

FAQs about Requests for Determination of whether IRB Review is Required

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GENERAL QUESTIONS

1. What **types of determinations** does OHSRP provide?

OHSRP provides determinations of ‘excluded from IRB review’ or ‘not excluded from IRB review’ for NIH research activities. In general, ‘Human subjects research’ requires IRB review unless it meets certain categories of research deemed “exempt” from this requirement.

Human subjects research refers to activities in which a researcher obtains (1) data about the subjects through intervention or interaction with them; (2) identifiable data about the subjects of research; or (3) obtains the informed consent of human subjects for research. The term ‘exempt’ applies to a specific subcategory of research activities that are considered ‘human subjects research’ under the human subjects regulations, but do not require IRB review (see FAQ #2 below or [45 CFR 46.101](#)). If you are only using de-identified specimens/data for research, you are not conducting ‘human subjects research’ and can likely get a determination of ‘excluded from IRB review’.

2. What does it mean to get an **exemption** for my research project?

Some researchers will receive a determination of ‘excluded from IRB review’ because under the regulations their activities are considered ‘exempt’ human subjects research. There are six categories of *exempt* research; two categories of *exempt* activities are commonly submitted to OHSRP for review. Exemption category 2 is used for research “involving the use of educational tests, survey procedures, interview procedures, or observation of public behavior”, e.g., survey research for which no private or sensitive information is collected. To meet the criteria for exemption category 2, when identifiers are recorded, “disclosure of the human subjects’

responses outside of the research cannot reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability or reputation".

Exemption category 4 is used for research "involving the collection or study of existing data, documents, records, pathological or diagnostic specimens" e.g., a retrospective medical chart review where no identifiers are retained. To meet the criteria for this category, the 'sources must be publicly available' or the research must be conducted without recording any identifiable information or codes that are linked to identifiable information. For example, at the Clinical Center, the medical record number is a code that links to the specific patient.

3. I am using [de-identified \(anonymous or coded\) specimens/data](#) for my research and have no access to identifiers. Do I need to submit a request for determination?

Per NIH policy, when an NIH investigator is conducting research with de-identified specimens/data, submission of a request for determination and receipt of a formal determination is required prior to any research being conducted. This includes research projects that use data that is publicly accessible from on-line sites.

4. I plan to obtain [de-identified \(anonymous or coded\) specimens/data](#) from a collaborator or outside source to use as part of [the research on an NIH IRB-approved protocol](#). Why can't I receive approval through a determination for this activity?

If the research with de-identified specimens/data will be conducted as part of an active NIH IRB-approved protocol, the new research activity cannot be approved through an OHSRP determination. The specimens/data and the planned research must be described in the protocol and there must be IRB review and approval.

5. I have some [specimens/data \(linked to identifiers\)](#) that were collected under an active NIH IRB-approved protocol. I would like to de-identify them and use them to conduct secondary research. Can I receive a determination for this activity?

When an NIH investigator has identifiers associated with the human sources of the specimens/data and is conducting research with these materials, he/she is considered 'engaged in human subjects research' under the regulations. As long as the protocol remains open with the IRB, the investigator should not de-identify the specimens/data under the protocol to be able to conduct new research without IRB review and approval. The IRB must review and approve the research. The IRB can provide guidance as to whether the research can be addressed through an amendment to the protocol or requires a new protocol.

6. I have some identified specimens/data that were collected under an active NIH IRB-approved protocol. I would like to [de-identify them and send them to a collaborator for secondary research](#). Can I receive a determination for this activity?

The answer is, it depends. If the protocol is still open and the specimens/data are linked to identifiers, you must first insure that you have obtained consent for sharing specimens/data for the planned research activity or broad consent for sharing for future research. Then, if you are simply sharing the specimens/data with another researcher and do not intend to be a collaborator in the planned research, you can submit a request for determination for the sharing and OHSRP is likely to determine that IRB review is not needed. If you are maintaining identifiers associated with the specimens/data and plan to collaborate in the research, e.g. receive results of analysis and co-author a paper with the collaborator, then you will need IRB approval for the new research. See FAQ #5 above.

7. I have [de-identified specimens/data from a closed IRB-approved protocol](#) that I would like to use for secondary research. I no longer have access to the code key or any identifiers associated with the materials. Can I receive a determination for this activity?

You should be able to receive a determination that IRB review is not needed for your activity. One exception is a situation in which even after identifiers are removed, you might be able to readily ascertain the identities of the subjects when reviewing the data. Sometimes this is possible because the data is from a very small group of individuals with whom you directly interacted. In this case, you may need IRB approval for the activity. Please consult OHSRP if you have questions.

8. Why can't I receive a determination if I have [already started or finished my project](#)?

The purpose of requesting and receiving an OHSRP determination is to ensure that your planned research project does not require IRB review and approval per NIH policy and to protect the rights and welfare of research participants. Generally OHSRP does not provide formal determinations once a project has already begun. In some cases, we will provide informal feedback. Please contact OHSRP if you have already started your project and require guidance.

9. What do you mean when you ask if NIH is conducting a research activity that is part of an [FDA-regulated protocol](#) approved by an outside IRB? Why is this important?

By FDA-regulated research, we mean research that is focused at least in part on studying the safety or efficacy of unapproved drugs or devices, or new uses of approved drugs or devices. These types of studies must meet additional requirements under FDA regulations. One situation when this is important is if samples are collected from subjects taking an investigational drug at an outside institution and sent to NIH, after de-identification, for assaying with a subsequent return of results to the outside investigator. If this is the case, you should confirm with your collaborator that the planned research activity at NIH is included in the IRB/ethics committee-approved *protocol and consent form* at the other institution. If you are engaging in a

collaboration involving IRB-approved research utilizing a drug or device at another institution, always verify that IRB review and appropriate consent have occurred before submitting your request for determination.

QUESTIONS ABOUT THE NEED FOR APPROVAL FOR RESEARCH WITH SPECIFIC TYPES OF SPECIMENS/DATA

10. I am using [derivatives](#) for my research. Do I need to submit a request for determination?

Research with certain derivative samples does not require an OHSRP determination. These include certain derivatives of materials originally obtained from humans, including: human cell lines (including iPSCs/hESCs), recombinant DNA clones of human genes, infectious agents isolated from human tissue, DNA, RNA, nucleic acid isolates, and cell fragments/subparts, if those materials are not individually identifiable or linked by a code to a living individual.

If additional information about the patient/subject is being shared along with the derivative, an OHSRP determination is required. Research with tissue, blood, or components of blood (e.g. plasma, serum, buffy coat, peripheral blood mononuclear cells, white blood cells, blood fractions), fecal material, urine, or sputum does not fall under this category, and requires an OHSRP determination.

11. Do I need to submit a request for determination or obtain IRB approval if I am conducting research using [iPSC lines](#)?

Research with de-identified iPSC lines does not require an OHSRP determination. If a new iPSC line is being derived from identified specimens, or the iPSC line is associated with identifiers, or the human donor is known to the investigator, IRB review and approval is required. Also if the iPSC line or the results of research will be used as part of an IRB approved protocol, the protocol should be amended to address the use of the line and submitted for IRB approval. Other important requirements can be found here: <https://oir.nih.gov/sourcebook/ethical-conduct/special-research-considerations/use-human-stem-cells/guidelines-human-embryonic-induced-pluripotent-stem-cells/induced>

12. Do I need to submit a request for determination or obtain IRB approval if I am conducting research using [hESC lines](#)?

Research with a de-identified hESC line does not require an OHSRP determination. If the hESC line is identified or the human donor is known to the investigator, IRB review and approval is required. Also if the hESC line or the results of research will be used as part of an IRB approved protocol, the protocol should be amended to address the use of the line and submitted for IRB approval. Other important requirements can be found here:

<https://oir.nih.gov/sourcebook/ethical-conduct/special-research-considerations/use-human-stem-cells/guidelines-human-embryonic-induced-pluripotent-stem-cells>

13. Do I need to submit a request for determination or obtain IRB approval if I am conducting research using specimens/ data from [deceased individuals/autopsy materials](#)?

Research with specimens/data from individuals who are confirmed to be deceased does not require an OHSRP determination or IRB approval. The exception is when the results of the research will be used as part of an IRB approved protocol. In this case, the protocol should be amended to obtain approval for the inclusion of the specimens/data as part of the research.

14. I am getting specimens/data from a [commercial repository](#) for my research? Does that mean no determination is required?

If you are purchasing de-identified specimens/data from a for-profit entity (e.g. the Coriell Biorepository), no OHSRP determination is required. An academic-affiliated institution or non-profit that only charges processing and shipping charges for specimens or prepared slides does not meet the definition of a commercial entity.

15. Do I need to submit a request for determination or obtain IRB approval if I am conducting research using [fetal tissue](#)? What are the requirements that need to be met?

The use of fetal tissue for research always requires submission of a request for determination or IRB review and approval. If the specimens are de-identified, OHSRP may determine that IRB review is not needed. However, if the specimens are identified or the investigator knows the identify of the human donor, IRB review and approval is required. Also, if the results of research with de-identified fetal tissue will be used as part of an IRB approved protocol, the protocol should be amended to address the use of the specimens (rather than requesting an OHSRP determination). In addition, research with fetal tissue requires submission of an Investigator Attestation and confirmation of donor consent to the reviewing entity (OHSRP or the IRB). The forms and other important requirements can be found here:

<https://oir.nih.gov/sourcebook/ethical-conduct/special-research-considerations/fetal-tissue-research>

16. Are there special requirements if I am [generating genomic data \(i.e. WES/WGS or GWAS\)](#) as part of my project and I am requesting a determination?

There is no special information that needs to be included as part of your submission for a determination, but NIH has a specific genomic data sharing policy that must be followed when an investigator is generating large-scale genomic data. The policy can be found here:

<https://gds.nih.gov/03policy2.html>

QUESTIONS RELATED TO DE-IDENTIFICATION OF SPECIMENS/DATA

17. What is a [de-identification agreement](#)? Do I need to submit a de-identification agreement as part of a submission in the new web-based system? What types of documents meet the requirements for a de-identification agreement?

When the NIH investigator is receiving coded specimens/data, and the person sending the specimens/data has the code key which links the specimens/data to individuals, the NIH investigator should obtain a **de-identification agreement** or other equivalent agreement indicating that the party providing the coded specimens/data will not reveal the link to re-identify the human source of the specimens/data.

The investigator does not need to upload the de-identification agreement into the new web-based system, but he/she must obtain the agreement and then attest that he/she has obtained it in the application.

Examples of de-identification agreements include an MTA, a data sharing policy, or data use or transfer agreement which states that personal identifiers will not be shared. Investigators may also exchange agreement language, e.g. over e-mail, that is modified to reflect the nature of the arrangement, using a variation on the sample language below:

Sender of coded specimens/data:

I, [Sender's Name] of [Sender's Institution], holder of the code-key, cipher or identifiers for the shared [specimens, data (specify)], promise not to release the individually identifiable information about the subjects from whom the [specimens, data (specify)] derive, to [Recipient's Name] at [Recipient's Institution] per the provisions of U.S. Code 45 C.F.R. 46.

Recipient of coded specimens/data:

I, [Recipient's Name] of [Recipient's Institution], recipient of the [specimens, data (specify)], promise not to request individually identifiable information about the subjects from whom the [specimens, data (specify)] derive, from [Sender's Name] at [Sender's Institution] per the provisions of U.S. Code 45 C.F.R. 46.

The de-identification email template can be found here:

<https://federation.nih.gov/ohsr/nih/formtmp.php>

18. What is an [honest broker](#) and when do I need one? Do I need to submit an honest broker form as part of a submission in the new web-based system?

An honest broker is an individual, who is not a member of the research team, who is tasked with de-identifying or re-coding specimens or data. When an NIH investigator wants to conduct new research with existing individually identified specimens/data that are currently part of an IRB-approved protocol, IRB review and approval is required. However, in some cases, the investigator does not need to maintain identifiers and the protocol is at a point when it can be closed, e.g. the research has already been published. In rare cases, an investigator may have access to identified specimens/data from a protocol that has been closed with the IRB. In these circumstances, to conduct new research without IRB review, the specimens/data would need to be de-identified by an independent party, i.e. the honest broker. An NIH investigator may want to obtain specimens/data (which are not under an active NIH IRB-approved protocol) from another NIH staff member, e.g. radiology, who is unable to de-identify the specimens/data prior to sharing them. The NIH investigator may identify and utilize an “honest broker” to do this. See FAQs #5 & 6 to learn more about the requirements when specimens/data were collected under an open NIH IRB-approved protocol. For more information on the honest broker process, please see HRPP SOP 6:

https://federation.nih.gov/ohsr/nih/ohrdocs/SOP_6_v1_9-17-13_508.pdf

In the new web-system, the investigator does not need to upload the signed honest broker agreement, but he/she must attest that he/she has obtained the agreement. The honest broker agreement and certification can be found here:

<https://federation.nih.gov/ohsr/nih/formtmp.php>

19. What constitutes an **identifier? Is date of birth considered an identifier?**

The following are examples of personal identifiers:

- Names or initials
- Date of birth* (if full date given)
- Social security number
- Street address
- Telephone and fax numbers
- Electronic mail addresses
- Medical record number
- Health plan identifier
- Biometric identifiers, including finger and voice prints
- Full face photographic images or any comparable images
- Research study/protocol subject number
- Pedigree – a diagram or text that indicates which individuals within a family express or carry a genetic trait or medical condition (i.e. in the case of families with a rare disease)
- Account numbers
- Certificate/license numbers
- Vehicle identifiers and serial numbers, including license plate numbers
- Identifying numbers related to devices, such as serial numbers
- Internet protocol (IP) address numbers

QUESTIONS ABOUT SURVEY/INTERVIEW/FOCUS GROUP RESEARCH

20. I am conducting surveys (interviews or focus groups) for research purposes. Is it possible to get a determination for my project?

If the NIH research team is collecting or receiving de-identified data through on-line surveys for research purposes, the activity is likely not considered 'human subjects research' and the senior investigator will probably receive an OHSRP determination of 'excluded from IRB review'.

When the NIH research team is interacting with subjects or collecting identifiable data through surveys, interviews, or focus groups, the activity may qualify for a determination of exempt from IRB review under certain circumstances. An exemption is possible for this type of activity, provided that none of the potential responses could harm the subject if the information was released outside of the research context. Please note, the project could also be determined to be exempt, when no identifiers are being collected, even if some of the data is considered sensitive. When this type of research involves collection of identifiable and sensitive data, there must be IRB review and approval. To provide a determination for this type of research, OHSRP needs to review the information sheet, consent language, or instructions, and the survey instrument, focus group script and/or questions, along with the information included in the request for determination application. Certain minimal information (or consent language) must be provided to the prospective subjects, either in writing or orally.

21. What type of information minimally needs to be in the information sheet/consent form provided to subjects for survey research?

Per NIH HRPP SOP 6, when conducting surveys (interviews or focus groups) for research purposes, the subject should be informed that the activity is being conducted for research purposes and that his/her participation is voluntary; and provided with a description of the procedures involved (e.g. approximate time commitment, number of questions, number of follow ups, etc.), and the name and contact information for the lead researcher. You should also consider addressing the following topics, when applicable: 1) purpose of the research; 2) description of the subjects being targeted (number and criteria); 3) any anticipated risks or benefits; 4) methods for withdrawal and whether data will be maintained if one withdraws; 5) whether identifiers will be collected or not; 6) if identifiers will be collected, how confidentiality will be insured, i.e. that no identifiers will be used in any resulting publications or presentations; and 7) compensation.

22. I am conducting surveys (interviews or focus groups) for research purposes. Do I need to collect planned and cumulative enrollment data? Why?

The project requires* submission of a planned enrollment report prior to project start and collection and submission of cumulative enrollment data for each fiscal year during enrollment if it:

1. Involves the prospective collection of survey, interview or focus group data and/or receipt of identifiable survey, interview or focus group data;
2. Meets the criteria of 'exemption category 2'; and
3. Qualifies as 'clinical research' as defined by the NIH (The NIH definition of clinical research can be found here:
<http://grants.nih.gov/grants/glossary.htm#ClinicalResearch>),

The Planned Enrollment Report and the Cumulative Inclusion Enrollment Report can be found here: <https://federation.nih.gov/ohsr/nih/formtmp.php>

*For more information about the requirements for the Inclusion of Women and Minorities as Participants in Research see:

http://grants.nih.gov/grants/funding/women_min/women_min.htm

QUESTIONS ABOUT THE NEED FOR APPROVAL FOR SPECIFIC OTHER ACTIVITIES

23. Do I need to submit a request for determination or obtain IRB approval if I am conducting a [QI/QA activity](#)?

When QA/QI activities are being conducted both for the purposes of quality assessment/improvement and to conduct research (i.e. to develop or contribute to generalizable knowledge about a topic), an OHSRP determination or IRB approval is required. If NIH staff will be interacting with the participants to collect specimens/data, or they will receive identifiable specimens/data to meet both goals, NIH IRB approval may be required. If QI/QA activities are being conducted to collect information solely to improve practices or services, without an intention to contribute to generalizable knowledge, no submission of a request for determination or IRB approval is required.

24. Do I need to submit a request for determination or obtain IRB approval for a [case report](#) about one patient? What about if I am doing a [case series](#)?

A case report about one patient, under the care of the NIH staff member, usually does not require a submission of a request for determination nor IRB review. This is true when no changes were made to the patient's care for the sake of reportability. An OHSRP determination or IRB approval is generally required when a case series (i.e. multiple patients) is envisioned. When the identities of the patients are known to the NIH staff members who are authoring the case series, IRB approval is generally required.

25. Do I need to submit a request for determination or obtain IRB approval if I am conducting a [program evaluation](#)?

When evaluation results will be shared outside of the relevant program or IC and/or the evaluation involves participants being assigned to groups for comparison; or a comparison of a standard versus non-standard intervention, an OHSRP determination or IRB approval is required. If NIH staff will be interacting with the participants to collect private information or they will receive identifiable, private information as part of the project, NIH IRB approval may be required.

26. Do I need to submit a request for determination for an [NIH BTRIS Query](#) in which I will get de-identified data for research purposes?

Most BTRIS requests will generate an automated determination after the information is entered in the BTRIS application. When a project requires that the BTRIS team do a manual data extraction, a request for determination is required. IRB approval is required when an investigator wishes to obtain and maintain identified data from BTRIS for his/her research project.