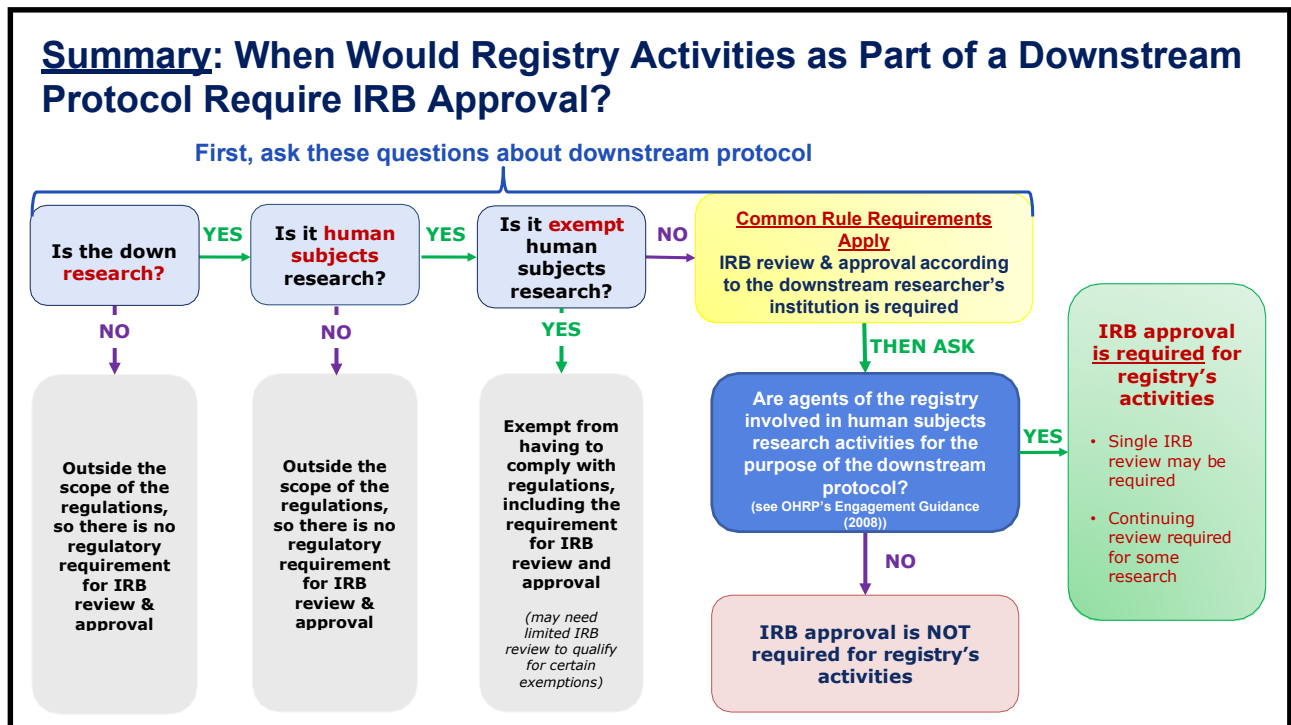
Registry employees or agents are involved in the research when they:

- Are part of the downstream protocol research team;
- Obtain for the purpose of (an HHS-funded) downstream protocol data about or biospecimens from study participants through intervention or interaction;
- Obtain Identifiable private information about the study participants; or
- Obtain informed consent of study participants for the research. Asking study participants for permission to be contacted by downstream investigators is NOT considered involvement.
- For more information visit: <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-engagement-of-institutions/index.html>.

8. Does the Common Rule require IRB continuing review for studies that meet expedited review criteria?

Unless an IRB determines otherwise, continuing review of research is not required for research eligible for expedited review in accordance with §46.110. [§46.109(f)(1)(i)].

Appendix 1: Flowchart for Downstream Protocol



¹ U.S. Department of Health & Human Services, Office for Human Research Protections. (2017, January 19). *Regulations*. Retrieved June 15, 2020 from <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/index.html>

² U.S. Department of Health & Human Services, Office for Human Research Protections. (2016, March 18). *Federal Policy for the Protection of Human Subjects ('Common Rule')*. Retrieved June 15, 2020 from <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html>

³ U.S. Government Publishing Office. (2017, January 19). *Federal Register: Rules and Regulations*. Vol. 82(7265) [PDF file]. Retrieved June 15, 2020 from <https://www.gpo.gov/fdsys/pkg/FR-2017-01-19/pdf/2017-01058.pdf>

⁴ *Public Welfare*, 45 C.F.R. § 46.102(7) (2017). Retrieved June 15, 2020 from https://www.ecfr.gov/cgi-bin/text-idx?SID=7f5862546652623faa6cddc27c5d1c02&mc=true&node=se45.1.46_1102&rgn=div8

⁵ *Considerations for Registries and Data Centers under the Revised Common Rule*. Jaime O. Hernandez, J.D., M.Be., Division of Education and Development (DED), Office for Human Research Protections (OHRP), August 14, 2020 webinar. Posted on the NAACCR website: <https://www.naacccr.org/irb-information-for-cina/>