“Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy…” 45CFR 46.101(b)

“The following categories of clinical investigations are exempt from the requirements of this part for IRB review…” 21 CFR 56.104

Institutional Review Board (IRB) staff will make a determination of exempt status after evaluating the application and appropriate supporting documents (e.g., instrument, consent) against a detailed worksheet. The IRB chair or members are involved in the evaluation and determination when requested by staff or when evaluating an expedited or full review application. The principal investigator (PI) is responsible for knowing and adhering to the ethical principles of human subject research and for informing the IRB immediately of any changes, adverse or unexpected events that would alter the exempt status, and any personnel changes. The investigator may not make the determination of exempt status. This is in compliance with the Terms of the Federal Wide Assurance that requires written procedures for “[v]erifying, by a qualified person or persons other than the investigator or research team, whether proposed human subject research activities qualify for exemption from the requirements of the Common Rule.”

A research study that is determined to meet the criteria for exempt status is exempt from further initial and continuing review by the IRB. The PI, however, is required to report to the IRB any expected modifications in the research activity that will cause the exempt status to change, i.e., the research to change from exempt to expedited or full review status, change the category of exemption. The PI is also required to report to the IRB any unexpected or adverse events that occur or new information obtained that may cause the research activity to change from exempt to expedited or full review status. The PI is also required to submit any personnel changes to the IRB via email. Because research determined to be exempt does not require continuing review, PIs are not required to notify the IRB when the research study is complete.

The Human Research Protection Program (HRPP) Manual 6 “IRB Evaluation Criteria” does not apply to research studies determined to be exempt.
Criteria for Exempt Status

The criteria for exempt status follow all applicable federal regulations including 45 CFR 46.101(b)(1) through (6), 45 CFR 46.301(a), 45 CFR 46.306(a) and (b), 45 CFR 46.401(b) and 21 CFR 56.104. The criteria are applied to all research regardless of funding or funding source, with limited exceptions outlined in HRPP Manual 8-8 “Demonstration Projects.”

These regulations identify specific categories of exempt research activities and also identify when there are exceptions. If a specific research activity meets the exemption criteria for one applicable regulation but not another, the research activity will not be given the exempt status but will be processed under procedures for expedited or full review.

To be classified as exempt, the research:

1. Must involve only procedures or be a type of research study listed in one or more of the exempt categories (see exempt categories sections below);
2. Cannot involve any of the exceptions for the exempt categories (see children and prisoners section below);
3. Cannot involve prisoners as research subjects; and
4. Cannot be greater than minimal risk. “Minimal risk means that 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(i)

U.S. Food and Drug Administration (FDA) Exempt Categories

The following exempt categories apply to research subject to FDA regulations (i.e., clinical investigations). 21 CFR 56.104 sub-categories (a), (b), and (c) cannot be applied to activities that are regulated by the U.S. Department of Health and Human Services (DHHS).

21 CFR 56.104 Exemptions from IRB requirement. “The following categories of clinical investigations are exempt from the requirements of this part for IRB review:

“(a) 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.”

“(b) 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.”

“(c) 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.”

“(d) 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
The following exempt categories apply to research subject to DHHS regulations. 45 CFR 46.101(b) subcategories (1), (2), (3), (4), and (5) cannot be applied to activities that are FDA-regulated.

45 CFR 46.101(b). “Unless otherwise required by Department or Agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:”

“(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.”

“(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.”

“The Office for Protection from Research Risks (OPRR) has determined that the following criteria (see 48 FR 9266-9270, March 4, 1983) must be satisfied to invoke the exemption for research and demonstration projects examining "public benefit or service programs" as specified under Department of Health and Human Services (HHS) regulations at 45 CFR 46.101(b)(5):

- The program under study must deliver 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).

- The research or demonstration project must be conducted pursuant to specific federal statutory authority.

approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.”
• There must be no statutory requirement that the project be reviewed by an Institutional Review Board (IRB).
• The project must not involve significant physical invasions or intrusions upon the privacy of participants.”

“(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.”

**Exempt Category 7 Demonstration Project**
See HRPP Manual 8-8 “Demonstration Projects” for applicability and restrictions on the use of exempt category (7).

(7) Research involving the study of a previously collected existing data set which may include documents, records, pathological specimens, or diagnostic specimens, if these sources are identifiable or if the information is recorded by the investigator in such a manner that subjects can be identified, directly or through identifiers linked to the subjects.

**Research Involving Children**
The regulations require additional protections for research involving children. All exempt categories above apply to children as research subjects with the exception of exempt category (2). This category applies to research involving children as subjects only under specific conditions as specified in 45 CFR 46.401(b):

“Exemptions at §46.101(b)(1) and (b)(3) through (b)(6) are applicable to this subpart. The exemption at §46.101(b)(2) regarding educational tests is also applicable to this subpart. However, the exemption at §46.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.” 45 CFR 46.401(b)

Research involving children cannot be classified as exempt under category (2) if the research involves:
• Survey
• Interview procedures
• Observations of public behavior when the investigator participates in the activities being observed

Research involving children can be classified as exempt category (2) if the research involves only educational tests and / or observation of public behavior where the investigator does not participate in the activities being observed and meets the other conditions of 45 CFR 46.101(b)(2).
Research Involving Prisoners
The DHHS regulations on exemptions do not apply to research involving prisoners. Research involving prisoners as subjects is not exempt from the regulations.

Criteria for Protection of Human Subjects in Exempt Research
Research that is determined to be exempt from IRB review is not exempt from protection of human subjects. The following criteria to protect human subjects must be met and the principal investigator must assure and assume responsibility to:

1. Ensure that researchers are trained in the ethical principles, relevant federal regulations, and institutional policies governing human subject research.
2. Ensure that the subjects are informed of the research through a documented or undocumented consent process, if appropriate.
3. Ensure that subjects are equitably selected.
4. Maintain confidentiality of the subjects and the data, and to maintain the privacy of the subjects and protection of the data through appropriate means. If data is anonymous, the investigators will make no attempt to identify any individuals.
5. Ensure that researchers adhere to the appropriate policies to protect human subjects, maintain confidentiality and privacy, and adhere to accepted ethical standards.
6. Inform the HRPP when additional researchers are added to an exempt research study.
7. Report any complaints from subjects regarding the risk and benefits of the research study to the HRPP.
8. Report any change in the research study which may raise the research study from exempt to an expedited or full review level to the HRPP. If there is any question about a change in protocol the PI should consult the IRB staff. Failure to submit changes which raise the research study out of the exempt category will be considered noncompliance and will be subject to investigation and action by the HRPP.
9. Submit any changes in the research study which may change the exempt category.

These criteria are specified in the PI assurance form for an exempt research study. The PI’s signature acknowledges that he/she understands and accepts these conditions. Investigators can refer to the HRPP website for specific information on training, voluntary informed consent, privacy, and how to notify the IRB of adverse or unexpected events.

Consideration of circumstances that may affect ethical principles should be taken into account when an exempt determination is made. For example, consideration such as whether the research involves student research pools, research on one’s own students, or course credit may affect equitable selection of subjects. Other considerations may
include whether the research involves incomplete disclosure and/or deception or whether the research involves audiotaping or videotaping. Involvement of these circumstances in the research does not preclude an exempt determination. However, consideration should be made as to whether inclusion of such circumstances affects the exempt determination.

**Determination of Exempt Status**
The investigator must submit an exempt application to the IRB including supporting documents, e.g., instruments, surveys, data abstraction sheet. The application requesting exempt status is a shortened version of the expedited/full review application and is designed to capture information needed to make the exempt determination. The exempt application is submitted through the MSU IRB online system and must be submitted by the PI. The PI must also submit the PI assurance form for an exempt research study acknowledging with a signature that they have read and accepted the responsibility to protect research subjects if the research study is determined exempt.

IRB staff will review the application to determine if the research meets the criteria for exempt research and meets the criteria that subjects are protected. The determinations are documented using an exempt determination worksheet. IRB staff will document how or why the research involves no more than minimal risk and how the research meets criteria for one or more of the exempt categories. The staff may consult or refer the research study to the IRB chair or members who will make the determination of whether the research meets the criteria after evaluating the exempt application and completing the exempt determination worksheet. The IRB chair or member may also make the exempt determination when assigned to review expedited or full review research studies. The completed exempt determination worksheet will reference all categories under which the exemption is granted.

Individuals assigned to review an exempt application in which she or he has a conflict of interest cannot review the application. The policy and procedure (e.g., notification procedures) described in HRPP Manual 10-1 “Conflict of Interest” shall be followed.

The completed exempt determination worksheet is placed in the file and the research study will be processed based on the level of review.

**Determination - Exempt**
An exempt determination requires that the research activity meet the criteria for exempt status and meets the criteria for protection of research subjects in exempt research. If the research study is determined to meet the criteria for exempt status and if the PI assurance form for an exempt research study has been received, the IRB staff will send an exempt determination letter to the investigator. If the PI assurance form for an exempt research study has not been received, the PI will be prompted.

**Determination - Not Exempt (Expedited or Full)**
If it is determined that the research study does not to meet the criteria for exempt status, IRB staff will communicate this to the PI informing him/her of the determination. The
communication will include an explanation of why the research study did not meet the exempt criteria and request that an initial application appendix be submitted. The IRB staff will assign the appropriate category to the application; request additional information as needed and initiate the relevant IRB review process, e.g., assign the chair to review the application.

**Determination - Not Human Subject Research**

See HRPP Manual 4-3 “Determination of Human Subject Research” for procedures when the IRB staff determines that the research study does not meet the definition of human subject research.

**Timeframe**

Processing of applications for exempt status is estimated to take 7-9 working days. Processing time may increase if the application is incomplete, unclear, or lacks all necessary supporting documents (e.g., signed cover sheet, consent process information, instruments).

**Modifications to Exempt Research**

In general, investigators are not required to submit modifications to the IRB once a research study is designated as exempt as long as those changes do not affect the exempt category or criteria for exempt determination (changing from exempt status to expedited or full review, changing exempt category). However, personnel changes should be submitted to the IRB via email.

Modifications in procedures that would change the exempt category approved by the IRB include but are not limited to:

- New knowledge that increases the risk level
- Use of any methods described in the expedited review categories that do not meet the exempt criteria (e.g., blood draws)
- Surveying or interviewing children or observing public behavior of children and participating in the activities being observed
- Change in the way identifiers are recorded (directly or indirectly) from existing data, documents, records, pathological specimens, or diagnostic specimens so that subjects can be identified
- Addition of an instrument, survey questions, etc. that would pose more than minimal risk to subjects
- Addition of an instrument, survey, etc. from which information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and 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
- Addition of prisoners as research subjects
- Addition of other vulnerable populations that may pose more than minimal risk
- Under certain circumstances, addition of a funding source
- Addition of exempt category not previously approved by the IRB
If there are plans to make any of the above changes, the investigator must contact the IRB staff. An initial application appendix must be submitted to the IRB with all appropriate supporting documents (e.g., new or revised instruments, consent forms) for review and approval by the IRB prior to initiation of such changes. The application will then be reviewed in accordance with HRPP Manual 8-2 “Expedited Review Procedure” and 8-3 “Full Board Review.”

If investigators are unsure of whether a proposed modification changes the exempt status and needs to be submitted, they are encouraged to contact the IRB staff. Investigators may send an email with a description of the proposed change to the IRB via email.

**Personnel Changes**
If researchers will have contact with subjects or identifiable private data, they must be listed on the IRB application. If researchers need to be added after determination of the exempt status, the PI must submit the personnel changes form requesting that the additional personnel be added. If there is a change to the PI, the personnel form must also be submitted to the IRB.

**Closure**
Because research determined to be exempt does not require continuing review, investigators are not required to notify the IRB when the research study is complete.

**Audit of Exempt Research**
The IRB maintains the authority to audit research determined to be exempt (see HRPP Manual 8-10 “Research Study Audits” for audit policies and procedures). If the audit reveals that the research activities differ from the application to the IRB for exempt status and no longer meet criteria for exempt status (e.g., conducting non-approved research that meets the criteria for expedited or full review status) or if investigators are not fulfilling the agreed upon assurances for subject protection, the research will be considered in noncompliance. See HRPP Manual 9-2 “Noncompliance” for policies and procedures. Investigators should retain records for audit following MSU guidelines, “Michigan State University Guidelines on Research Data: Management, Control and Access.”