Review of Research

What are some of the different kinds of risks found in studies?

Risks can be categorized as physical, psychological, sociological, economic, and legal. The IRB should consider all the various types of risks the subjects are exposed to in the research when categorizing research and making risk determinations. Risks to subjects must be reasonable in relation to anticipated benefits, if any, to subjects and to the importance of knowledge that may reasonably be expected to result from the research.

What are the different risk levels?

Although, there are several types of risk, there are only two levels of risk:

(1) **Minimal risk:** The probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

(2) **Greater than Minimal Risk:** The probability and magnitude of harm or discomfort anticipated in the research are greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

What the two methods of IRB review?

The two different risk levels are responsible for the two different methods of IRB Review.

(1) Full-board review at a Convened Meeting:

a. Greater-than-minimal risk research

i. Research involving FDA regulated drugs and devices (IRB member only)

ii. Invasive Procedures (IRB member only)

iii. Sensitive subject matter (IRB member only)

(2) Non-Committee review by Designated Reviewers

a. Minimal Risk Research

i. Non-Human Subjects Determinations (IRB member and Administrative staff)

ii. Personnel Changes (Administrative staff)

iii. Exemption Determinations (Administrative staff)

iv. Expedited Reviews (IRB member only)

The IRB must document the risk level for each study.

The IRB records for each study must indicate the level of risk determined by the IRB. The records include the minutes of convened board proceedings, correspondence letters and electronic checklists in iRIS or check-sheets uploaded into iRIS.

What is the difference between exempt human subjects research and not-human- subjects research?

Certain activities have characteristics of research but do not meet the regulatory definition of human subjects research. Some studies fall in gray areas and it is difficult to determine if in fact they are human subjects research and require submission to the IRB through iRIS for a determination. To be considered research, a study must first be research and then involve human subjects. Below are the federal definitions of each.

To be Research, the activity must be a ***systematic investigation*** including research, development, testing and evaluation **AND** the activity must be designed to ***develop or contribute to generalizable knowledge***.

To involve human subjects, the study must involve a living individual about whom an investigator conducting research ***obtains data through intervention or interaction with the individual*** **OR** the study must involve a living individual about whom an investigator conducting research ***obtains identifiable private information***.

If a study does not meet both definitions, it is "not-human-subjects research" and does not require IRB review. However, this is different from human subjects research that falls into one of the exempt categories.

What are the Exempt categories?

In accordance with 45 CFR 46.101 http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.101 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.

(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.

Currently there is no regulatory basis for Continuing Review for studies that are Exempt. After 5 years the investigators need to check-in with the IRB and apply for another Exemption Determination if the study is still ongoing.

What are the requirements for Expedited Review?

All expedited protocols must be reviewed by a member of the IRB and must undergo continuing review at least once per year. https://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html

- Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.
- The categories in this list apply regardless of the age of subjects, except as noted.
- The expedited review procedure may not be used where identification of the subjects and/or

their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects= financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

- IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.
- Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

Expedited Research Categories

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
    a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
    b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
    a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
    b) from other adults and children[2], considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or

mouth washings; (j) sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject=s privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

8. Continuing review of research previously approved by the convened IRB as follows:
   a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for **long-term follow-up** of subjects; or
   b) where no subjects have been enrolled and no additional risks have been identified; or
   c) where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

What is the meaning of long-term follow-up?

Under expedited review category (8)(a), OHRP interprets "long-term follow-up" to include:

- Research *interactions* that involve no more than minimal risk to subjects (e.g., quality of life surveys); and
- Collection of follow-up data from procedures or interventions that would have been done as part of routine clinical practice to monitor a subject for disease progression or recurrence, regardless of whether the procedures or interventions are described in the research protocol.

In contrast, OHRP interprets "long-term follow-up" to exclude:

- Research *interventions* that would not have been performed for clinical purposes, even if the research interventions involve no more than minimal risk.

What criteria must be met for the IRB to approve research?

45 CFR 46.111 applies to research that is reviewed through expedited procedure or the full board. Each element of the criteria should be considered during the review and discussed during convened meetings.

> (1) Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
>
> (2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
>
> (3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
>
> (4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by federal regulations.
>
> (5) Informed consent will be appropriately documented, in accordance with, and to the extent required by federal regulations.

(6) When the study is greater than minimal risk, clinical research, or an FDA regulated clinical trial, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(8) Where any of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect subjects.

This is the basic criteria to consider. Additional criteria must be met depending upon the type of research such as FDA regulated research and research involving vulnerable populations.

An IRB must determine that **ALL** of the criteria are met prior to issuing an IRB approval.

http://rcb.tamu.edu/humansubjects/forms/HRP314WORKSHEETCriteriaforApproval.pdf

What additional protections are required for Children's research?

When reviewing research with children as subjects, in addition to determining that all the criteria for approval are met as indicated above, the IRB should consider the justification for their inclusion in the research and the circumstances of the children to be enrolled in the study-for example their health status, age, and ability to understand what is involved in the research-as well as potential benefits.

*** For any protocol involving children, the IRB must determine which of the four categories of research apply to that study, if any. The IRB should document the rationale for this choice.**

45 CFR 46.404- Research not involving greater than minimal risk to the children.

To approve this category of research, the IRB must make the following determinations:

- the research presents no greater than minimal risk to the children; ***and***
- adequate provisions are made for soliciting the assent of the children and the permission the permission of **one parent** is sufficient for research to be conducted.

45 CFR 46.405- Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child subjects involved in the research.

To approve research in this category, the IRB must make the following determinations:

- the risk is justified by the anticipated benefits to the subjects;
- the relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by available alternative approaches; ***and***
- adequate provisions are made for soliciting the assent of the children and the permission the permission of **one parent** is sufficient for research to be conducted.

45 CFR 46.406- Research involving greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research, but likely to yield generalizable knowledge about the subject's disorder or condition.

In order to approve research in this category, the IRB must make the following determinations:

- the risk of the research represents a minor increase over minimal risk;
- the intervention or procedure presents experiences to the child subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations;
- the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; ***and***
- adequate provisions are made for soliciting the assent of the children and permission is to be obtained from parents, **both parents** must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

The fourth category, *45 CFR 46.407*, cannot be conducted without permission from DHHS.

45 CFR 46.407 Research that the IRB believes does not meet the conditions of 45 CFR 46.404, 46.405, or 46.406, but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.

If the IRB believes that the research does not meet the requirements of 45 CFR 46.404, 46.405, or 46.406, but finds that it presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, it may refer the protocol to HHS for review. The research may proceed only if the Secretary, HHS, or his or her designee, after consulting with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following an opportunity for public review and comment, determines either: (1) that the research in fact satisfies the conditions of 45 CFR 46.404, 46.405, or 46.406, or (2) the following:

- the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- the research will be conducted in accordance with sound ethical principles; ***and***
- adequate provisions are made for soliciting the assent of children and permission is to be obtained from parents, **both parents** must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

What is the policy for assent of children?

In general assent from children 7 or older should be obtained but this may vary depending on other factors. The IRB shall take into account the ages, maturity, and psychological state of the children involved. Once the IRB has enough information it can determines whether assent is a

requirement of all children, some of the children or none of the children. An assent document should be provided to children that are capable of providing assent when required by the IRB.

What is a Data Safety Monitoring Plan?

A data and safety monitoring plan (DSMP) is a specific plan, developed by the sponsor or the local principal investigator that outlines how study outcomes and progress will be monitored throughout the course of the research to ensure the safety of subjects as well as the integrity of the data.

All studies that are greater than minimal risk or when required by the funding agency must have a data safety monitoring plan submitted as part of the IRB application.

There are four main issues that must be addressed in each plan.

1. **Who**, is the individual or entity that is responsible for the oversight of the data and safety monitoring plan (DSBP)?
    a. Generally the plan can be carried out by the PI and research team. However, there are circumstances when a more extensive plan that includes an outside expert, a board or committee may be needed. A data safety monitoring board (DSMB) is usually needed for large scale multisite clinical trials or very high risk studies.
    b. A DSMP does not always have a DSMB, especially for single site studies.
2. **What** will be monitored?
    a. Monitoring should include a review of the outcome data collected (including adverse events, unanticipated problems, and subject withdrawals) to determine whether there is any change to the anticipated benefits or to the known risks and whether the study should continue as originally designed, should be changed, or should be terminated. Sometimes an interim analyses should be conducted.
    b. Also, the monitoring may include an evaluation of the progress of the research study, including subject recruitment and retention, and an assessment of the quality of the data.
3. **When or how often will the monitoring occur?**
    a. The frequency of data and safety monitoring will be dependent on the nature of the research study. The PI must indicate how often there will be a formal review of the outcome data (monthly, semi-annually, etc.)
4. **What will be reported to the IRB?** At a minimum, the results should be reported at the time of continuing review; or, the frequency should be based upon the complexity or risk of the study. In any case, if the data and safety monitoring reveal an unanticipated problem, or other serious issues it should be reported immediately.

What is the difference between privacy and confidentiality?

- **Privacy is related to setting;** will research procedures, interviews or the informed consent process take place in setting that ensures privacy? Does the subject have control over the extent and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others that may or may not be part of the research team?
- **Confidentiality is related to information/data;** it pertains to an individual's personal information. The IRB must take into account the degree of sensitivity of the information that may be obtained in the research and the protections put in place by the investigator to prevent access by unauthorized persons. Both physical and electronic protections should be addressed.

What is a controverted issue?

- The minutes of IRB meetings must be in sufficient detail to show a written summary of the discussion of controverted issues and their resolution (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)). Many IRBs struggle with the amount of detail that is necessary to satisfy this regulatory requirement.
- Controverted issues are those that cause controversy and dispute among the IRB membership during a convened meeting. Controverted issues that arise during the convened meeting usually are the result of opposition to some aspect of the proposed research. During the review of proposed research, IRB members may express a difference of opinion, or raise issues, questions or concerns that cause debate among the IRB members, or even result in disagreement. Some research, by its very nature, is considered to be controversial (e.g., emergency research where informed consent may not be obtained for all subjects or some research involving vulnerable populations).
- IRB members may resolve controverted issues and concerns with continued discussion and deliberation, decide to seek further clarification from the investigator or sponsor of the proposed research, or an outside consultant. The board may decide to settle the issue by vote. The minutes must summarize the IRB's discussion and resolution of any controverted issues (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)).

What is the policy for non-compliance in human subjects research?

Investigators are required to promptly report any instances of noncompliance that involves a potential risk to subjects or others, or involves failure to comply with federal regulations, state laws, Institutional policies, and/or requirements or determinations of the IRB or provisions of the approved protocol.

- Noncompliance will be reviewed by the IRB Chair or designee to see:
  - If immediate action needs to be taken to ensure subject safety.
  - If the allegation has no basis in fact correspondence will be issued indicating such.

- If the noncompliance is serious and/or continuing it will be sent to the full board.
- If there is noncompliance but it is not serious or continuing it does not require full board review and can be managed by the chair or designee.

- The IRB Chair or designee may request as needed:
  - Additional information from the PI.
  - Consultation with General Counsel.
  - An investigative sub-committee that may include outside expertise.
  - The Post Approval Monitoring (PAM) team to conduct an inquiry/review into the allegation.
- The investigator will be given the opportunity to respond to the allegations of suspected noncompliance.
- The PAM will prepare a written report of any inquiry/
  - The PAM's report will be submitted to the IRB and a copy will be provided to the investigator.
  - If the allegation involves the IRB or any other component of the institution, the PAM will forward a copy of the report to the HRPP Director, Associate VPR and Institutional Official as appropriate.
- When required, a corrective action plan will be developed.
  - The corrective action plan will outline what steps the investigator has taken or will take to resolve the noncompliance and sufficient detail to ensure adequate measures or training is taken to prevent future noncompliance.
- If the noncompliance cannot be resolved as described above or an appropriate corrective action plan that is acceptable to the IRB cannot be developed, the IRB has the authority to impose corrective actions, take additional measures to protect human subjects or to refer the non-compliance to the Institutional Official (IO) with recommendations.

What New Information Items need to be Promptly Reported to the IRB?

New safety, risk and compliance related information, including Unanticipated Problems, require prompt reporting to the IRB. Within 5 business day of being notified of the reportable new information item, investigators are to submit a report through iRIS.

All of the following types of information are to be submitted:

1) Information that indicates a new or increased risk, or a new safety issue. For example:
   a) New information that indicates an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk (e.g., an interim analysis, safety monitoring report, publication in the literature, sponsor report, or investigator finding).
   b) An investigator drug brochure, package insert, or device labeling is revised to indicate an increase in the frequency or magnitude of a previously known risk, or describe a new risk.

   c) Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol.
   d) Protocol deviation that harmed subjects or others or that indicates subjects or others might be at increased risk of harm.
   e) Complaint of a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm.
   f) Any changes significantly affecting the conduct of the research
2) Harm experienced by a subject or other individual, which in the opinion of the investigator are **unexpected** and **probably related** to the research procedures.
   a) A harm is "**unexpected**" when its specificity or severity are inconsistent with risk information previously reviewed and approved by the IRB in terms of nature, severity, frequency, and characteristics of the study population.
   b) A harm is "**probably related**" to the research procedures if in the opinion of the investigator, the research procedures more likely than not caused the harm.
3) Non-compliance with the federal regulations governing human research or with the requirements or determinations of the IRB or the institution, or an allegation of such non-compliance.
4) Audit, inspection, or inquiry by a federal agency or any other outside entity and any resulting reports (e.g. FDA Form 483.)
5) Written reports of study monitors.
6) Failure to follow the protocol due to the action or inaction of the investigator or research staff whether planned or unplanned (deviations).
7) Breach of confidentiality (inappropriate disclosure of or access to confidential information).
8) Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject.
9) Incarceration of a subject in a study not approved by the IRB to involve prisoners.
10) Complaint of a subject that cannot be resolved by the research team.
11) Premature suspension or termination of the protocol by the sponsor, investigator, or institution.
12) Unanticipated adverse device effect (any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.)

Iris will be modified in the near future to capture all of the events above.

http://rcb.tamu.edu/humansubjects/forms/HRP029SOPReportableNewInformation.pdf

What is the process for reviewing reportable new information?
http://rcb.tamu.edu/humansubjects/forms/HRP024SOPNewInformationProcess.pdf

The primary goal for the IRB in reviewing non-compliance or unanticipated problems is to determine what needs to be done to protect human subjects.

What are the outcomes or determinations the IRB can make on research protocols at a convened meeting?

Approve: If the research meets all the federal criteria of approval as submitted, the IRB can approve the research as submitted. An approval period must be set based upon degree of risk but the period cannot be greater than one year.

Approve Pending Modifications to Secure Approval: If minor revisions or additional information is required, but the research otherwise meets the regulatory criteria for approval, the research can be approved pending verification of the required changes. The changes required by the board should be very specific so that when the changes are submitted they can be verified without judging whether or not the changes meet the regulatory criteria for approval. The investigator's response to the requested changes can be verified by a designated reviewer or HRRP staff and the research is not required to come back to a convened board meeting.

Deferred: A protocol is deferred if it does not qualify for Approval Pending Modifications. The research currently does not meet one or more of the criteria for approval without the requested changes or additional information. The IRB must provide the reason for the deferral as well as recommendations to make the research approvable. The research must be reviewed at a subsequent convened meeting of the IRB after the changes are made.

Disapproved: The full IRB has the authority to disapprove proposed research projects that do not meet the federal criteria for approval. This type of vote means that the IRB may consider the research project inappropriate for the local subject population or the risk/benefit ratio is too unfavorable. The IRB may have no recommendations that might make the research approvable.

What are the outcomes or determinations a reviewer can make on research that is reviewed through expedited procedures (non-committee review)?

Approve: If the research meets all the federal criteria of approval as submitted, the reviewer can approve the research as submitted. The research should be no more than minimal risk and the continuing review period cannot be greater than one year.

Approve Pending Modifications to Secure Approval: The reviewer can ask for changes until the study meets the regulatory criteria for approval. If all the criteria for approval are met but minor revisions are necessary the research can be approved pending verification of the required changes.

Send to Full Board: If the research is unable to be approved by the reviewer through expedited procedures, the study must be sent to a convened meeting of the IRB. Research cannot be disapproved through expedited procedures.

How does the IRB address Investigator Conflict of Interest (COI)?

Financial Conflicts of Interest of investigators are managed in accordance with Texas A&M University System Regulation 15.01.03 and University Rule 15.01.03.M1 'Financial Conflicts of Interest in Sponsored Research'.

However, the IRB has the final authority to determine whether the research in which the researcher has a financial conflict of interest and the management plan of that conflict, if any, allow the research to be approved.