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**Return this guide to the
IRB Program Coordinator
prior to leaving the meeting.**

IRB MEMBER CONFLICT OF INTEREST

IRB member is said to have a conflict of interest whenever that person, his or her spouse, or dependent child falls under any of the following conditions:

1. Is an investigator or sub-investigator on the protocol (IRB members only, not applicable to PIs)
2. Has entered into a financial arrangement with the sponsor or agent of the sponsor, whereby the outcome of the study could influence the value of the economic interest.
3. Acts as an officer or a director of the sponsor or an agent of the sponsor.
4. Has any equity interest in the sponsor of \$10,000 or greater or 5% or greater of the equity of the sponsor.
5. Has received payments or other incentives from any sponsor that when aggregated for the member, spouse and dependent children, total of \$10,000 or greater.
6. Has identified him or herself for any other reason as having conflict of interest.

ADVERSE AND UNANTICIPATED PROBLEM REPORT

If the following three conditions apply, then the incident must be reported to OHRP.

1. The event was unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied.
2. The event was related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).
3. The event suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

In consideration of the above items, review the overall study as follows:

- a. Is the risk/benefit ratio still acceptable?
- b. Is a modification needed in the protocol to define or minimize the risk?
- c. Does the consent/permission form appropriately list the current event?
- d. Does the protocol require any revisions?
- e. Does the consent/permission form require any revisions?
- f. Should all research subjects be informed of the event?
- g. Overall, does approval of the study still meet the criteria of 45 CFR 46.111?
- h. Does the event represent an incident of non-compliance?
- i. Should the study continue?

§46.111 Criteria for IRB approval of research

In order to approve human subject research the IRB shall determine that all of the following requirements are satisfied:

(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 §46.116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117.

(6) When appropriate, 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) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Required Elements of Informed Consent
45 CFR 46.116

1. a statement that the study involves research;
2. an explanation of the purposes of the research;
3. the expected duration of the subject's participation;
4. a description of the procedures to be followed;
5. identification of which procedures are experimental;
6. a description of reasonably foreseeable risks or discomforts that the subjects may encounter, and if appropriate, a statement that some risks are currently unforeseeable;
7. a description of possible benefits, if any, to the subject and others which may be reasonably expected. It should be stated that since it is an experimental treatment or procedure, no benefits can be guaranteed.
8. a disclosure of appropriate alternative procedures or treatments, if any, which are available and might be advantageous to the subject. One alternate might be to choose not to participate in the research;
9. a statement describing the manner and extent, if any, to which confidentiality of records identifying the subject will be maintained and, if applicable, a statement that the IRB, FDA and other entities may inspect the records;
10. for research involving more than minimal risk, an explanation as to whether any compensation or any medical treatments are available if injury occurs and, if so, what they consist of or where further information may be obtained;
11. a description of whether or not reimbursement for time, inconvenience, etc. will be given, including the schedule of payments;
12. an explanation of who to contact for answers about the research and in the event there is a research-related injury (This is generally the PI or another staff member closely associated with the study). A separate contact must be named for questions concerning the subject's rights.
13. a statement that the subjects' participation is voluntary, that refusal to participate will not involve penalty or loss of benefits to which the subject is entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is entitled.

SEE OTHER SIDE FOR ADDITIONAL ELEMENTS THAT MUST BE ADDED WHERE APPROPRIATE

Additional Elements of Informed Consent
45 CFR 46.116

1. A statement that the particular treatment and/or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable; ***This element should be included when the research involves an investigational drug or device or involves procedures for which the risk profile is not well known***
2. anticipated circumstances under which the subject's participation may be terminated by the investigator with or without the subject's consent; ***Include when there are known circumstances under which the subject's participation may be terminated by the investigator or sponsor.***
3. a description of any additional costs for which the subject will be responsible, that may result from participation in the research study; ***Include when there are additional costs to subjects, over and above standard care, e.g., additional MRI's radiograph's, DEXA scans; additional visits that may not be covered by insurance/Medicare/Medicaid***
4. a description of the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject; ***This element should be included when there is a likelihood that abrupt termination from the research would result in adverse events to the subject and alternative procedures/medications should be administered, e.g., study drug would need to be tapered and replaced with an approved drug so that the subject was not placed at increased risk of injury.***
5. a statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject; ***Included when there is likelihood that interim findings might indicate increased risk, lack of efficacy, etc. and a reasonable person would wish to reconsider participation.***
6. the approximate number of subjects that will be involved in the study, totally and at UT Austin. ***Include when such information might affect a subject's willingness to participate.***

Short Form Written Consent Document

If use of a short form of consent documentation is requested, the IRB must determine that:

1. the consent document (short form) states that the required elements of consent have been presented orally to the subject or the subject's legally authorized representative (LAR);
2. there is written summary that embodies the basic and appropriate additional elements of consent and what will be said to the subject or the subject's LAR;
3. There will be a witness to the oral presentation;
4. for subjects who do not speak English, the witness will be fluent in both English and the language of the participant of the subject's LAR.
5. The subject or the subject's LAR will sign the short form (if the study is FDA-regulated, the subject or the subject's LAR will sign and date the short form);
6. The witness will sign both the short form and a copy of the summary;
7. The person obtaining consent will sign a copy of the summary;
8. A copy of the short form will be given to the subject or the subject's LAR;
9. A copy of the summary will be given to the subject's or the subject's LAR.

FOR STUDIES INVOLVING CHILDREN

Definitions:

Minimal Risk Research - Research in which 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 (of normal subjects) or during the performance of routine physical or psychological examinations or tests.

Assent - A child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Consent/Permission - the agreement of parent(s) or guardian to the participation of their child or ward in research.

Parent - a child's biological or adoptive parent.

Ward - A child who is placed in the legal custody of the state or other agency, institution or entity consistent with applicable Federal, State, or local law.

Questions:

1. Determine according to the definition of minimal risk shown above if the proposed research investigation minimal or more than minimal risk.
2. Does the proposed research activity hold the prospect of direct benefit to the individual subject?
3. If the study intends to include wards in the research, is the research related to their status as wards or conducted in schools, camps, hospitals, institutions or similar settings in which the majority of children involved as subjects are not wards?
4. Generally assent is required from all children who are enrolled in research activities, has the investigator considered the ages, majority and psychological state of the potential subjects to determine if obtaining assent is a reasonable expectation?
5. If a waiver to obtain assent is being requested is one of the following justifications given:
 - The children are not capable of providing assent base on age, maturity or psychological state.
 - The capability of the children is so limited that they cannot reasonably assent to the research.
 - The interventions or procedures involved in the research holds out a prospect of direct benefit that is important to the health and well-being of the children and is available only in the context of the research.
 - Assent is waived using criteria for waiver of informed consent. . **(45 CFR 46.116(d))**
6. Is there a requirement for a written documentation of assent?

Permissible Categories of Research:

Research investigation not involving greater than minimal risk. (45 CFR 46.404)(21 CFR 50.51)

1. Does the research investigation involve no greater than minimal risk?
2. Are adequate provisions made for obtaining assent of the children?
3. The informed permission of the parent(s) or guardian(s) will be obtained?

Research investigation involving more than minimal risk, but presenting the prospect of direct benefit to the individual subjects. (45 CFR 46.405)(21 CFR 50.52)

1. Does the research involve greater than minimal risk?
2. Does the research present the prospect of direct benefit to the individual subject?
3. Are the risks justified by the anticipated benefits?
4. Is the relationship of the anticipated benefit at least as favorable as alternative approaches?
5. Are adequate provisions made for obtaining assent of the children?
6. Will the informed permission of the parent(s) or guardian(s) be obtained?

Research investigation involving more than minimal risk with no prospect of direct benefit to the individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition. (45 CFR 46.406)(21 CFR 50.53)

1. The research involves more than minimal risks to subjects with no prospect of direct benefit to the individual but is likely to yield generalizable knowledge about the subject's disorder or condition?

2. Does the risk represent a minor increase over minimal risk?
3. Is the intervention or procedure present experience commensurate with those inherent in the subjects' actual or expected medical, dental or psychological, social or educational experience?
4. Are adequate provisions made for obtaining assent of the children?
5. Will the informed permission of the parent(s) or guardian(s) be obtained?

In order to approve research investigation under this category all questions above must be "Yes".

Research investigation not otherwise approvable which presents an opportunity to understand, prevents, or alleviates a serious problem affecting the health or welfare of children. (45 CFR 46.407)(21 CFR 50.54)

1. The IRB must find 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?
2. If the IRB makes this determination and the research will be federally funded, a request may be made by the PI through the IRB, to the secretary of Health and Human Services who, after convening a panel of experts and following opportunity for public comment, may approve the research.

FOR STUDIES WITH PREGNANT WOMEN AND FETUSES

46.204 - Research involving pregnant women or fetuses.

Pregnant women or fetuses may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
2. a) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or,
b) If there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.
3. Any risk is the least possible for achieving the objectives of the research;
4. If a or b from #2 above is "Yes", the woman's consent is obtained in accord with the informed consent provisions of 45 CFR 46.116.
5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of 45 CFR 46.116, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
6. Each individual providing consent under numbers 4 or 5 above is fully informed regarding the reasonably foreseeable impact of the research on the fetus;
7. For children as defined in 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
10. Individuals engaged in the research will have no part in determining the viability of a neonate.

46.207 - Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates.

The Secretary will conduct or fund research that the IRB does not believe meets the requirements of 46.204 or 46.205 only if:

- (a) The IRB 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 pregnant women, fetuses or neonates; and
- (b) The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either:
 - (1) That the research in fact satisfies the conditions of 46.204, as applicable; or
 - (2) The following: (i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; (ii) The research will be conducted in accord with sound ethical principles; and (iii) Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part.

FOR STUDIES INVOLVING PRISONERS

45 CFR 46.305

A) Approval may be given only if the IRB finds that:

1. any possible advantages accruing to the prisoner through his or her participation in the research, (when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison) that are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired.
2. the risks involved in the research commensurate with the risks that would be accepted by non-prisoner volunteers;
3. procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. (Note: Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project);
4. the information is presented in language which is understandable to the subject population;
5. assure that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and
6. each prisoner is clearly informed in advance that participation in the research will have not effect on his or her parole;
7. when the research requires follow-up beyond the period of incarceration, have provisions been made for locating the individual;
8. participants informed of how follow-up will take place, if such is required;

B) Where the Board finds there may be a need for follow-up the following must be included:

1. are there potential complications that may result form participation in the research;
2. is the possible duration of such complications stated;
3. types of examinations and care that would be typically be needed for such complications;
4. adequate provisions for such examinations or care to subjects after their participation in the research has ended; taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

45 CFR 46.306

Behavioral research conducted or supported by DHHS may involve prisoners as subjects only if it involves:

1. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
2. Study of prisons as institutional structures or of prisoners as incarcerated persons provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
3. Research on conditions particularly affecting prisoners as a class (e.g., vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary (DHHS) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of his or her intent to approve such research (Does the proposed treatment benefit at least as many individuals as the last available standard therapy and that number is greater than any other eligible treatment).
4. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subjects. In cases in which those studies requires assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups that may not benefit from the research, the study may continue only after the Secretary (DHHS) has consulted with appropriate

FOR STUDIES INVOLVING PRISONERS

experts, including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of his or her the intent to approve such research. (Does the proposed treatment benefit at least as many individuals as the last available standard therapy and that number is greater than other eligible treatment).

5. In accordance with the federal regulations, the IRB has the authority to waive the requirement that research activities fit in Categories 1-4 listed above if the proposed research meets the following specific criteria: 1) the research involves epidemiologic studies in which the sole purposes are (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study potential risk factor associations for a disease, and (2) the IRB has determined that items A and B have been appropriately addressed and has also determined that (i) the research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and (ii) prisoners are not a particular focus of the research.

CATEGORIES FOR RESEARCH ELIGIBLE FOR EXPEDITED REVIEW

Research activities that present no more than minimal risk and 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 46.111** and **21 CFR 56.110**.

- 1. Clinical studies of drugs and medical devices only when conditions above are met.**
 - a. Research on drugs for which an investigational new drug (IND) 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 or 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, non-pregnant 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, 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 include:
 - a. Hair and nail clippings in a non-disfiguring 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 sub-gingival 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 eth medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications).** Examples include:
 - 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 non-research purposes (such as medical treatment or diagnosis).** NOTE: Some research in this category may be exempt from HHS regulations for the protection of human subjects. 45 CFR 46.111 (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 HHS regulations for the protection of human subjects. 45 CFR 46.111 (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.**

CRITERIA FOR RESEARCH ELIGIBLE FOR EXEMPT REVIEW

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. These regulations identify specific categories of Exempt research activities and also identify when there are exceptions.

To be classified as Exempt, the research:

1. **Must involve only procedures or be a type of study listed in one or more of the Exempt Categories (listed above);**
2. **Cannot involve children being surveyed, interviewed or interactively publicly observed;**
3. **Cannot involve prisoners as research subjects;**
4. **Cannot be greater than minimal risk, and**
5. **Cannot be FDA-regulated, except for category (6).**

“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)

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 Board Review.