



THE OHIO STATE UNIVERSITY

Secondary Use of Data and Specimens

Biomedical & Cancer

Part 2: What type of Review is Required?

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Regulatory & Exempt Determinations



Objectives

- ✓ Review relevant definitions related to secondary use of data and/or specimens
- ✓ Review exempt and expedited IRB categories that apply to secondary use projects
- ✓ Explore the process used to determine review requirements for secondary use of materials
- ✓ Discuss possible review outcomes



Overview

- Background
- Considerations and types of reviews/determinations
- Review categories, definitions, examples, and FAQs
- Related Ohio State Human Research Protection Program (HRPP) policies and guidance



Background

- The volume of research involving secondary use of data and bio-specimens has grown exponentially over the past several years
- Current practices have evolved nationally to place greater emphasis on the ethical obligation to obtain prospective informed consent for collection and use of data and/or specimens for research and to reconsider research uses of data and specimens (particularly identifiable materials) for which consent was never obtained



Background (cont.)

- A multidisciplinary working group representing investigators, IRB leaders, and research administrators was convened
- Existing guidance, national and international standards, and peer institutions' policies and practices were considered and recommendations were forwarded to the IRB Policy Committee (IPC)
- The Research Involving Data and/or Biological Specimens Policy was updated and approved by the IPC to include recommendations from this working group



How are review requirements determined?



There are three main questions to determine if review is required*:

Definitions	Yes	No
Is the project <i>research</i> according to the applicable regulations (DHHS, FDA, etc.)?	continue	stop
Does the project involve <i>human subjects</i> according to the applicable regulations (DHHS, FDA, etc.)?	continue	stop
Is our institution <i>engaged</i> in the research involving human subjects?	continue	stop

*the order of the questions matters!



After asking the three questions, there are four possible determinations:

1. The proposed project/activity is not regulated human subjects research (HSR) and may be conducted without requesting exemption or IRB review (no formal application needed); or
2. The proposed project/activity is regulated HSR, but Ohio State is not engaged in the research and the project may be conducted without requesting exemption or IRB review (no formal application needed); or



Possible Review Determinations (cont.)

3. The proposed project/activity is regulated HSR, Ohio State is engaged, and the project appears to meet the criteria for exemption from IRB review (an exempt application should be submitted to request an exemption determination by ORRP staff); or
4. The proposed project/activity is regulated HSR, Ohio State is engaged, and the project requires IRB review (an IRB application should be submitted for Expedited or Convened review)



As a reminder:

We previously addressed the first two outcomes in Part 1 of this presentation series. You can access the Part 1 presentation online on the ORRP website at [ORRP Education Sessions](#)





Once we establish review is required, we ask these questions to determine the level of review required:

Definitions	Yes	No
Do <u>all</u> activities for the project fall under one or more of the six <i>exemption</i> categories?	Stop (submit exempt application)	Continue
Do <u>all</u> activities fall under one or more of the seven main <i>expedited</i> IRB review categories?	Stop (submit expedited IRB application)	Stop (submit regular IRB application to proceed with convened review)



Applicable Categories of Exempt Review



General Exemption Requirements (as related to secondary use)

- Only research that is limited to activities in one or more of the exempt categories may be determined to be exempt from IRB review
- Research that includes both exempt and non-exempt activities cannot be split apart in order to request exemption for one activity. This stipulation is true both internally and when collaborating with outside universities. If all activities to be conducted for the study as a whole do not fall under one or more of the exemption categories, then no portion of the project can be submitted for exemption



General Exemption Requirements as related to secondary use (cont.)

- Research involving prisoners may not be determined to be exempt
- Research that is subject to FDA regulations may not be determined to be exempt under DHHS exemption categories
- At Ohio State, proposed research may not be greater than minimal risk to be determined exempt



Exempt Category #1:

Research conducted in established or commonly accepted educational settings (e.g., schools, colleges, and other sites where educational activities regularly occur), involving normal educational practices, such as:

- a. Research on regular and special education instructional strategies; or
- b. Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods



Exempt Category #1 reminders:

- Research must be on *normal* educational practices (not just using data collected in/from schools for other purposes)
- Data accessed under exempt category #1 can be prospective, retrospective, or both
- Data collected can be identifiable or potentially identifiable (however, if identifiable, the project should not pose risk to participants)
- Consent should be obtained when practicable



Exempt Category #1 examples:

- A research study involving the collection of student data to compare student performance on a professional exam before and after a new required course is implemented
- A research project looking at student records, demographics, satisfaction, and graduation rates in field X across institutions
- A research project analyzing standardized testing data over several years



Exempt Category #4:

Research involving the collection or study of *existing* data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that participants cannot be identified, directly or through identifiers linked to the participants



Existing

“Existing data or specimens” means that the materials must be “on the shelf” at the time (or before) the research is submitted for an exemption determination

- There must be no plans for ongoing collection
- Serial applications (e.g., intending to submit an application at the end of each year to obtain the year’s data) are not permitted



Individually Identifiable

Materials are considered “individually identifiable” when the identity of the participant is, or may readily be ascertained by, the investigator or the investigator’s staff, or associated with the information

For research involving use of or access to protected health information (PHI), this means that no HIPAA identifiers (which include dates, zip codes, etc.) can be collected or received

Note: Limited data sets released from data repositories with IRB approval to release such data sets to other investigators (such as the Information Warehouse at Ohio State) may not be considered individually identifiable with data use agreements in place



Individually Identifiable (cont.)

In order for a project involving patient information to be considered to be de-identified at Ohio State, there must be more than 25 potential subjects that fit the inclusion criteria

Please note that projects with more than 25 individuals may still be considered potentially identifiable. The ability to de-identify data depends on the specific project, the data point(s) in question, and the potential for indirect identification. Materials are considered de-identified when all direct personal identifiers are permanently removed (e.g., from data or specimens), no code or key exists to link the information or materials back to their original source(s), and the remaining information cannot reasonably be used by anyone to identify the source(s)



Protected Health Information (PHI)

Health information that is individually identifiable (contains at least one of the 18 HIPAA identifiers) and created or held by a covered entity





HIPAA Identifiers

1. Names
2. All geographical subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code in certain circumstances
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
4. Phone numbers
5. Fax numbers
6. Electronic mail addresses



HIPAA Identifiers (cont.)

7. Social Security numbers
8. Medical record numbers
9. Health plan beneficiary numbers
10. Account numbers
11. Certificate/license numbers
12. Vehicle identifiers and serial numbers, including license plate numbers
13. Device identifiers and serial numbers
14. Web Universal Resource Locators (URLs)
15. Internet Protocol (IP) address numbers
16. Biometric identifiers, including finger and voice prints
17. Full face photographic images and any comparable images
18. Any other unique identifying number, characteristic, or code



Exempt Category #4 reminders:

- Cannot be FDA regulated (no device development, research results cannot be held for review or intended for submission to the FDA in support of a report or marketing permit)
- “Existing data or specimens” means that the materials must be “on the shelf” at the time (or before) the research is submitted for an exemption determination
- No identifiers can be collected as part of the data intended for analysis
- No keys to subject identifiers can be retained



Exempt Category #4 reminders (cont.):

- In some instances, investigators can create and use a temporary list or key to access information from more than one location, but only if it is part of the same record (e.g. the patient's regular Ohio State medical record information is housed in two different databases, or exists partially in paper, partially electronically). Only a simple list (e.g., a list of MRNs) or a simple key (e.g., MRN = random study number) can be created, and this list/key must be destroyed immediately after collection, prior to any analysis, processing, or use of the data/specimens. If investigators need to retain a link, IRB review is required.
- The link can only be used to access information for a single source (e.g. the patient's Ohio State medical record), and it cannot be used to combine completely separate sources of data (e.g. the Ohio State medical record with data from the patient's nursing home record, QI record, school record, work record, and/or private physician's record)



Exempt Category #4 example:

A research project that involves data collection from IHIS to investigate the relationship between age, medication type, and outcomes of three common medications used to treat X

- The date range of data to be collected is 01/01/2010 – 01/01/2016
- Only age, race, gender, medication type, dose, comorbidities, and outcome are collected (no HIPAA identifiers)
- Investigators will create a separate, temporary list of MRNs to aid in data collection, but the list will be destroyed immediately after collection, prior to any analysis



Exempt Category #5:

Research and demonstration projects that are conducted by, or subject to, the approval of (federal) department or agency heads, and that are designed to study, evaluate, or otherwise examine:

- a. (federal) public benefit or service programs;
- b. procedures for obtaining benefits or services under those programs;
- c. possible changes in or alternatives to those programs or procedures; or
- d. possible changes in methods or levels of payment for benefits or services under those programs



Exempt Category #5 (cont.):

Additional requirements (all must apply):

- The programs under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act);
- The research or demonstration project must be conducted pursuant to specific federal statutory authority;
- There must be no statutory requirement that the project be reviewed by an IRB; and
- The project must not involve significant physical invasions or intrusions upon the privacy of participants



Exempt Category #5 helpful reminders:

- In order to qualify under category 5, the research must be on federal programs and subject to the approval of federal department or agency heads—research on a local/state program does not qualify under this exemption (thought it may fall under one or more of the other exemption categories)
- In general, if your research is eligible for this exemption, the federal agency will provide a letter indicating that the research is eligible for exemption under category 5



Exempt Category #5 examples:

- At the request of The U.S. Department of Agriculture, an Ohio State investigator will conduct research to compare the current use of the Supplemental Nutrition Assistance Program (i.e., food stamps) by Americans compared to twenty years ago
- At the request of DHHS Centers for Medicare & Medicaid Services, an Ohio State researcher will study elements of the implementation of the Affordable Care Act



Applicable Categories of IRB Review



Expedited IRB Category #5:

Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes, such as medical treatment or diagnosis

Note: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. This listing refers only to research that is not exempt



How does expedited category #5 differ from exempt category #4?

Expedited IRB Category #5 is used for accessing data originally collected for non-research purposes when:

- Separate sources need to be combined (e.g., education record with medical record);
- Fewer than 25 individuals at Ohio State meet the inclusion criteria;
- Potential or actual identifiers are needed (e.g., HIPAA identifiers, need to retain key during analysis); or
- Data needs to be collected that will come into existence after the date the research is proposed (i.e., not all currently existing)



Expedited IRB Category #5 example:

A research project that involves data collection from IHIS to investigate the relationship between age, medication type, and outcomes of three common medications used to treat X

- The date range of data to be collected is 01/01/2010 – 01/01/2018 as there is an additional drug that was only recently approved and investigators want to compare data on its outcomes as well
- Investigators need to collect HIPAA identifiers (such as dates) for analysis
- Investigators need to retain a key to identifiers during analysis in case they need to go back and confirm the data collected or determine the need to collect additional data points



Expedited IRB Category #7:

Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies

Note: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. This listing refers only to research that is not exempt



Expedited IRB Category #7 examples:

- Research utilizing existing national datasets where non-public, potentially identifiable (or identifiable) versions are utilized but the research is intended to study group characteristics or behavior
- Accessing identifiable information and recordings from a private linguistics bank for a secondary study on elements of language X
- Secondary analysis research utilizing existing, identifiable Ohio State research data where the secondary research is intended to study group characteristics or behavior



Full (Convened) IRB Review:

Whenever non-exempt human subjects research contains activities that do not fall under one or more of the expedited review categories, or if the project is potentially greater than minimal risk, then convened review is required





Full (Convened) IRB Review examples:

- Investigators need to access their own research data or banks to collect data to use for a secondary study that does not fall under expedited category #7, and the original sources contain identifiers (even if researchers do not intend to use the identifiers for the secondary project)
- Research that intends to collect and analyze existing, identifiable data that poses greater than minimal risk to individuals (e.g., data about criminal behavior, illegal drug use, etc.)



Frequently Asked Questions



How do I receive a written determination about the review requirements necessary for my project?

A determination can be requested from ORRP via email at ORRPDeterminations@osu.edu

- Investigators will need to provide sufficient materials for a determination: e.g., research protocol/description, grant (as applicable), information about collaborators, contracts/agreements (if any), and any study-specific materials (e.g., data points to be obtained)
- Upon receipt of complete information, review requirement determinations are usually made within five business days (additional information may be requested)



What is the difference between prospective and retrospective studies?

Retrospective studies collect or evaluate materials that are existing (on the shelf) at the time that the research is conceived and submitted for IRB review or exemption

Prospective studies plan to collect/evaluate at least some materials that are not yet in existence at the time the research is conceived and submitted for IRB review or exemption

Note: Studies may have both prospective and retrospective elements





Is there a difference between the rules for use of data and use of tissue?

In general, human subjects review requirements hinge on the DHHS and FDA (as applicable) definitions of **research** and **human subject**, and are therefore treated similarly in the human subjects research review process

It is important to remember that FDA-regulated research has a different definition of human subject that can include de-identified specimens. Also, there may be additional laws, rules, processes, considerations, and required protections for the use of data vs. specimens (e.g., FERPA, HIPAA, GINA, IBC, etc.)



I am only using data and/or specimens from deceased individuals; do I need IRB review or exemption?

No. Use of existing materials from deceased individuals (e.g., autopsy materials) does not constitute research with human subjects. Please note that other laws, university processes, and requirements may still apply (e.g., biosafety/IBC review, HIPAA, material transfer agreements (MTAs), DUAs, etc.)





Do case reports require IRB review or exemption?

It depends. If the project is limited to one or two case reports, (defined as a factual description of the clinical features and/or outcomes of the case(s) without any additional testing, evaluation, analysis, or review of others for comparison), then no review is required. Three or more reports, or projects involving additional testing, evaluation, analysis, or comparison require IRB review or exemption (as applicable)

Even if no IRB review or exemption is required, investigators will still need to work with the stewards of the records to determine whether permission is required, to satisfy other requirements (e.g., FERPA, HIPAA), and to fill out the proper forms for access to and use of the data



I have left-over or existing materials from a research project; can I de-identify them and share them with other investigators or use them myself without review?

No. An investigator may not de-identify data and/or specimens under his or her control (such as materials collected by the investigator for another study) in order to share them with others or to use them for future research without IRB review and approval

Secondary (i.e., “new”) use of materials obtained for primary research purposes by an investigator with IRB approval (or exemption) requires either IRB review of an amendment or a new protocol describing the proposed secondary use, depending on the previous approval (or exemption) and the new research objective. Informed consent may also be required for this new use, depending on the scope of the original consent and the newly proposed research



Do I need to obtain consent if I am only collecting data/specimens that will come into existence regardless of the research?

Maybe. In order to qualify for a waiver of consent (and a waiver of HIPAA authorization if PHI is involved), investigators must meet certain regulatory criteria. In some instances the IRB may determine that consent (and authorization, when applicable) is required if the investigator does not meet the required waiver criteria (e.g., unable to justify why it is impracticable to conduct the research without a waiver). For information on the requirements for a waiver of informed consent, see the policy [Informed Consent and the Elements of Informed Consent](#)



For secondary research with previously collected data and/or specimens, is additional informed consent or a waiver request required, or is the original consent that was obtained for the data/specimen's collection adequate for the new research?

In certain, limited circumstances, the secondary research activities may be adequately anticipated and described in the informed consent obtained for the data and/or specimen collection, and further informed consent or waiver is not required. However, in cases where the additional research is not sufficiently addressed in and “covered” by the previous consent process, then the IRB must either approve a new consent process or a waiver of the informed consent process

Note: Waiver of informed consent for secondary use of data and/or specimens is generally not permitted in FDA-regulated research



Does obtaining exemption or IRB approval for my research automatically grant me access to the materials I need at Ohio State or elsewhere?

Not necessarily; the stewards of the materials have ultimate control over access to the materials in question, and they decide whether to grant access to researchers

Obtaining an exemption or approval from the IRB is only the first step in starting research involving access to PHI. Once obtained, the research team will need to contact the appropriate Privacy Officer or records steward to request access to the materials in question and provide proof of the exemption or IRB approval. As applicable, investigators will also need to provide documentation of any approved waivers or partial waivers of consent and/or HIPAA authorization. Additional forms may need to be completed



HRPP Policies, Links, and Guidance



HRPP Polices

<http://orpp.osu.edu/irb/osuirbpolicies/hrpppolicies/>

HRPP Glossary

<http://orpp.osu.edu/irb/osuirbpolicies/hrppglossary/>

FAQs

<http://orpp.osu.edu/irb/irb-faqs/>



Exempt Guidance Page

<http://orpp.osu.edu/irb/investigator-guidance/exempt/>



Ohio State Research Involving Data and/or Biological Specimens Policy:

<http://orpp.osu.edu/irb/osuirbpolicies/hrpppolicies/>

FERPA Policy

https://registrar.osu.edu/policies/privacy_release_student_records.pdf

Student Data

<http://oesar.osu.edu/>

HIPAA Guidance

<http://orpp.osu.edu/irb/investigator-guidance/hipaa/>

Ohio State University Privacy Officers

http://orpp.osu.edu/files/2011/10/privacyofficers_060115.doc



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Protecting Human Subjects in Research at Ohio State



Human Subjects

The Human Research Protection Program is responsible for all Ohio State research involving human subjects. The HRPP's primary responsibility is to protect the rights and welfare of human research subjects, in accordance with Department of Health and Human Services (DHHS) and Food and Drug Administration (FDA) regulations.

NEWS

[Spring 2015 IRB Newsletter now available](#)

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[New System for IRB and Exempt Submissions](#)