ISSUES TO BE ADDRESSED WHEN CONDUCTING EXEMPT REVIEW

University of Kentucky Educational Resource
45 CFR 46 Revised

Below are examples of issues IRB reviewers should consider when conducting Exemption Review. Categories apply to review of research approved after January 21, 2019.

Additional Regulatory Protection for Children and Prisoners

The revised common rule regulations now allow for the application of all exempt categories to research involving the use of pregnant women, human fetuses, and neonates, assuming all the research activities fall within one or more exempt categories as determined by the IRB.

Certain research activities **cannot** be exempt because additional protection has been granted by federal regulations for vulnerable populations. The kinds of research that **cannot** be exempt because they are subject to the federal requirements of subparts C and D are as follows:

1. Research that involves surveying and/or interviewing children;
2. Research involving the administration of educational tests and/or the observation of public behavior of children if the investigators actively participate in the test administration or the activities being observed;
3. Research involving benign behavioral intervention with children (exempt category 3);
4. Research involving prisoners when prisoners are the intended/targeted population for enrollment (Note: prisoners may be allowed if the research is aimed at involving a broader subject population and the involvement of the prisoner(s) is only incidental).

All Research Activities Must Fit Within Six Federal Categories

For a study to be eligible for exemption all of the research activities must fit in one or more of the six categories listed below. Please note the University of Kentucky does not review research protocols for exemption under regulatory categories #7 or #8 at this time.

Risk Assessment Considerations

Research eligible for exemption usually involves little or no risk to subjects. Some reviewers apply the “minimal risk” standard when conducting exempt review. Minimal risk is defined, as “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.”

Exemption Applications that Do Not Meet the Definition of Human Research

The exemption process is further complicated because, occasionally, an activity that is sent to the IRB using an Exemption Application does not meet the federal definitions of “research” or “human subject.” These definitions are included on the UK “What Needs IRB Review?” page of the ORI website at http://www.research.uky.edu/ori/human/WhatNeedsIRBReview.htm. Research is defined as a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Knowing the intent if the activity helps determine whether it is being conducted to contribute to generalizable knowledge.

In analyzing whether activities involve human subjects, it is important to focus on what is being **obtained** by the investigators. If the investigator (a) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (b) obtains uses studies, analyzes, or generates identifiable private information or identifiable biospecimens, then the research DOES involve human subjects. Reviewers should contact ORI staff if they think the activity does not meet the above definition.

Guidance for Applying the Six Exemption Categories

(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 instruction strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

Exemption 1 applies to research in established or commonly accepted educational settings that involves certain normal educational practices, such as research on instructional techniques already in use or classroom management. The IRB reviewer must keep three things in mind when considering this category.

First, the IRB reviewer has to consider whether the proposed activities constitute "normal educational practice" and if the setting is a "commonly accepted educational setting." For example, a study to develop an innovative method for teaching math in the second grade would be eligible under this exemption provided the curriculum development methods reflected normal educational practices. Typically, the educational setting would be a classroom. However, teaching students to drive in a driver's education class or teaching children or adults to cook in a formal cooking class could be considered a "normal educational setting." The IRB reviewer can contact one of the IRB College of Education representatives for guidance regarding whether the research is occurring in an "accepted educational setting" or whether it involves "normal educational practices."

Second, the IRB reviewer must determine if a research project draws enough time and attention away from the delivery of the regular educational curriculum that the research project could have a detrimental effect on student's achievement. If the study meets either of the criteria above, it would not meet the criteria for exempt category 1.

Third, the IRB reviewer must determine that the proposal does not adversely impact the assessment of educators providing instruction. For example, a researcher could not rate an instructor's teaching method and report the findings to the instructor's supervisor.

This category does not apply to Food and Drug Administration (FDA) regulated research.

(2) Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation 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;

[*Information collected may be sensitive*. *Researcher may see the identifiers, but will not record them. This means the information cannot be linked to the subjects directly or by some coding system if the researchers can access the codes. An example would be a survey collecting responses but no identifier(s) or code(s) to enable re-identification*]

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

[*This means if a third party were to gain access to the information, a subject would not be placed at risk for (a) criminal or civil liability or (b) having his/her financial standing, employability, educational advancement, or reputation damaged. Information collected should not be sensitive.*]

(iii) 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 by §46.111(a)(7) which states there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

[*Information collected may be sensitive*. *Researcher may record identifiers. However the researcher completes a Limited Review Form and the IRB considers the adequacy of investigators proposed safeguards to protect the privacy and confidentiality of the subjects*.]

This category involves data collection (including audio or video) only. Research involving interventions that are distinct from those information collection methods allowable under this exemption do not satisfy the conditions of this exemption. For example, if a research study were to randomly assign students to take an educational test in a quiet room or in a room with a moderate level of noise, or to consume a snack (or not) before taking the test, this research would not be exempt under this exemption. Research in which the purpose of the research is to see whether respondents answer survey questions differently depending on the gender of the interviewer would not satisfy the conditions of the exemption, because the manipulation of the interviewer would be a distinct intervention. Research involving observation of public behavior does not qualify for this exemption if the investigator intervenes with subjects, for example, by offering them an ostensibly lost wallet to see if they will accept it.

The category presumes adults would understand that actively providing responses to educational tests, surveys, or interviews constitutes agreement to participate. In some cases, the IRB may ask for a waiver of informed consent or may require informed consent from an ethical perspective.

The category is narrowed in scope by 45 CFR 46 Subpart D's additional protections for research involving children. Where children will be involved as research subjects, the use of survey or interview procedures is eliminated from this exemption, and so is any research involving the investigator's administering educational tests and/or participating in an activity being observed for the research. Observing a classroom would not constitute public behavior and would generally not be permitted for this exempt category.

This category does not include interventions such as manipulating conditions or the environment to determine response. For example, observation of public behavior does not qualify for this exemption if the investigator intervenes with subjects (e.g., offering someone in public an ostensibly lost wallet to see if they will accept it.

This category does not apply to FDA regulated research.

(3) Research involving 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;

[*Information collected may be sensitive*. *Researcher will not record identifiers].*

(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

[Information collected should not be sensitive.]

(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 by §46.111(a)(7) which states there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

[*Information collected may be sensitive*. *Researcher may record identifiers. However the researcher completes a Limited Review Form and the IRB considers the adequacy of investigators proposed safeguards to protect the privacy and confidentiality of the subjects*.]

This new category requires adult participants to prospectively agree to participation. Depending on the context of the study, prospective agreement may be obtained via standard informed consent or the Consent Cover Letter template delivered as a written document or verbal consent script along with a waiver of documentation (signature).

This exemption category may **NOT** be applied to research involving minors. Subjects must be adults, but the provision does not specify that they must be competent, and therefore tests of competency are not generally required, unless there is a potential of exploitation.

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 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. [The IRB may consider whether debriefing is appropriate given the context of the research.]

Medical interventions (including medical tests, procedures, and devices) are not permitted in this category. Also note the methods of data collection are somewhat specific (verbal, written, or audiovisual). So, a study that might otherwise meet the criteria for exemption under this category but involved, for example, the collection of body measurement data for research purposes would not qualify.

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.

This exemption allows for the intervention to be distinct from the data collection method; for example, a research study comparing test performance of test takers in quiet or noisy surroundings would qualify for this exemption. Also, subjects could be asked to perform cognitive tasks, and audiovisual recording could be used to collect the data, without any educational test, survey or interview procedure occurring, and this research would qualify for this exemption.

This category does not apply to FDA regulated research.

(4) Secondary research for which 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;

[What is meant by "publicly available"? This language in the regulation was intended to apply to public sources of data. This would apply to secondary research use of archives in a public library, for example, or to government or other institutional records where public access is provided on request, or from a commercial entity if the information is provided to members of the public on request or if the only requirement for obtaining the information is paying a user fee, registering or signing in as a visitor to an archive. It would also apply if a commercial entity made identifiable biospecimens publicly available to anyone on request or for a fee. Note: student records which are covered by the Family Educational Rights and Privacy Act (FERPA) are not public records].

(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;

[What is meant by "identifiers linked to the subjects"? Identifiers can include names, social security numbers, medical record numbers, or other codes that permit specimens or data to be linked to living individuals and, perhaps, also to associated medical information. If an investigator records information about individuals in a nonidentifiable manner, the investigator must not attempt to re-identify or contact the research 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 parts 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) [Note that HIPAA does not apply to biospecimens, so this provision applies only to the secondary use of identifiable private health information (which can include information obtained from biospecimens]; or

[Note: it is not clear what is meant by "investigator's use" as stated in (iii). This language may prohibit the sharing of protected health information (PHI) from data repositories. If there is any chance that the protocol will involve sharing, you are advised to submit an expedited or full review protocol and obtain informed consent.

Also, if protected health information (PHI) will be used, appropriate HIPAA provisions must be applied. In most cases this will involve requesting a HIPAA waiver of Authorization Form].

(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 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 applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 *et seq.*
[Note: This category is unlikely to be used. If you believe that it is applicable, please contact the Office of Research Integrity for assistance.]

It is important to recognize that this exemption does not cover any primary collections of either information or biospecimens. For example, if an investigator wants to collect information directly from research subjects by asking them to complete a questionnaire, that would not be covered by this exemption. If an investigator wants to collect biospecimens by having subjects swab their cheek, that would similarly not be covered by this exemption. On the other hand, an investigator who wants to use information that is in an existing data or specimen bank, or use biospecimens that are in a pathology laboratory, or use the "excess" portion of blood that was drawn for clinical purposes, could use this exemption assuming all of the relevant conditions are met.

However, this exemption does allow both retrospective and prospective collection. Under this category, private information and biospecimens no longer have to be in existence prior to the start of the research. A research study that proposes to analyze samples or information that will be collected for clinical purposes in the future could qualify for this exemption if it meets at least one of the applicability provisions. For example, an investigator could start a study that involves using biospecimens from clinical pathology laboratories, and could include specimens that are added to the laboratories during the course of the study (again assuming that the other conditions of the exemption are met).

While this category involves secondary research for which consent is not required, the IRB could request the investigator to obtain informed consent or request a waiver of informed consent for prospectively collected data under sub-category (iii). Informed consent would not apply to category (i) public available or (ii) researcher agrees not to record identifiers or re-identify or re-contact subject. However, the IRB may ask the researcher to justify why informed consent is not practicable for prospective collections under (iii).

This category does not apply to FDA regulated research.

(5) Research and 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 or alternatives to those programs or procedures, or 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.

This category does not apply to FDA regulated research.

(6) Taste and food quality evaluation and consumer studies:

(i) If wholesome food without additives are consumed [The IRB reviewer must verify the food product being researched is “wholesome,” meaning there are no additives in it. An example of such a research project would be a taste-test conducted on different types of grapefruit to determine consumer preference. The grapefruits are those normally grown in different sections of the country using normal agricultural practices and do not

involve the addition of food additives or chemicals. The subjects merely indicate which of the grapefruits tasted they prefer.]; 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.

The Food and Drug Administration (FDA) has determined levels of safety for various agricultural chemicals, referred to as GRAS (generally recognized as safe) and GRAE (generally recognized as effective) additives which are fed to animals raised for food production. If these agricultural additives are given to animals at or below the levels found to be safe by FDA, the research can receive exempt review.

An example of such research would be taste-testing pork products where the swine have been fed corn and a chemical additive at a level designated below FDA guidelines that make the animal gain weight more quickly. The objective of the study is to determine whether the addition of the chemical changes the flavor of the pork.

There are also approved levels for environmental contaminants set forth by the Food and Drug Administration, the Environmental Protection Agency (EPA) or the Food Safety and Inspection Service of the U.S. Department of Agriculture (USDA) that may affect the grass or grain consumed by grazing food animals such as chemicals sprayed on a field to combat chickweed. If the research involves taste-testing of food products that come from animals exposed to environmental contaminants and the investigator can show that the use of these contaminants was at or below those approved levels, the research can receive exempt review.

In all of these situations, the investigator should provide some documentation that the alterations, either chemical, environmental or agricultural, have been found to be safe by FDA, USDA, and/or EPA.

However, if there have been food and color additives incorporated into the food product and these additives are used in research with the intent to apply to FDA for marketing that additive, the research would not qualify for exemption. Even if the procedures are preliminary in nature, if the research would eventually lead to FDA approval for marketing the food or color additive, it would not qualify for exempt review. The additives are viewed as investigational by FDA and, therefore, do meet the exemption criteria.

(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 determinations required by §46.111(a)(8).

Exemption category 7 is not an option at the University of Kentucky at this time.

(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 §46.116(a)(1) through (4), (a)(6), and (d);

(ii) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with §46.117;

(iii) An IRB conducts a limited IRB review and makes the determination required by §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)(i) 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.

Exemption category 8 is not an option at the University of Kentucky at this time.

2008 Guidance from OHRP regarding exemptions and the HIPAA Privacy Rule

The Privacy Rule and the IRB regulations differ with respect on what is considered individually identifiable.

The Privacy Rule is a Federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 (see 45 CFR part 160 and subparts A and E of part 164). The Privacy Rule permits covered entities under the Rule to determine that health information is de-identified even if the health information has been assigned, and retains, a code or other means of record identification, provided that:

(1) the code is not derived from or related to the information about the individual;

(2) the code could not be translated to identify the individual; and

(3)the covered entity under the Privacy Rule does not use or disclose the code for other purposes or disclose the mechanism for re-identification (see HHS guidance entitled, *Institutional Review Boards and the HIPAA Privacy Rule*, page 6, Q and A #3, at http://privacyruleandresearch.nih.gov/pdf/IRB_Factsheet.pdf).

Regarding condition (1) above, in contrast to the Privacy Rule, information that is linked with a code derived from identifying information or related to information about the individual is not considered to be individually identifiable under the HHS regulations for the protection of human subjects at 45 CFR 46.102(f), if the investigators cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimen pertains. Therefore, some coded information, in which the code has been derived from identifying information linked to or related to the individual, would be individually identifiable under the Privacy Rule, but might not be individually identifiable under 45 CFR part 46.

References:

Office for Human Research Protections Revised Common Rule Q & A
www.hhs.gov/ohrp/education-and-outreach/revised-common-rule/revised-common-rule-q-and-a/index.html#exemptions

2018 Federal Policy for the Protection of Human Subjects**, 45 CFR 46.104**

National Institutes of Health (2006, January 18). *SF424 (R&R) Application Guide for NIH and Other PHS Agencies: A guide developed and maintained by NIH for preparing and submitting applications via Grants.gov to NIH and other PHS agencies using the SF424 (R&R)*. Updated March 25, 2011, Retrieved April 4, 2011, from
http://grants.nih.gov/grants/funding/424/SF424_RR_Guide_General_Adobe_VerB.pdf

Office of Human Research Protections, Department of Health and Human Services (2008, October 16). *Guidance on Research Involving Coded Private Information or Biological Specimens*. Retrieved April 4, 2011, from **http://www.hhs.gov/ohrp/policy/cdebiol.html**

September 24, 2004 OHRP Human Subject Regulations Decisions Charts (charts 1 - 7) at
http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html

Office for Human Research Protections, Department of Health and Human Services Frequently Asked Question Section: **http://answers.hhs.gov/ohrp/categories**