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

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).

Please note: 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 categories of exempt research as determined by the IRB.

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 reviews apply the “minimal risk” standard when conducting exempt review. When determining “minimal risk,” the IRB reviewer must first identify all risks associated with the study. The U.S. Department of Health & Human Services (HHS) defines “minimal risk” to mean “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.” [45 CFR 46.102(j)].

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.
In analyzing whether activities involve human subjects, it is important to focus on what is being obtained by the investigators. If the investigators are not obtaining either (a) data about living individuals through intervention or interaction, or (b) identifiable private information, then the research does not involve human subjects. Reviewers should contact ORI staff if they think that might be the case in a specific application.

**Guidance for Applying the Six Exemption Categories**

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(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 3 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 time and attention away from the delivery of the regular educational curriculum and if the research project could have a detrimental effect on student’s opportunity to learn. 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. If the study poses a greater than minimum risk to the instructor, then the study could not be reviewed as exempt category 1. 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;

[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 or 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.]

(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.

[This means the information gathered during these activities can be linked to the subjects, either directly or by some coding system if the researchers can access the codes and the IRB determines the investigator has proposed putting adequate safeguards in place to protect the privacy and confidentiality of the subjects.]

This exemption 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. OHRP has also stated that observing a classroom does not constitute public behavior and is not permitted for this exempt category.

This category does not apply to FDA regulated research.
(3) (i) 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;

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

[Medical interventions (including medical tests, procedures, and devices) are not permitted.]

(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 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.]

This exemption category may NOT be applied to research involving minors. 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.

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*;

(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 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

(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.]

Under this category, private information and biospecimens no longer have to be in existence prior to the start of the research. For example, 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.

*What is meant by "publicly available"? This language in the regulation was intended to apply to public sources of data, such as local telephone directory information. For example, student records which are covered by the Family Educational Rights and Privacy Act (FERPA) are not public records. The meaning of this language with respect to human tissue specimens is widely debated. Although there are organizations that make human cells and tissues broadly accessible to the research community, these materials are not usually available to the public at large and are not generally considered to be publicly available.
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.

***Note: it is not clear what is meant by “investigator’s use” as stated in (iii). This language may not allow the sharing of protected health information (PHI) from data repositories. If you believe the protocol involves sharing of PHI, please contact the Office of Research Integrity for assistance.

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 not 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](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


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

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