GUIDANCE TO RESEARCH USING HUMAN SUBJECTS

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1. Introduction

The Department of Public Health (Department or DPH) maintains an Institutional Review Board which is charged with assuring that the rights of human subjects of research conducted or sponsored by the Department are protected as outlined in federal and state policies and regulations. The Board is guided by the ethical principles set forth in the publication: "The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research."

All research projects that involve human subjects must be submitted to the Board and approved by the Board prior to their initiation. These and other requirements for continuing contacts between the investigators and the Board are enumerated in this manual. The Board has the authority to suspend or terminate approval for research projects when certain requirements are not met. Approval of research projects is based on the determination that all aspects of the project are in accordance with the procedures that are outlined in this manual and other applicable regulations and considerations, including 45 C.F.R. 46 and 21 C.F.R. 50 & 56.

Insuring the rights of human subjects of research is a collaborative effort of all those persons who are involved with the research project. The procedures that are outlined in this manual constitute the minimum framework to assure that subjects' rights are protected. It is the Board's responsibility to assess whether or not these minimum standards are met based on what is submitted to them. It is in the conduct of the research project, however, that the standards are implemented. The process of protecting subjects' rights, then, hinges on the performance of the investigators as they carry out the project.

It is hoped that the intent of these procedures will be helpful as a guide to investigators as they make the innumerable decisions necessary to conduct a research project. If there are questions, the Board may be reached at:

Georgia Department of Public Health
Institutional Review Board
2 Peachtree Street, NW, Suite 16-432
Atlanta, Georgia 30303-3142
(404) 657-6645

2. Definitions

The IRB uses the following definitions in determining whether a project requires IRB review and approval:

1. *Research* – means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

2. *Human subject* – means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.
3. *Private information* – means information that is individually identifiable (i.e. the identity of the subject is or may be readily ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.
4. *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.

3. Application Process

3.1. Who Should Apply

Approval must be obtained for all research involving human subjects when:

a. the research is conducted by or sponsored by the Department;
b. the research requires access to the Department's subject pool;
c. the subjects are employees of the Department;
d. the research requires access to data held by the Department;
e. before implementing any amendments to previously approved research protocols.

Approval must be obtained prior to any involvement of the human subjects. The approval by the Board is limited to no more than a 12-month period and must be renewed at least annually to continue the involvement of human subjects. Researchers must have no involvement with human subjects unless they have current approval from the Board.

3.2. Application Procedures

Applications for approval are filed with the IRB Director. Applications are submitted via e-mail using the "Initial Application" form. Only electronic applications submitted on the official DPH forms will be accepted for review. Applicants are to follow the instructions listed on the forms.

The information that is submitted on the application form should represent the procedures, forms, activities, etc. that are subject to the IRB approval. The approval will be only for what is contained in the application - not for the entire protocol (assuming there is a protocol and it is different). No application will be considered until all required information is received by the Board.

If the investigator translates any of the materials both, the English and foreign language versions must be submitted with the application. Note that the IRB approves only the English language version of all submitted materials and it is the investigator's responsibility to assure an appropriate and accurate translation.

The application should be submitted at least six weeks prior to the desired start time. No activity may begin until a written approval from the Board is received.

3.3. Processing Fees

All externally funded projects are subject to a processing fee. The fee is non-refundable regardless of the outcome of the review and must be paid before the initial review of the application. The fee schedule is as follows:

Initial Applications:
- $1,500 for expedited or full reviews
- No fee for studies meeting the criteria for exemption from IRB review

Amendments:
- $250 for major changes that must be reviewed by the full Board
- No fee for minor changes that can be reviewed using the expedited review procedures

Continuing Reviews:
- $750 for studies with ongoing data collection/contact with human subjects
- $250 for studies where only data analysis/manuscript preparation is ongoing

The following types of projects are exempt from the processing fees:
1) Projects conducted by faculty, unless the project is funded from external sources
2) Projects conducted by undergraduate or graduate students, unless the project is funded from external sources
3) Projects where the Principal Investigator is a Georgia state employee, unless the project is funded from external sources

Checks should be made payable to DPH IRB. *Include a short version of the title and the name of the Principal Investigator on the check*. Mail payment to:

Georgia Department of Public Health
Attention: Financial Services - IRB
2 Peachtree Street, NW, 15th Floor
Atlanta, Georgia 30303

4. Informed Consent

Except as provided elsewhere in this directive, no investigator may involve a human subject in a research project unless the investigator has obtained the legally effective informed consent of the subject or the subject's legal representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the subject's legal representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the subject's legal representative shall be in language that is understandable to the subject or the subject's legal representative. No informed consent shall contain any language that waives or appears to waive any of the subject's legal rights, or

releases or appears to release the investigator, the sponsor, or the institution or its agents from liability for negligence.

The IRB approves an English language version of informed consent. If the investigator translates the informed consent, it is his or her responsibility to assure an appropriate and accurate translation. Both, the English and foreign language version of the informed consent must be submitted with the application.

When the application has been approved, the IRB Chair will stamp the approved consent form and return the stamped copies to the Principal Investigator. These stamped copies include an expiration date and are to be used in the study.

4.1. Elements of Informed Consent

The minimum elements of informed consent are as follows:

a. a statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
b. a description of any reasonably foreseeable risks or discomforts to the subject;
c. a description of any benefits to the subject or to others which may reasonably be expected from the research;
d. a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
e. a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;
f. for research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
g. an explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and
h. a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

When appropriate, one or more of the following elements of information shall also be provided to each subject as part of the consent form:

a. a statement that the particular treatment 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;
b. anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
c. any additional costs to the subject that may result from participation in the research;

d. all appropriate alternatives to participation, including nonparticipation;
e. the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
f. a statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject;
g. the approximate number of subjects involved in the study;
h. if the design includes treatment and control groups (and/or placebo control groups), statements that describe how the subject will be assigned to groups; and,
i. for certain subjects, including patients in any institution of the Division of Mental Health, Developmental Disabilities and Addictive Diseases, a statement from the subject's attending physician that the subject understands the informed consent and is competent to give consent for participation in the study.

4.2. Situations When Written Consent Is Not Required

The Board may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the Board finds and documents that (1) the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: public benefit of service programs; 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; and, (2) the research could not practicably be carried out without the waiver or alteration.

The Board may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirements to obtain informed consent provided the Board finds and documents that:

1. the research involves no more than minimum risk to the subjects;
2. the waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. the research could not practicably be carried out without the waiver or alteration; and,
4. whenever appropriate, the subjects will be provided with additional pertinent information after participation.

The Board may waive the requirement for a signed informed consent form (but not the requirement for informed consent) if it finds that either (1) the only record linking the subject and the research would be the signed informed consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research and the subject's wishes will govern, or (2) the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. An example would be an anonymous mailed questionnaire. In this situation, a cover letter could contain the elements of informed consent and a signature of the subject would not be required.

There are certain other "emergency" situations, detailed in 21 C.F.R. 50.23 & 50.24 where an intervention may occur without prior informed consent.

5. Approval Process

To seek approval of a protocol from the Department's IRB, the investigator must submit a completed and signed "Initial Application" form and all supporting documents to the IRB Director. All actions of the Board concerning an application are communicated in writing to the investigator and the sponsor.

5.1. Types of Review Procedures and Criteria

The Board may follow one of three procedures for review of an application, depending on the characteristics of the project. The types of review and the criteria for each type are listed below.

5.1.1. Exempt Review Procedure

Applications for projects in which the only involvement of human subjects is in categories that are described below is exempt from the requirement for IRB review and approval. The categories are:

a. research conducted in established or commonly accepted education settings, involving normal educational practices, such as
    1. research on regular and special education instructional strategies, or
    2. research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods;
b. research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior unless
    1. the information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects, and
    2. 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;
c. 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 subparagraph 2. above, if
    1. the human subjects are elected or appointed public officials or candidates for public office or
    2. federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter;
d. 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;

e. 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:
    1. public benefit or service programs,
    2. procedures for obtaining benefits or services under those programs,
    3. possible changes in or alternatives to those programs or procedures, or
    4. possible changes in methods or levels of payment for benefits or services under those programs;

    For projects in this category, the investigator must submit, along with the other requirements for application, the agreement concerning confidentiality of records and the statement from the appropriate official that the proposed project meets the requirements of O.C.G.A. 50-18-101 and other DPH Directives.
f. taste and food quality evaluation and consumer acceptance studies if:
    1. wholesome foods without additives are consumed, or
    2. 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.

Note that, although federal regulations do not require a signed informed consent for exempt research, the DPH IRB requires that all exempt studies include an informed consent to allow potential participant to voluntarily agree to take part in the study.

The IRB Chair will make the final determination if the protocol can be granted exempt status. The Chair may contact the investigator to request additional documentation or clarification. If exempt status cannot be granted, the application will be reviewed using Expedited or Full Board review procedures.

5.1.2. Expedited Review Procedure

For applications for projects meeting the below described eligibility requirements for expedited review, the review may be performed by the IRB Chair or by one or more Board members, designated by the IRB Chair, who are experienced reviewers. In reviewing the research, the reviewers may exercise all the authorities of the Board except the reviewers may not disapprove the research. The reviewers may approve the application, or they may require modifications and grant approval once these modifications have been made. If they do not approve the application, it will be forwarded to the Board for a full Board review.

The eligibility requirements for research for which the IRB may use expedited review are as follows:

1. the application represents minor changes in a currently approved project, or
2. the research is found to involve no more than minimal risk to the subject and falls under one of the following categories established by the U.S. Department of Health and Human Services (DHHS) and listed below. This list will be amended, as appropriate, through periodic republication by DHHS in the Federal Register. A

copy of the list is available from the Office of Human Research Protections, DHHS. The investigator must check with DHHS for any amendments to the list.

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, 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.

5.1.3. Full Board Review Procedure

Full Board review is required for all eligible projects that are neither exempt from review nor qualify for expedited review. Protocols are assigned a Primary Reviewer and are reviewed at the convened IRB meeting. Each member of the IRB receives a complete copy of the application. The

Primary Reviewer is responsible for conducting an in-depth review of the protocol and presenting a summary of the study and any concerns or comments at the convened meeting. The members of the Board discuss the project and vote on the decision. The investigator will be notified of the Board's decision in writing.

If the protocol is "*conditionally approved*" a notice listing the required changes will be sent to the investigator. If the requested changes are minor, the investigator's response will be reviewed by the IRB Chair who will then make the decision on the protocol. If the requested changes are extensive, they will be forwarded to the full Board for review.

5.2. Review Criteria

In order to approve a protocol, the IRB will determine if all of the following are met:

a. risks to subjects are reasonable in relation to any anticipated benefits to subjects and the importance of the knowledge to be gained;
b. risks to subjects are minimized
    1. by using procedures that are consistent with sound research design and which do not unnecessarily expose subjects to risk, and,
    2. whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes;
c. selection of subjects is equitable;
d. appropriate measures are in place to obtain and document the prior informed consent of the subjects or the subjects' guardians, and the prior legally effective informed consent of the subjects or the subjects' legal guardians have been obtained and documented;
e. there are adequate provisions for monitoring the collected data to ensure the safety of subjects and to protect their privacy by maintaining anonymity or confidentiality of the data.
f. additional safeguards are in place to protect the rights and welfare of participants from vulnerable populations.

5.3. Types of Decisions

The IRB review of research proposals will result in one of the following status categories:

1. *Approved* – this decision is issued when the project meets the criteria outlined above. A written approval notice that includes the approval expiration date will be sent to the investigator. No activities involving human subjects may begin until the investigator receives the written approval notice.
2. *Conditionally Approved* – This decision is issued when changes or clarifications to the initial protocol are required. A written notice outlining the conditions that must be met before approval is granted will be sent to the investigator. The investigator must respond to these conditions in writing within 30 days from the date of the notice. If the Board does not receive a response within 30 days, the protocol will be automatically disapproved. The investigator's response is reviewed by the IRB Chair and, if necessary, the full Board. If it is determined that the conditions have been met, a letter of approval

will be sent to the investigator. No activities involving human subjects may begin until full approval is granted.

3. *Disapproved* – This decision is issued if the project does not meet the criteria for approval and there are serious risks to participants and not enough safeguards are in place to minimize those risks. A written notice outlining the reasons for denial will be sent to the investigator. The investigator may appeal the decision of the Board as described in Section 7 of this manual.
4. *Tabled* – This status will only be assigned if an initial application, amendment, or request for continuation is not reviewed at the meeting for which it was originally scheduled. The submission will be re-scheduled for review at the next meeting. A notice explaining the reason for this decision will be sent to the investigator.
5. *Closed* – This status indicates that the investigator finished all research related activities involving human subjects and requested to permanently close the project. If the project has been closed, it cannot be re-opened. If the investigator wished to restart the project in the future, he or she must submit a new IRB application.
6. *Terminated* – This decision indicates that the approval of a project has been permanently terminated by the IRB. The Board may terminate a study if the investigator does not comply with IRB requirements or federal regulations, or if there has been serious or unexpected harm to subjects. Termination of a project means that the approval has been withdrawn and all research related activities involving human subjects must cease. A notice explaining the reason for this decision will be sent to the investigator, appropriate Divisions of the Department, DHHS, the Food and Drug Administration and other appropriate organizations. If the approval has been terminated, the project cannot be re-opened. If the investigator wishes to restart the project in the future, he or she must submit a new IRB application.
7. *Suspended* – This decision indicates that an approval of a project has been temporarily put on hold by the IRB. This decision does not indicate termination of the project. The Board may suspend a project that does not comply with IRB requirement or federal regulations, or that has been associated with unexpected serious harm to subjects. A notice of this action listing conditions that must be met to remove the hold will be sent to the investigator, appropriate Divisions of the Department, DHHS, the Food and Drug Administration and other appropriate organizations. The investigator must respond to these conditions in writing within 30 days from the date of the notice. If the Board does not receive a response within 30 days, the approval of the project will be automatically terminated. All research related activities involving human subjects must cease until the IRB removes the hold.

5.4. Amendments to Approved Protocols

If the investigator wishes to amend the protocol after it has been approved, she or he must submit the "Application for an Amendment to an Existing Protocol" form and any additional documents that have been introduced or changed.

To qualify for an expedited review, the changes proposed in the amendment must meet the requirements of Section 5.1.2 in that they must be minor. Minor changes are ones that do not substantially alter:

a. risks to participants
b. research design or methodology
c. participant population
d. other factors that may warrant review by the full Board.

Amendments that meet the above criteria will be reviewed by the IRB Chair or the Primary Reviewer of the initial protocol. If the reviewer determines that the proposed amendment substantially alters the protocol, the amendment will be forwarded to the full Board for review.

5.5. Continuing Review

Approval to conduct a project may be granted for a period of no more than 12 months. If the project is not completed by the end of the approved period, the investigator must apply for a continuation of approval. The length of the approval period and the extent of continued review will be determined by the Board at the time of approval and will be communicated to the investigator. It is the responsibility of the investigator to keep track of the expiration date and submit "Continuing Review Application" to the IRB. The Board considers the renewal request and notifies the investigator of the decision. The investigator should submit the renewal application well in advance of the expiration of the previous IRB approval to allow the Board enough time to review the application. Submitting the "Continuing Review Application" does not automatically extend the approval period. If previous approval expires before the Board reviews the renewal application, the investigator must stop any activities involving human subject until the renewal application is approved.

The continuing review application may qualify for expedited processing if:

1. the study continues to meet the criteria for expedited review, or
2. participant enrollment is on-going and no additional risks or adverse events have been identified, or
3. enrollment of new participants has been completed and all research related activities involving human subject have been completed; the research remains open only for data analysis or long-term follow-up of participants, or
4. no participants have been enrolled and no additional risks have been identified.

Continuing Review Applications that qualify for the expedited review procedures will be reviewed by the IRB Chair or by one or more Board members, designated by the Chair, who are experienced reviewers.

5.5.1. Frequency and Extent Considerations

The length of time of approval for each project will be based on a consideration of the vulnerability of the subject population, the extent of risks to subjects, and a consideration of other factors of the research administration and design. Special attention will be given to

projects involving new procedures or treatments and projects involving placebo control groups. The following is a frequency guideline for approval periods:

a. new drug trials - 6 month approval period;
b. projects involving pregnant women, children, or other vulnerable populations - 9 to 12 month review period; and
c. projects involving minimal risks to subjects - 12 month approval period.

5.5.2. Suspension or Termination of Projects

The Review Board may suspend or terminate approval of research that is not being conducted in accordance with requirements for the protection of human subjects and any research associated with unexpected serious harm to subjects. Any suspension or termination of approval will include a statement of the reasons for the Board's action, including any procedures that were not followed in the course of the research project, and will be reported promptly to the investigator, the institution with which the investigator is affiliated, the appropriate Division or Office of DPH, and, if appropriate, to DHHS, the Food and Drug Administration (FDA), and other organizations.

5.5.3. Lapse In Approval

The continuation of a research project after the expiration of the Board's approval is a violation of federal regulations. If the Board's approval has expired, research activities must stop. No new subjects may be enrolled in the project. If the investigator is actively pursuing renewal of approval with the Board and the current approval expires before the Board reviews the renewal application, no activities involving human subject may be performed until the Board approves the renewal application or grants an extension of approval until decision on the continuing review application is made.

When the Board terminates protocol approval, in addition to stopping all research activities, any subjects currently participating should be notified that the study has been terminated due to lapse in approval.

Procedures for withdrawal of enrolled subjects should consider the rights and welfare of the subjects. If discontinuation of research activities would result in increased risk or harm to participants, the investigator may appeal the requirement to stop all research related activities by sending a written request to the IRB Chair. The appeal must specify which research activities should continue and explain why discontinuation of these activities would increase the risk or harm the participants. If follow-up of subjects for safety reasons is permitted by the IRB Chair, the subjects should be so informed and any adverse events or outcomes should be reported to the Board. If the appeal is denied, a new application must be submitted for IRB review and approval.

6. Responsibilities of Investigators

It is the responsibility of the investigator to design the project in such a way that minimizes risks to subjects and to continuously monitor the activities of the project to assure that the risks remain at a

minimum. It is the responsibility of the investigator to report in writing the following information to the Board:

a. any reports requested by the Board;
b. any changes in the project's protocol, including a change of DPH Sponsor or a change of Principal Investigator;
c. requests for continuing review, and,
d. any adverse events associated with the project.

Any proposed changes in previously approved projects must be approved by the Board and cannot become effective prior to being approved. Consideration of changes will be accomplished in the manner described for initial approval of applications. Changes in DPH Sponsors or Investigators do not require the approval of the IRB but the contact information for the new DPH Sponsor and/or Investigators must be provided to the IRB Chair.

In addition to reporting to the Board, the investigator must report adverse events as required to the Food and Drug Administration and must indicate to the Board such notification. The Board will acknowledge these reports in writing and will indicate one of the following: 1) the Board will review the report at the next meeting and the project may continue until a formal Board action is taken; or 2) the project must be discontinued immediately. The IRB Chair has the authority to make the decision concerning which course of action will be followed.

7. Appeals

A decision to disapprove a research project may be appealed by submitting a written request for reconsideration by the Board, including any additional data pertinent to the decision. Upon receipt, the request and any related documents will be conveyed to the Board for reconsideration. The reconsideration will be accomplished in the manner described for initial review. A negative decision by the Board cannot be reversed except by a vote of Board members.

8. Research Involving Vulnerable Populations

For research projects that involve the participation of vulnerable subjects, there are specific requirements contained in the federal regulations. Compliance with these regulations will be assessed by the Board when a project involves any of these groups of subjects. The investigator must demonstrate that inclusion of participants from these populations is justified and that additional safeguards have been implemented to protect the rights and welfare of these participants. The types of subjects and the associated federal regulation(s) are listed below.

8.1. Pregnant Women, Human Fetuses and Neonates

Studies on pregnant women, human fetuses and neonates may qualify for expedited review if they meet the criteria outlined in Section 5.1.2. The IRB Chair will make the final determination. Studies that do not qualify for expedited review will be reviewed by the full Board in accordance with the criteria of 45 CFR 46 Subpart A and B. Pregnant women or human 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 on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
2. the risks 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, 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 the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit to both the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means; and her consent is obtained;
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, 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 of incest;
6. each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. for children who are pregnant, assent and permission are obtained in accordance with 45 C.F.R. 46 Subpart D;
8. no inducements, monetary or otherwise, will be offered to the 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 pregnancy; and,
10. individuals engaged in the research will have no part in determining the viability of a neonate.

Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

1. where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
2. each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
3. individuals engaged in the research will have no part in determining the viability of a neonate.

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this section unless:

1. The IRB determines that the research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or
2. The IRB determines that the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
3. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

After delivery nonviable neonate may not be involved in research covered by this section unless all of the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
2. The research will not terminate the heartbeat or respiration of the neonate;
3. There will be no added risk to the neonate resulting from the research;
4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
5. The legally effective informed consent of both parents of the neonate is obtained. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accordance with the provisions of this manual that relate to general protection of human research subjects and additional protections for children involved as subject, as well as 45 C.F.R. 46 subparts A & D.

Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus:

1. Such research may be conducted only if the IRB finds that it is in accord with any applicable federal, state, or local laws and regulations regarding such activities.
2. If information associated with the material collected is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent regulations are applicable.

8.2. Prisoners

All initial applications for studies involving prisoners must be reviewed by the full Board in accordance with 45 CFR Subpart C. To comply with 45 CFR Subpart C 46.304, the membership of the board will include at least one member who is a prisoner or a prisoner representative with the appropriate background and experience to serve in that capacity. The prisoner representative will be assigned as the Primary Reviewer.

As it relates to prisoners, federal regulations defined *minimal risk* as **"**the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons." When assessing the level of risks, the IRB will only allow risks that would be acceptable for non-prison volunteers. The Board will not use risks that face prisoners in the prison environment as a standard for acceptable risks.

Amendments to protocols involving prisoners that propose minor alteration to the previously approved protocol that do not change the level of involvement of prisoners or the level of risk will be reviewed using the expedited review procedure. All other changes will be reviewed by the full board. The IRB Chair, in consultation with the prisoner representative, will make the final determination.

Continuing review of protocols involving prisoners will be reviewed using the expedited review procedures only if they meet the criteria for expedited review outlined in Section 5.1.2 and:

1. enrollment of new participants has been completed and all research related activities involving human subject have been completed; the research remains open only for data analysis; or
2. no participants have been enrolled and no additional risks have been identified.

Continuing review applications that do not meet the above criteria will be reviewed by the full Board.

When reviewing studies involving prisoners, the IRB will ensure that the research falls under one of the following categories:

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 (for example, 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 of DHHS has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research; or

4. research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary of DHHS has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research.

As stated in 45 CFR 46.305(a)(2-7), when reviewing research involving prisoners, the IRB will also ensure 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, 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 are commensurate with risks that would be accepted by nonprisoner 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. 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. adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and
6. where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

8.3. Children and Wards

When reviewing research potentially involving children the IRB uses the following definitions:

1. *Children* – means persons who have not attained the legal age for consent to treatment or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted (Georgia – 18 years of age).
2. *Assent* – means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.
3. *Permission* – means the agreement of parent(s) or guardian to the participation of their child or ward in research.
4. *Parent* – means a child's biological or adoptive parent.

5. *Guardian* – means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

For research not involving greater than minimal risk, the investigator must demonstrate that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians pursuant to 45 C.F.R 46.408.

For research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects the investigators must demonstrate that:

1. the risk is justified by the anticipated benefit to the subject;
2. the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches, and
3. adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians pursuant to 45 C.F.R. 46.408.

For research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or conditions, the investigator must demonstrate that:

1. the risk represents a minor increase over minimal risk;
2. the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
3. the intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
4. adequate provisions are made for soliciting assent of the children and permission of their parents or guardians pursuant to 45 C.F.R. 46.408.

For research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children, the investigator must demonstrate that:

1. research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
2. for research funded by DHHS, the Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either that the research in fact satisfied the conditions described above or the following:
    a. the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
    b. the research will be conducted in accordance with sound ethical principles;
    c. adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians pursuant to 45 C.F.R. 46.408.

Children who are wards of the state or any other agency, institution or entity can be included in research approved as 1) involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subjects' disorder or conditions, or 2) research not otherwise approvable but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. Wards may be included in such research only if the research is related to their status as wards, or is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

If the research is approved, the IRB will require that an advocate is appointed for each child who is a ward. One individual may serve as advocate for more than one child. The advocate must have the background and experience to act in, and agrees to act in, the best interest of the child for the duration of the child's participation in the research, and must not be associated in any way with the research, the investigators or the guardian organization.