Harvard Pilgrim Health Care, Inc.
Harvard Pilgrim Health Care Institute, LLC
Office of Sponsored Programs

Policy and Procedure

TITLE: Exemption Determination

PURPOSE:

To set forth the policy and procedure for:

- determining when certain human subjects research activities are exempt from applicable statutes, regulations, codes and guidance; and
- conducting the ethical evaluation of exempt research.

PERSONS AFFECTED:

This policy & procedure (P/P) applies to all Harvard Pilgrim Health Care, Inc. (HPHC) and Harvard Pilgrim Health Care Institute, LLC (HPHCI) (collectively, HPHC/I) personnel engaged in research, teaching or research administration activities in support of the charitable and educational mission of HPHC.

POLICY:

The Institutional Review Board (IRB) shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities, including exempt research activities under 45 CFR 46.104 for which limited IRB review is a condition of exemption (under §46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7), and (8)).

The authority to determine whether any research activity is exempt from applicable statutes, regulations, codes and guidance rests with the IRB Chair or delegate. The IRB Chair or delegate shall:

- have the authority to represent the HPHC IRB;
- have no direct involvement in the activity he or she is examining; and

- be familiar with the federal, state, local and foreign statutes, regulations, codes and guidance governing the research, organizational policies, and the nature of the research.

The determination of the IRB Chair or delegate will consider the exemption criteria for all federal, state, local and foreign statutes, regulations, codes and guidance applicable to the research, recognizing that research activities that are exempt from one set of rules might not be exempt from another set of rules.

The HPHC IRB shall:

- provide the determination decision to the investigator(s) via IRBNet;
- indicate in the determination, the reference to one or more categories under which the exemption is granted; and
- maintain records of exemption determinations.

Although most exempt research requires no further oversight to be conducted ethically, some exempt research raises ethical concerns or requires certain measures to protect research participants. Therefore, the IRB Chair or delegate shall also conduct the ethical evaluation of exempt research.

All human subjects research that is exempt under 45 CFR 46.104(d)(1) through (8) will be conducted in accordance with other applicable federal, state, local and foreign statutes, regulations, codes and guidance applicable to the research activity as well as applicable policies and procedures and the Belmont Report.

DEFINITIONS:

For the purposes of this policy:

Authority to Determine that Research is Exempt
The authority to determine whether the research meets 45 CFR 46.104 exemption criteria belongs to the IRB, via the IRB Chair or delegate. Investigators are not permitted to determine whether research is exempt.

Common Rule (See **Glossary**)

Ethical Exemption Criteria
Research must meet the following ethical criteria in order to be approved, even if it falls into one or more exemption categories:

1. Research presents no more than minimal risk to research subjects.
2. Selection of research subjects is equitable.

3. If research involves interaction with research subjects, the IRB shall determine whether there should be an informed consent process that will disclose such information as:
   a. the activity involves research;
   b. a description of the procedures involved in the research;
   c. that participation in the research is voluntary; and
   d. name and contact information for the investigator.
4. If private identifiable data are recorded, provisions for maintaining confidentiality of data are adequate.

Exempt Categories

Unless otherwise required by law or governmental agencies, research activities in which the only involvement of human subjects will be in one or more of the categories listed below in section (d), are exempt from the requirements of the 2018 Revised Common Rule except that these research activities must still comply with the requirements of this section and as specified in each category. Use of the exemption categories for research subject to the requirements of subparts B, C, and D is as follows:

(a) Subpart B (Additional Protections for **Pregnant Women, Human Fetuses and Neonates**) – Each of the exemptions at this section may be applied to research subject to Subpart B **if the conditions of the exemptions are met.**

(b) Subpart C (Additional Protections Pertaining to Biomedical and Behavioral Research Involving **Prisoners** as subjects) – The exemptions at this section do not apply to research subject to Subpart C, **except for research aimed at involving a broader subject population that only incidentally includes prisoners**.

(c) Subpart D (Additional Protections for **Children** Involved as Subjects in Research) – The exemptions at (d)(1), (4), (5), (6), (7), and (8) may be applied to research subject to subpart D if the conditions of the exemptions are met. Paragraphs (d)(2)(i) and (ii) of this section only may apply to research subject to Subpart D involving educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed. Paragraph (d)(2)(iii) of this section may not be applied to research subject to Subpart D.

(d) Except as described in the above paragraph, the following categories of human subjects research are exempt from this policy:

(1) Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the

comparison among instructional techniques, curricula, or classroom management methods.

(2) Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observations of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(ii) Any disclosure of the human subject's responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained I 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, and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7) to determine if there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of the data.

(3) (i) Research involves benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

(A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(C) The 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, and an IRB conducts a limited IRB review to make the determination required by45 CFR 46.111(a)(7) to determine if there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of the data.

(ii) For the purpose of this provision, benign behavioral interventions are 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. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in a research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

(4) Secondary research for which informed consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of , a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on t information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S. C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S. C. 552a, and if, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

(5) Research or demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act as amended.

(i) each Federal department or agency conducting or supporting the research and demonstration projects must establish on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

(ii) [Intentionally blank].

(6) Taste and food quality evaluation and consumer acceptance studies: (i) if wholesome foods without additives are consumed, or (ii) if a food is consumed that contains a food ingredient oat or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

(7) Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determination required by 45 CFR 46.111(a)(8).

(8) Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met: (i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with 45 CFR 46.116(a)(1) through (4), (a)(6), and (d); (ii) Documentation of informed consent or waiver of documentation of informed consent was obtained in accordance with 45 CFR 46.117; (iii) An IRB conducts a limited IRB review and makes the determination required by 45 CFR 46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph(d)(8)(1) of this section; and (iv) The investigator does not include returning individual research

results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results

The following categories of clinical investigations are exempt from FDA regulation (21 CFR 56.104):

1. Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before July 27, 1981.

2. Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.

3. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.

4. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Any other research subject to FDA regulation cannot be exempt. Research is subject to FDA regulation if it involves a drug, medical device, food, or other product regulated by the FDA.

Exempt Research

Research that involves research subjects that presents no more than minimal risk and falls within one or more of the exempt categories set forth in 45 CFR 46.104(d) and 21 CFR 50 and 56, may qualify as exempt from IRB review. However, before this determination is made, the IRB Chair or delegate shall also determine whether the research is subject to applicable state, local or federal law. Note: IRB submission is required for all exempt research. Research that involves prisoners, human fetal tissue or surveys and interviews with children may or may not qualify as exempt depending on specific categories as noted.

Human Subject (see GLOSSARY)

Interaction
Communication or interpersonal contact between investigator and subject.

Intervention
Includes both physical procedures by which information or biospecimens are gathered (for example venipuncture) and manipulation of the subject or the subject's environment that are performed for research purposes.

Minimal Risk
The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than that ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Private Information
Includes information about:

1. behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place; and
2. information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator associated with the information) in order to constitute research involving human research subjects.

Research
A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:

- Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

- Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are 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 (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products) Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
- Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
- Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions. (45 CFR 46.102(l)).

PROCEDURE:

1. IRB staff is alerted to a new project submission in IRBNet via email and by the appearance of the *New Project* submission flagged in the *Submissions Manager* page in IRBNet.

2. A new project submission must include the following:
   a. a completed HPHC IRB Exemption Determination Form (the investigator's request for a determination from the IRB as to whether the research is exempt from compliance with the Common Rule) and applicable attachments;
   b. the study protocol;
   c. the PI's electronic signature; and
   d. the grant manager's signature (for HPHC studies) or Atrius Health Director of Research signature (for Harvard Vanguard Medical Associates/Atrius Health studies).

3. The new project submission should also include the following:
   a. The investigator is instructed on the exemption form that if HPHC is the prime recipient of a federal award through a grant, contract or cooperative agreement but another institution or entity will carry out the non-exempt human subjects research activities, the Office for Human Research Protections (OHRP) considers HPHC engaged in human subjects research and HPHC IRB approval is required;
   b. IRB approvals from other institutions (when appropriate); and
   c. other materials as requested.

4. If the submission is missing information or requires clarification, the submission package is "unlocked" in IRBNet by IRB staff and the required follow-up is listed in the message to the

investigator detailing the reasons for this action. Once the required information is present and all updates are made, the investigator (or investigator's designee) will mark the revisions complete in IRBNet which queues the submission back to IRB staff.

5. When the submission is complete, the IRB Chair or delegate shall determine whether a research proposal meets the exemption criteria by reviewing the research against the exempt categories listed above.

6. Whether the PI requests an exemption determination or not, the IRB Chair or delegate at the same time shall also review the research and determine whether the research is exempt from any other state, local or country regulations where the research is being conducted.

7. If the exemption requires a limited IRB review as applicable to exempt categories 2, 3, 7 or 8, the submission will be assigned to the IRB Chair or delegate to conduct the limited review via expedited review assignment. A limited IRB review does not require a continuing review.

8. The Senior Compliance Manager (SCM) shall:
    a. update the *Review Details* of the submission in IRBNet, adding the agenda date and review type;
    b. *share* the submission assigning her/himself as the primary reviewer and the IRB Chair if a secondary review is necessary. If the exempt review requires a limited IRB review, the reviewer will be denoted as an expedited reviewer. The SCM will click on the alarm bell if assigning the submission to the IRB Chair to ensure automatic notification of a completed review;
    c. if assigning the submission to the IRB Chair, the SCM will also notify the IRB Chair the submission is ready by clicking to notify users that access to the submission has been granted and including a note regarding the submission.

9. The IRB Chair or delegate will conduct the exemption determination, and limited IRB review as applicable, review using the Exempt Determination Checklist.

10. Following the determination that research is exempt, the IRB Chair or delegate will conduct the ethical evaluation of the exempt research applying the Ethical Exemption Criteria section on the Reviewer Sheet – Exemption Determination.

11. The SCM and IRB Chair (as applicable) will:
    a. record any comments regarding their review in the *Reviewer Comments* section in IRBNet;
    b. upload a completed reviewer worksheet (if necessary);
    c. record the determination of the review; and

d. mark the review complete.

12. If the IRB Chair requests additional information prior to completing the review, the SCM will follow-up with the investigator and/or Project Manager and will notify the IRB Chair when a reply has been received.

13. After the exemption determination has been made, the SCM will update IRBNet with the appropriate determination within five (5) days following the review. The following fields will be updated:

a. Review type, Action, Effective Date, Project Status; and
b. the meeting minutes will be recorded as appropriate.

14. An exemption determination letter will be generated using the Exemption Determination Letter template, edited to indicate the reference to one or more categories under which the exemption was granted.

15. The letter will be published in IRBNet and the notification of the published letter will automatically be sent to the investigator in IRBNet to indicate that an exemption determination letter has been produced.

16. The SCM will apply submission tag(s) as applicable to the study.

17. If applicable, the *Project Notes* section in IRBNet will be used to document any special requirements or notes that apply to the entire study that are unavailable by tag. *Project Notes* can only be viewed and edited by users with Administrator access.

18. If the submission is determined to be non-exempt, the determination letter will include a requirement that the investigator submit an Initial Application in response.

19. For research that is determined to be non-exempt, follow the *Policy and Procedure on Initial Full Review*.

20. For research determined exempt prior to the effective date of the 2018 Rule, the research will remain under the regulations of the pre-2018 Rule.

REVISION HISTORY:

Department: OSP - Research Integrity & Compliance	**Title**: Exemption Determination
Effective Date: 01/22/20	**Owner:** Senior Compliance Manager

Replaces P/P Dated: IRB SOPs (02/08/17); IRB Procedure: 001.03 (12/10/13); P/P (01/2/19, 07/18/18)
Related Documents: Exemption Determination Form; Exemption Determination Letter Template; Submission Checklist – Initial; Reviewer Sheet – Exemption Determination
References: 45 CFR 46.101(b); 21 CFR 56.104(d); 45 CFR 46.301(a); 45 CFR 46.401(b); OHRP Guidance on the Involvement of Prisoners in Research, May 23, 2003; AAHRPP Elements: II.2.A and II.2.B; AAHRPP Tip Sheets: 8, 9, 18