The Christ Hospital IRB **Number:** 1.16
Submitted By: Emily Humbert **Effective Date:** 01/12
Reviewed By: Steve Roberts, MD & M. Jennings, MD **Revised/Reviewed Date:** 03/17
Approved By: Steve Roberts, MD
(II.2.A, II,2,B)

STANDARD OPERATING PROCEDURE

Exempt Research: Determination of Human Subject Research and Research Exempt from Federal Human Subjects Protection Regulations

POLICY:

This policy is to describe the federal requirements for the determination of research that qualifies for exempt status and to define the policy and process of The Christ Hospitals review of exempt research.

The Department of Health and Human Services (DHHS) regulations describe six categories of research that may qualify for exempt status. Although the regulations do not address a maximum risk level, it is implicit within the concept of exempt research that there must be very little, if any, associated risk. Therefore, research that qualifies for exemption from the requirements of 45 CFR 46 must meet the aforementioned risk threshold and fall within one or more of the six exempt categories.

In some cases, research that is technically exempt has associated risk that is greater than minimal. The Christ Hospital IRB (TCH IRB) requires all greater than minimal risk studies to be submitted to TCH IRB via the protocol submission for Full Board review. Therefore, such studies are not subject to exempt review by TCH IRB.

Research involving prisoners is not exempt from the federal regulations because this class of subjects is considered vulnerable. The Christ Hospital does not do research on prisoners. See IRB SOP 3.19 (Research Involving Vulnerable Populations) for further clarification on research involving the use of prisoners.

Exemptions are not applicable to research involving some subjects considered vulnerable including the decisionally impaired, the homeless, and nursing home residents.

The exemptions are applicable to research involving pregnant women, human fetuses and neonates per 45 CFR 46 Subpart B.

Research involving children can be considered exempt from further IRB review in accordance with the pertinent regulations. The Christ Hospital does do research on children. See IRB SOP 3.19 (Research Involving Vulnerable Populations) for further clarification on research involving the use of children. However, the exemption for research involving the use of educational tests (cognitive, diagnostic, aptitude achievement), survey procedures, interview procedures or observation of a minor's public behavior cannot be used for research involving children *unless*

the research involves only the observation of public behavior when the investigator does not participate in the activities being observed. These protections are found within 45 CFR 46: Protection of Human Subjects (DHHS).

The regulations do not specify who has or does not have the authority to decide whether a research project is exempt. Recognizing that this is an area where federal regulations are silent, the Office of Human Research Protections (OHRP) recommends that the decision to exempt a study from IRB review be made by someone other than a research investigator associated with the project. Many investigators do not have sufficient knowledge of the federal regulations to determine properly, in all cases, whether research is exempt. In addition, investigators have an obvious conflict of interest. The Christ Hospital has given the authority to make the determination of exempt status to TCH IRB chairman or designee. Research classified as exempt is not subject to continuing review or the other requirements of 45 CFR 46.

A research project that is exempt from human research subject IRB requirements may not be exempt from HIPAA provisions.

Criteria Allowing Exemption from Federal Regulations
The following are the six categories of exempt research specified by DHHS (45 CFR 46, 101(b):

Category 1

a) The research is conducted in established or commonly accepted educational settings.
b) The research involves normal educational practices, such as:
    i. Research on regular and special education instructional strategies.
    ii. Research on the effectiveness of or the comparison among instructional techniques, curricula or classroom management methods.
c) The research does not involve prisoners as participants
d) The research is not FDA-regulated

Category 1 is limited to the study of normal educational practices that will be conducted in commonly accepted setting such as elementary, secondary, or post-secondary schools. Thus, a study that involves evaluation of a radically new instructional strategy or use of random assignment of subjects to different instructional methods is usually not exempt because the methods employed in the studies deviate from normal educational practices. Educational research that involves deception or withholding of information from subjects is not considered exempt. Exemptions are not granted for research on physical education that involved exercise if the activity is altered in a significant way for the purposes of the research. Even if the exercise is considered normal educational practice, an element of risk may be introduced with physical activity, particularly intense exercise.

Category 2

a. The research involved the use of one or more of the following:
    i. Educational tests (cognitive, diagnostic, aptitude, achievement)
    ii. Survey procedures
    iii. Interview procedures
    iv. Observation of public behavior

b. If any disclosure of the participants' responses outside the research could reasonably place the participants at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, or reputation.
    i. Information obtained is not recorded in such a manner that participants can be identified, directly or indirectly through identifiers linked to the participants.
c. If the research is regulated by the Department of Veterans Affairs:
    i. If any disclosure of the participants' responses outside the research could reasonably place the participants at risk of loss of insurability.
        A. Information obtained is not recorded in such a manner that human subjects can be identified directly or through identifiers linked to the subjects, and
        B. Participants can be identified, directly or through identifiers linked to the participants
d. If the research involves children as participants:
    i. The procedures do not involve any of the following:
        A. Survey procedures
        B. Interview procedures
        C. Observation of public behavior where the Researchers participate in the activities being observed
e. The research does not involve prisoners as participants
f. The research is not FDA-regulated

Category 2 reflects concern about protecting the subject's privacy and avoiding any risks associated with breach of confidentiality. Therefore, if the research data contains any subject identifiers and if disclosure of data to unauthorized persons could harm the subject in any way, the research is not exempt. For example, survey research that deals with sensitive and private aspects of the subject's behavior, such as sexual preferences, substance abuse, or illegal conduct, is not exempt if the data is linked to individual subjects. If there are no subject identifiers, then the research is technically exempt. TCH IRB chair or designee will consider all potential risks associated with this kind of research in determining exempt status. In this example, there may be more than minimal risk involved even in the absence of subject identifiers. Such surveys can contain invasive questions that may cause the subject to experience emotional distress or discomfort while answering them. This research technically qualifies for exemption because there are no subject identifiers, however, the potential risks of the research should negate exemption. Such research should use an unsigned consent form that clearly describes the nature and possible risks of the research.
Research involving cognitive or diagnostic testing will not be exempt if the testing is psychologically invasive in nature (e.g., detailed personality inventory) and could potentially cause the subject some discomfort or distress. Again, although the research is technically exempt, if no subject identifiers are used, it will be considered as nonexempt research, by TCH IRB chair or designee, because of the risk level. Furthermore, TCH IRB chair or designee will guard against the possibility that an investigator may inappropriately characterize testing as normal educational practice and apply for exempt status under Category 1, which is less stringent in its requirements than Category 2.

Category 3

a) The research is not exempt under Category 2
b) Research involving the use of one or more of the following:
c) Either of the following is true
d) The research does not include prisoners as participants
e) The research is not FDA-regulated

Category 3 represents an extension of Category 2, but without the same level of oversight of the subject's right to privacy. Personal identifiers can be maintained if there is a federal statute that protects confidentiality or if the subject is either a public official or a candidate for public office. Category 3 effectively holds public officials who become research subjects to a different standard by providing less protection of their rights than for other members of society. Nevertheless, despite the loophole created by this exemption, the rights of individuals who hold public official will be protected by TCH IRB conducting a thorough review of the proposed research as addressed under Category 2.

Category 4

a) The research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens.
b) Either of the following is true:
    i. The sources are publicly available
    ii. The Researchers records information in such a manner that participants cannot be identified, directly or indirectly through identifiers linked to the participants.
c) The research does not involve prisoners as participants
d) The research is not FDA-regulated

The Health Insurance Portability and Accountability Act or HIPAA Privacy Rule (45 CFR 160 and 164) applies to research involving protected health information but does not recognize exemptions. For research to qualify for exempt status under Category 4 the information derived from use of the data, records, or biological specimens must be recorded so that subjects cannot be identified. This means there must be no direct or indirect subject identifiers (e.g., demographic information) that can be linked to the subjects. Some investigators erroneously assume that if they do not have access to the subject's name, which is, however, linked to the data or specimen, the research is exempt. However, the existence of even a one-way identifier, such as a code that can then be used to identify a subject, disqualifies the research from exemption under Category 4. It should also be noted that the research material must be existent "on-the-shelf" at the time the research begins. Any use of additional research material collected after the research is initiated constitutes a prospective study and obviously disqualifies the study from exempt status. Exempt research under Category 4 must be totally retrospective in nature.

Category 5

a) The project is a research or demonstration project
b) The research is conducted by or subject to the approval of a Federal Department Agency head
c) The research is designed to study, evaluate or otherwise examine one or more of the following:
    i. Public benefit or service programs

ii. Procedures for obtaining benefits or services under those programs.
iii. Possible changes in or alternatives to those programs or procedures
iv. Possible changes in methods or levels of payment for benefits or services under those programs.

d) The program under study delivers 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).
e) The research is conducted pursuant to specific federal statutory authority.
f) There is no statutory requirement that an IRB or EC review the research.
g) The research does not involve significant physical invasions or intrusions upon the privacy of participants.
h) The research does not involve prisoners as participants
i) The research is not FDA-regulated.

Category 5 allows research on public benefit or service programs, such as welfare, Medicaid, unemployment, and Social Security. This research may, however, involve vulnerable subjects such as economically disadvantaged persons or elderly individuals who are decisionally impaired. Research under Category 5 may also involve analysis of data that are routinely complied by the public office that administers the program but would be considered private by the subject. A thorough review of the research project, by TCH IRB, will help protect the rights and welfare of the participants, particularly those who may be vulnerable.

Category 6

a) The research involves taste and food quality evaluation or is a consumer acceptance study
b) Either of the following is true:
    i. Wholesome foods without additives are consumed
    ii. If a food is consumed that contains a food ingredient or an agricultural chemical or environmental contaminant, the food ingredient or agricultural chemical or environmental contaminant is at or below the level and for a use found to be safe by one of the following:
        A. The Food and Drug Administration
        B. The Environmental Protection Agency
        C. The Food Safety and Inspection Service of the U.S. Department of Agriculture.
c) The research does not involve prisoners as participants

Category 6 is limited to taste and food quality evaluation studies that do not involve consumption by the subject of any type or volume of food that has any potential risks such as indigestion or vitamin deficiencies. The food consumed by the subject and the time frame in which this is accomplished should constitute reasonable eating behaviors. Studies that involve consumption of alcohol, vitamins, or supplements such as protein powder, creatine, and glucosamine chondroitin sulfate do not qualify for exempt status.

REFERENCES:

1. OHRP Decision Charts for Determination of Exemption: www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm
2. The term *federal human research subjects protection regulations* refers to 45 CFR Part 46 and 21 CFR Parts 50 and 56. Exemptions from all or part of the federal human research protections regulations are listed at 21 CFR Sec. 56.104, 45 CFR Sec. 46.101(b)(1) – (6), 45 CFR 46.101 (i), 45 CFR 46.301(a), 45 CFR 46.401(b).
3. OHRP Guidance: Guidance on Research Involving Coded Private Information or Biological Specimens.

PROCEDURE:

This procedure describes how human materials or data not involving human subjects under the definition of 45 CFR Part 46 and 21 CRF Part 56 may receive a designation of "no humans" research. Use of the "no humans" designation is applicable to research activities that involve cadaver materials, use of outdated blood products (from the Red Cross or other blood banks), commercially available cell lines, or coded private information (OHRP, Guidance on Research Involving Coded Private Information or Biological Specimens)[3] unless the sponsoring agency determines otherwise.

INVESTIGATOR:

Submitting a "No Humans" Research Designation Application:

- Submits one copy of the following materials to the IRB Office:
  - Completed form: "No Humans" Research Designation Application, including the faculty advisor/course instructor signature if the investigator is a student.
  - Grant or funding application, if applicable.
  - Investigator Agreement.
  - Written policies and procedures for repository.
- Responds to all requests for more information from the IRB Office.
- Submits any changes to the protocol during the course of the research by resubmitting the "No Humans" Application Form.
- The investigator may not initiate any changes prior to TCH IRB review and approval.

Submitting an Exempt Application the Investigator will submit the following materials to the IRB Office:

- Submits one copy of the Exempt Application Form
- Grant or funding application, if applicable
- Financial Disclosure Form for anyone involved in the study
- HIPAA Waiver Form, if applicable
- Informed Consent or applicable waiver form
- CITI training certificate
- Advertising material, if applicable

Investigator will respond to all requests for more information from the IRB Office.

The investigator may not initiate any changes prior to TCH IRB review and approval

IRB OFFICE:

IRB Staff:

- Document receipt of Application for No Humans Research application using date stamp; or
- Document receipt of Exempt Application using date stamp
- Forwards application to IRB Chair or designee for review.

IRB Chair or Designee:

- Reviews application to determine if the research involves human subjects in accordance with guidelines outlined above; OHRP Human Subject Decision Charts September 24; and OHRP definitions and FDA definitions of human subject and research. (See "Criteria to Determine Exemption" below.)
- Examines proposed research for any problematic issues on the basis of the Belmont Principles or TCH-adopted guidelines, and if identified, refers to IRB for further review.
- Requests additional information as necessary to complete above review.
- Takes one of the following actions:
    - Exemption Application Approved: Investigator is sent an approval letter. A report upon completion of the study may be required at the Chairman's discretion.
    - Additional Information Requested: The investigator is sent a letter describing the information requested. The investigator returns two copies to the IRB Chairman for review. If the reviewer is satisfied that the protocol meets the exemption criteria, then approval letter is sent to the investigator.
    - Exemption Certification Disapproved: The investigator is sent a letter indicating that the new protocol does not fall within the exemption categories. A new application must be prepared and submitted for either expedited (if appropriate) or full review by the IRB.
- Documents the determination of "No Humans," or "Exemption" using IRB Exempt Checklist, signs, and dates application.
- Files determinations in the IRB records.
- Review will be reported to the IRB members via the monthly IRB agenda.

REVISION HISTORY:

Date Revised	Reason For Change	Revised By
04/09/15	Added submission requirements for Exempt research	Becky