Exempt Human Research

Definitions:

Research: As defined by DHHS any systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Clinical Investigation: Any experiment that involves a test article and one or more human subjects, and that is subject to the FDA regulations. FDA regulations consider the terms "clinical investigation" and "research" to be synonymous. The following are considered experiments subject to FDA regulations:

- Any use of a drug, other than the use of an approved drug in the course of medical practice.
- Any use of a medical device to evaluate safety or efficacy of that device.
- Any activity where data are being collection to submit to FDA or to be held for inspection by FDA.

Test article: Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to FDA regulation.

Human Subject: A defined by DHHS: a human subject is a living individual about whom an investigator (whether professional or student) conducting research obtains either data through intervention or interaction with the individual, or identifiable private information. As defined by FDA: An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. A subject is also an individual on whose specimen a medical device is used.

Intervention: Includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subjects' environment that are performed for research purposes.

Interaction: Includes communication or interpersonal contact between an Investigator or his/her research staff and the research participant or their private identifiable information.

Private Information: Includes information about behavior that occurs in a setting in which an individual can reasonably expect that no observation or recording is taking place. It includes information, which has been provided for specific purposes by an individual, and the individual can reasonably expect will not be made public (e.g., 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 or associated with the

information) in order to be considered information to constitute research involving human participants.

Research Activities Involving Human Subjects: Activities that either (1) meet the DHHS definition of "research" and involve "human subjects" as defined by DHHS OR (2) meet the FDA definition of "research" and involve "human subjects" as defined by FDA.

Policy:

All research activities involving human subjects under the jurisdiction of the UHCMC IRB will be reviewed to determine (i) whether the research meets one or more of the exemption categories described in the federal regulations and (ii) whether it complies with UHCMC's ethical standards. Research conducted under exempt review is also subject to all applicable institutional and IRB polices and procedures.

A) Exempt Eligibility:

The Federal regulations allow certain research activities involving human subjects to be exempt from IRB full or expedited review [*see* 45 CFR 46.101(b) (1-6); 45 CFR 46.401(b); and 21 CFR 56.104(d)]. There are however restrictions for research involving children (*see* 45 CFR 46, Subpart D); and research involving prisoners does not qualify as exempt research (*see* 45 CFR 46, Subpart C). In addition, any HHS- funded research using newborn dried blood spots **collected on or after March 18, 2015** does not qualify as exempt research: (*see* NOT-OD-12-127 Preliminary Guidance Related to Informed Consent for Research on Dried Blood Spots Obtained Through Newborn Screening**).**

FDA-regulated research does not qualify for IRB exemption unless it falls under the FDA's emergency use provision for the use of a test article [21 CFR 56.104(c)] or Taste and Food Quality Evaluations and Consumer Acceptance studies [21 CFR 56.104(d)]. [Exempt Category 6]

The following are a list of categories as noted in the Federal Regulations 45 CFR 46.101 (b) that are permitted to be classified as research that is "exempt" from IRB full or expedited review:

> (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
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> (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

(i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

(3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:
(i) The human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

(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 subjects cannot be identified, directly or through identifiers linked to the subjects.

(5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:
(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; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

(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 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.

Only one category of will apply to the project. Only the IRB may determine what human subject research activities qualify as "exempt" under the Federal regulations. Investigators do not have the authority to make an independent determination that research involving human subjects is exempt. IRB approval of exempt status is required prior to initiation of the research.

A request for determination as to whether or not a human research protocol may be considered "exempt" may be submitted electronically through the iRIS system by adding a new study. In order to receive the questions related to exemption, you must answer yes

to the question "*Are you requesting determination as to whether your project qualifies for exemption as described in 45 CFR 46 / 21 CFR 56.104*?"
Upon review of the request, a determination of applicability will be made by either the IRB Chair, Vice-Chair, designated IRB member or Senior IRB staff member who is familiar with the regulations. The request will also be reviewed in accordance with the UHCMC HRPP's ethical standards including:

- That the research holds no more than minimal risk to the participant
- Selection of participants is equitable
- If the research involves recording of identifiable data, that there are adequate provisions in the plan to maintain the confidentiality of the data
- If there are interactions with participants, whether a consent process is required to disclose:
    1. the activity involves research;
    2. a description of the procedures;
    3. that participation is voluntary;
    4. the name and contact information for the researcher(s).
- There are adequate provisions to maintain privacy interests of the participants.

If the request is approved, the investigator will receive an approval notification in the iRIS system. The approval letter will list the applicable exempt category under the Federal regulations; the expiration date of the research; and a statement to indicate that the IRB must review any changes prior to implementation to determine if the study still qualifies for exemption and a statement that a new application is required if the study is to be continued after the expiration date.

If the request is disapproved, the IRB staff will indicate that the study does not meet the Federal requirements to be classified as "exempt" and will be given instruction about how to proceed. Depending on the type of research, minor revisions may need to be made in order to qualify for exempt status or a new application for full or expedited IRB review will have to be submitted for reconsideration.

B) Department Research Scientific Review:

All IRB Exemption requests must be reviewed and approved by the Department Research Scientific Review Committee (or Chairperson as appropriate) prior to being submitted to the IRB office. A copy of the department research review committee approval must be attached to the application in iRIS or the application may be forwarded for department chair for electronic signature in iRIS.

C) Duration of approval:

Continuing review is not required for research that has been determined to be exempt. However, all research determined to be exempt, will be awarded an expiration date of six years from the time the exemption was approved. If the investigator wishes to continue

the research project after the six year period, the investigator must re-submit the project as a new "Request for Exemption" for IRB review and approval. The request should include an updated protocol and summary of the work and results obtained during the previous approval period.

D) Amendments:

Proposed changes to an exempt study after initial IRB approval must be submitted to the IRB for review prior to implementation. Certain changes may disqualify the research from exempt status (i.e., recruiting prisoners). Any changes must be submitted in the iRIS system as an "amendment" to your currently approved exempt study. You must be sure to include a narrative which discusses the changes that are being made, as well as include any revisions to electronic components that were affected by the change (e.g., study application, information sheets, surveys, etc).

The IRB will review the proposed changes to determine if the project still qualifies for Exempt status. If the project is still considered Exempt, changes proposed may be implemented once the investigator receives an approval for the amendment through the iRIS system. Approved amendments do not change the current Exemption IRB number or current expiration date. If the IRB determines that the project no longer qualifies for Exemption, the investigator will be notified accordingly. The investigator may then choose to forego the proposed changes and continue with the study as currently approved or to close out the current exemption and resubmit for full or expedited IRB review and approval.

E) Use and Disclosure of PHI (applicability of the HIPAA Privacy Rule):

If the proposed research involves utilization of Protected Health Information (PHI), HIPAA regulations still apply, even if the IRB has determined that the research qualifies for IRB Exemption. Investigators must indicate applicability of HIPAA Privacy Rule as part of the IRB application process. Investigators must also submit the appropriate supporting documentation for review.

F) Certification in Human Subjects Protections:

Investigators requesting a determination of exemption are required to be certified in Human Subjects Protections through the Case CREC (Continuing Research Education Credit) Program.

References and/or Regulatory Citations:

NOT-OD-15-127: Preliminary Guidance Related to Informed Consent for Research on Dried Blood Spots Obtained Through Newborn Screening

45 CFR 46.101(b) (1-6)
45 CFR 46.401(b)
21 CFR 56.104(c)
21 CFR 56.104(d)

Related Policies:

IRB Policy, Protocol Submission Requirements
IRB Policy, Certification in Human Subjects' Protections
IRB Policy, Assent from Children in Research Studies
IRB Policy, Use and Disclosure of Protected Health information (PHI) for Research Purposes – HIPAA and the Privacy Rule