NEOMED Institutional Review Board for Studies Involving Human Subjects

POLICY AND PROCEDURES MANUAL

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Reference materials provided by:
American Society for Reproductive Medicine
Endocrine Society
Jerry L. Pettis Veterans Medical Center
Loma Linda University
Long Beach Memorial Medical Center
National Bioethics Advisory Committee
University of California, Los Angeles
University of California, San Francisco
University of Kentucky
Western Michigan University
University of Washington
MD Anderson, Orlando
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**Introduction**

This manual will provide faculty, staff and students with a comprehensive over-view of the regulations, procedures, and guidelines for conducting human subject research at Northeast Ohio Medical University (hereinafter NEOMED). In accord with the intent of federal legislation, this institution’s process has its own style, reflecting local community standards. However, the legal and ethical framework is consistent with national practices and is carefully monitored by the Office for Human Research Protections.

**What Constitutes Human Subject Research?**

For the purpose of applying policies about human subject protection, research is defined as a systematic investigation designed to develop or contribute to generalizable knowledge.

“Human subject” is defined as 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. Pathological specimens of any type from humans.

Genetics research projects can present dilemmas as to whether or not relatives of a research participant are in fact research subjects themselves. Refer to the Section of this Manual entitled “Genetic Research” for guidance.

**NEOMED Policy**

The ethical conduct of biomedical research assumes that the researcher and the subjects are always fellow human beings, equal in dignity and rights. The researcher’s quest for knowledge must always be balanced with respect for the person, their rights and welfare. Thus College policy is intended to support legitimate scientific inquiry within the context of human values and ethical principles.

Research involving human subjects conducted by faculty, staff, or students on its premises or under its sponsorship, whether supported by outside funds or not, must be reviewed and approved by the NEOMED Institutional Review Board (IRB) for human subject research. NEOMED IRB retains final judgment, to the extent allowed by Federal regulations, as to whether a particular activity is covered by this policy.

**Federal Regulations**

**Background.**

In the early and mid-1960’s reports of abuses of the rights and welfare of human subjects and of unethical research precipitated the U.S. Surgeon General’s Policy of 1966 requiring institutions to review the rights of subjects participating in research projects funded by the Public Health Services (PHS). In 1972 this policy was promulgated well beyond the PHS to include all research supported by any Federal agency. In July 1974 the National Research Act created the National Commission of Human Subjects of Biomedical and/or Behavioral Research to oversee the process. The Commission
produced the “Ethical Principles and Guidelines for the Protection of Human Subjects of Research” (also known as “The Belmont Report”).

One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines, which should be followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider:

1) The boundaries between biomedical and behavioral research and the accepted and routine practice of medicine,
2) The role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects,
3) Appropriate guidelines for the selection of human subjects for participation in such research and
4) The nature and definition of informed consent in various research settings.

Current regulations and implementation:
Federal policy for the protection of human subjects applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any Federal department or agency. For example, both the FDA and the Department of Health and Human Services (DHHS) have regulations pertaining to human subject research. Regulations by different agencies are generally consistent with each other, however exceptions exist in areas relating to constitution of the IRB and certain informed consent requirements. Copies of pertinent Federal regulations are available at NEOMED’s Office of Research and Sponsored Programs and on the Internet


DHHS Regulations:  [http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm](http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm)

NEOMED is in full compliance with State and Federal regulations for the protection of human subjects and further extends such policies to include all human research projects, whether sponsored by Federal agencies or not. The manner in which the University will implement the appropriate Federal regulations for the protection of human research subjects is detailed in its Federalwide Assurance of Compliance, filed with the U.S. Department of Health and Human Services Office for Human Research Protections. Documentation of this compliance is designated by NEOMED’s receipt of Federalwide Assurance, which is on file in the Office of Research and Sponsored Programs and available for review.

Federalwide Assurance No.  FWA00000027
IRB Registration Number  IRB00000824
Organization Number:  ORG0000501
**IRB Purpose and Philosophy**

NEOMED shares with most research institutions the philosophy that human subjects are a valuable resource and that this resource should not be expended on meaningless investigations, **even if participation carries no apparent risk.** The IRB encourages and supports quality research.

NEOMED’s IRB is guided by the ethical principles regarding all research involving humans as subjects as set forth in:

1. The “Declaration of Helsinki” of the World Medical Association which sets international ethical guidelines for human subject research; and
2. The “Belmont Report” which identifies basic ethical principles for the conduct of research involving human subjects

In summary the three basic principles outlined by the Belmont Report are:

a. **Respect for Persons**
   i. Acknowledge autonomy
   ii. Protect those with diminished autonomy

b. **Beneficence**
   i. Do no harm.
   ii. Maximize possible benefits and minimize possible harm.

c. **Justice**
   In selecting subjects, distribute the burdens and benefits of research equally among the various classes of society.

**IRB Responsibilities**

The IRB at NEOMED processes new research protocols, and maintains previously approved studies. By Federal regulation and College policy, the IRB has a great deal of authority as to the way that research can be conducted relative to the involvement of human subjects.

The IRB has the authority to approve, require modification, or disapprove proposed studies and to require modification, suspend or terminate approval of on-going studies (21 CFR 56.113 and 45 CFR 46.109). Its decisions may only be modified by other institutions, groups, or individuals to be more restrictive, **not less so**.

**No research can be conducted after IRB disapproval!**

In reviewing all research activities involving humans, NEOMED’s IRB follows national standards and approves research according to these criteria:

1) The risks shall be minimized as far as possible by sound research, safeguards against the risks, and avoidance of unnecessary risks.
2) The risks are reasonable in relation to the benefits to the subject or the importance of the knowledge to be gained for humanity.
3) The selection of subjects is equitable.
4) The informed consent of subjects will be obtained and documented.
5) Provision will be made for monitoring the data to protect subjects.
6) The privacy and confidentiality of the subjects will be protected, as well as their rights and welfare.
**IRB Staff and Membership**

NEOMED assures that its policies regarding the review of research involving human subjects are implemented systematically by distributing the responsibilities at several levels. The Institutional Review Board Chair is the Authorized Institutional Official designated by the President and Dean of the College to be responsible for the oversight of research involving humans and IRB functions.

The Office of Research and Sponsored Programs (OR&SP) is responsible for coordinating the functions of the IRB with other activities relating to sponsored research. This responsibility is assigned to the Human Protections Administrator /Institutional Review Board Administrator (HPA/IRB), who oversees staff support to the IRB.

The OR&SP is responsible for developing and maintaining those systems relating to IRB applications, written procedures, meeting notices, agenda, minutes, approval notices, and ongoing review. The HPA/IRB Administrator assures that the IRB Chair is provided staff support, and upon request to fulfill the Chair’s responsibilities. OR&SP is responsible for maintaining the computerized sponsored research database, which contains timely and appropriate information regarding IRB activities and College research projects.

In order to ensure complete and adequate review of College research activities, IRB membership is a composite of experience and expertise reflecting the consortium’s research climate. A member from each Consortium Institution is represented on the IRB. The scope of IRB membership should also provide for representation of the various populations involved as subjects in College research. Specific federal regulations require that the IRB include representation by both men and women and by at least one member whose primary concern is non-scientific and one who is not affiliated with the institution. The number of members required to accomplish this is at the discretion of the HPA/IRB Administrator and IRB Chair.

The Vice President for Research, who takes into consideration the range of topics typically reviewed by the Board, nominates prospective IRB members and what expertise is available and appropriate to participate in such review. The Vice President's recommendations are developed in consultation with OR&SP personnel who are familiar with the scope of the University’s research community. The President and Dean reviews the final list of nominations, and awards final approval. Membership is for three years, coinciding with the academic calendar, and is renewable.

A profile of the IRB’s membership is maintained with the U.S. Office for Human Research Protections (hereinafter OHRP). If an IRB is not established in accordance with Federal regulations, the study sponsor may not accept the resulting data and funding will likely be withdrawn.

The IRB reviews each project on an annual basis and more frequently according to the degree of subject risk and/or the subject population. Continuing review, which is an IRB function, is differentiated from monitoring or surveillance.
The Office of Human Research Protections (OHRP) charges the IRB with monitoring the research. It will periodically review currently approved research activities. The HPA/IRB Administrator assures that monitoring is effective and that human studies research complies with Federal and State regulations and University policies. The IRB, IRB Chair or HPA/IRB Administrator may audit a human study at any time without advance notice.

Responsibilities of NEOMED Investigators
Research investigators acknowledge and accept their responsibility for protecting the rights, safety, and welfare of human research subjects and for complying with all State, Federal, and College policies.

NEOMED investigators must familiarize themselves with the provision of NEOMED’s Federalwide Assurance of Compliance with the OHRP, which describes how these policies are implemented locally. Investigators are also reminded that most scientific/medical journals will not publish papers that lack required IRB review.

Only a College faculty member may serve as principal investigator for research conducted under the auspices of NEOMED. Investigators are responsible for obtaining approval by the IRB of all research proposals involving human subjects prior to the initiation of any activity and then assuring that the research does not continue beyond the period of time approved by the IRB.

The principal investigator is responsible for implementing the project in accord with the IRB-approved protocol, basic ethical and scientific principles, College policies, and any pertinent laws and regulations. The principal investigator ensures that informed consent is obtained in an ethical and legal manner, adverse events are reported to the IRB, and periodic reports are submitted as required by the IRB. The principal investigator also ensures that all participating researchers, staff, and other key personnel are aware of their responsibility to comply with College policies regarding human studies education (see Section “Human Studies Education”), and the confidentiality and storage of project data (see Section “Record-Keeping – Investigators”).

Student Research/Projects:
As part of their academic role, faculty members are responsible for teaching students ethical principles relating to human subject research and guiding them through the mechanisms of obtaining IRB approval. Student-initiated research involving human subjects, whether dissertation, thesis or other research projects must be submitted in the name of the faculty member designated by the academic department to be responsible for coordinating the student project(s) with the IRB. This faculty member assumes responsibility for ensuring that the student’s research complies with State, Federal and College policies regarding the protection of human research subjects. All records and correspondence with the IRB will be done under the faculty member’s name. Thus the faculty advisor, as the principal investigator, must keep the student investigator informed about IRB decisions and communications.

*See also “Faculty Guidelines For Student Projects Involving Human Subjects”
Annual Progress Report: The Office of the Research and Sponsored Programs (ORSP) will send investigators a reminder to submit their annual progress report by the deadline. Failure to do so may result in the suspension of ongoing studies or the disbursement of federal funding.

Required Human Studies Education.
NEOMED requires that all key personnel involved in human subject research complete its specified program of education. The requirement for initial certification includes:

- All key personnel are required to complete the training required by the National Institutes of Health (NIH) located at http://phrp.nihtraining.com/users/login.php
- Read (1) the Belmont Report,
- NEOMED Guidelines for Protection of Human Subjects in Research,
- NEOMED IRB Manual of Standard Operating Procedures, and
- NEOMED’s Federalwide Assurance with OHRP.

By signing the IRB application, the principal investigator agrees that he or she accepts the responsibility to ensure that only personnel that have read the required reading and possess current certification for human studies education from NEOMED will be involved in the study. The principal investigator will submit in advance the names of key personnel to OR&SP for verification that their education certification is current. Certificates must be included with the IRB application.

How is IRB review obtained?
Application guidelines and forms are available from the Research and Sponsored Programs web site (http://www.neoucom.edu/DEPTS/GRAN/index.html). All NEOMED faculty should consult with OR&SP regarding IRB processes. OR&SP staff are available to answer questions and preview consent documents. Investigators involved in human subject research for the first time are particularly encouraged to avail themselves of this service.

Conduct of Meetings
A packet of materials is distributed by e-mail to all IRB members prior to the meeting. The packet contains an agenda, minutes of the last meeting, copies of all proposals to be discussed, and annual reports for projects reviewed by full board whose approval period is expiring, and a summary of administrative actions occurring between meetings.

Unscheduled meetings may be called at the IRB Chair’s discretion. Such meetings are subject to all standards of a routine IRB meeting, including the requirement for a quorum. A majority of the appointed IRB membership and one non-scientific member constitutes a quorum for fully convened IRB meetings. A simple majority of those attending is required to pass a motion. The IRB Chair presides over the meeting. If unable to attend, the IRB Vice-Chair will serve as alternate chair.

Any action of the IRB involving the identity of an investigator or a subject is considered confidential. Thus the deliberations leading to such an action are closed to the public.
The IRB Application Packet contains the following:
All of the information and applications to the IRB are located on the Research & Sponsored Programs web site: http://www.neoucom.edu/audience/research/offices_programs/research_programs

1) IRB Application Form (IRB Application for interventional studies and IRB Behavioral Sciences Application for studies involving surveys and behavioral studies)

2) NEOMED Guidelines for preparation of a human subject protocol

3) NEOMED Guidelines for Written Consent and/or Informational Sheets

NEOMED’s IRB Guidelines specify the number of copies of the completed IRB application package the investigator will need to prepare for submission and deadlines for applying to a specific IRB meeting agenda. Before completing an IRB application, investigators should verify that they have the most recent version since changing regulations, policies, and procedures affect submission requirements.

How to submit an IRB application...the right way!
Before starting: identify collaborators, write protocol, identify/design data collection instruments, get peer review, obtain collaborative agreements, read Assurance and Belmont Report regarding human subjects.

1. Call OR&SP for latest forms and schedule of IRB meetings or http://www.neoucom.edu/audience/research/offices_programs/research_programs/forms
2. Complete forms - answer all questions; attach protocol
3. Write consent document
4. Get OR&SP to preview
5. Verify whether the application will receive Expedited, Exempt, Full IRB review -- plan accordingly
6. Submit required number of copies and original to OR&SP: packet to include IRB application form, summary of project, complete protocol, consent form, questionnaires or other data-collection tools (unless a referenced, tested tool), advertising, documentation of collaboration, copies of human research subject training certificates for all key personnel, conflict of interest disclosure, approval from the Radioactive Drug Safety Committee (as appropriate). Also submit a copy of the drug/device/biologic’s product literature (e.g., brochure, Instructions for Use, User Manual, etc.)
7. Obtain hard copy interim results from OR&SP for completion of requested changes/corrections. Refer to itemized number when answering questions.
8. Provide clean master of corrected consent document
9. Obtain official, stamped consent form and signed approval notice from IRB Chair through OR&SP. Note approval period.
10. Implement project.
11. Notify IRB via OR&SP of any adverse events, changes or additions to protocol; obtain acknowledgment from OR&SP
12. One month prior to expiration, complete Research Report Form and submit to OR&SP.
13. When new project period is approved, if still enrolling subjects, submit clean master of current consent form for updated authorization stamp.
Preparing the Literature Cited section.
The protocol should reference only key literature. Such references might provide background information on related in vitro studies, animal and/or human studies, as well as documentation of the rationale and of methods selected.

Subject Selection
Investigators are responsible for ensuring that women and racial and ethnic groups are included in research projects involving human subjects whenever feasible and appropriate. Because the practice of medicine has shown that advanced age is not necessarily a predictor of clinical outcome, the elderly should not necessarily be excluded from research based solely upon a categorical age limit. Racial and ethnic groups include American Indian, Alaskan Native, Asian, Pacific Islander, Black, and Hispanic. (See “Special Populations" for further guidance.)

Preparing Your IRB Protocol
To make sure the IRB has adequate information to complete its review expediently, be sure the following questions and topics are addressed in the protocol. If you are not providing a protocol please make sure this information is included in the application and the abstract

1) Is the information the IRB needs to know (compared to the information contained in a dissertation or funding proposal) clearly presented?
   a) Provide a summary of the research design, highlighting techniques used, data analysis, and statistical methods (see NEOMED Guidelines in the IRB application).
   b) If lengthy documents are involved, (more than 100 pages) three copies should be provided for reference purposes only, as a supplement to, NOT replacement for, the IRB’s required protocol.

2) What are your inclusion/exclusion criteria?
   a) Don’t forget the obvious: disease state, contraindicated medications, sex, or age.
   b) Reflect on psychosocial variables that may impact subject risk and study compliance.
   c) Don’t insult the reader by stating exclusion criteria that are merely stating the opposite of the inclusion criteria.

3) Does the selection of subject demonstrate an awareness of possible duplicate use of populations already being studied at NEOMED?
   a) Be alert to the pitfall of selecting a population just because they are easily available: students, patients, school groups (see “Special Populations”).

4) How will subjects be recruited?
   a) If advertising, describe your plan for using media, provide a copy of any advertising (ads, posters, hand-outs), wording of public service announcements.
   b) If access to subjects is by way of an institutional relationship (i.e., patients of another facility), obtain a letter of cooperation from the “gatekeeper” for that facility.
5) How will human subjects be involved?
   a) Describe step-by-step how the subject will be approached/solicited, who will do the
      informing and consenting, the conditions under which the subject will be approached,
      exactly what they will be told, etc.
   b) Be frank about potential for coercion and present a plan for managing such possibilities.
   c) If the process involves telephone contact, provide a script of what will be covered in
      telephone conversation.

6) What is the step-by-step plan for interacting with the subject in terms of how confidentiality
   and privacy will be respected?
   a) Describe the setting in which research will be administered to subject with regard to
      physical comfort, privacy, convenience, travel required.
   b) Demonstrate consideration for subject’s ability (mental, physical, developmental),
      environment, educational level, geographical location, and social context (especially for
      children and teens and other vulnerable populations).

7) Will human tissue be collected?
   a) If human biological samples are to be stored for future use, subjects should be advised of
      this fact.

8) Will the study involve genetic testing?
   a) Research subjects should have the option of selecting whether or not they want access to
      the genetic information generated by the study.
   b) Their decision should be recorded in the informed consent form.

9) Will the study involve radioactive material or X-rays?
   a) If yes, please ensure your protocol is reviewed and approved by the Radioactive Drug
      Research Committee.

10) Will the study involve any infectious material?
    a) If yes, please consult with the Office of Hazardous Materials Safety for safety guidance.

11) In addition to human research participants, will the study involve concurrent investigational
    use of animals?
    a) If yes, please provide evidence of review and approval by the NEOMED Institutional
       Animal Care and Use Committee.

12) What ethical concerns are involved? As the expert in the field, your insights are helpful.
    a) Be open about your concerns, sharing your methods for preventing or managing ethical
       dilemmas.
    b) For example, if deception is required, justify the need and describe any possibility for
       debriefing.
    c) If you anticipate concerns about the social impact of the research or its associated
       technologies, you are invited to consult the NEOMED IRB for counsel.
Grant Applications

Grant applications that involve human subjects in research require a carefully thought-out, detailed plan. Grant applications to Federal sponsors require a complete description of such a plan as illustrated in the following excerpt from the guidelines for Public Health Service Grants application:

- Provide a detailed description of the proposed involvement of human subjects in the work previously outlined in the Research Design and Methods section. Describe the population of subjects from which the sample is to be drawn. Specify inclusion and exclusion criteria. If compensation is being offered to subjects, provide the amounts and terms of payment. State whether there are costs to the subjects. Note the number of subjects required to test the primary hypothesis and power analysis. Describe the characteristics of the subject population, including their anticipated number, age range, and health status. Identify the criteria for inclusion or exclusion of any subpopulation. Explain the rationale for the involvement of special classes of subjects, such as fetuses, pregnant women, children, prisoners, institutionalized individuals, or others who are likely to be vulnerable.

- Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records, or data.

- Describe plans for the recruitment of subjects and the consent procedures to be followed. Include the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. State if the IRB has authorized a modification or waiver of the elements of consent or the requirement for documentation of consent. The informed consent form, which must have IRB approval, should be submitted to the PHS only if requested.

- Describe potential risks (physical, psychological, social, legal, or other) and assess their likelihood and seriousness. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects.

- Describe the procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Also, where appropriate, describe the provisions for monitoring the data collected to ensure the safety of subjects.

- Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and in relation to the importance of the knowledge that may reasonably be expected to result.

- If a test article (investigational new drug, device or biologic) is involved, name the test article and state whether the 30-day interval between submission of applicant certification to the Food and Drug administration and its response has elapsed or has been waived and/or whether use of the test article has been withheld or restricted by the FDA.
How long does the IRB review cycle take?
The length of the IRB review cycle varies from project to project. On average, complete application packets submitted for expedited and/or exempted reviews take approximately 2 weeks for review. Submission of a complete application packet requiring full board approval from the IRB to receipt of the formal approval notice from IRB Chair is dependant upon the date of the next IRB meeting. Please remember that the IRB meets every other month. All applications must be in the OR&SP 14 days prior to the IRB meeting. After the IRB meeting, approval is granted approximately within two business days if the application receives an unconditional approval.

The amount of time required to complete the processing of applications receiving “conditional approval” depends on the investigator’s ability to respond to the corrections and clarifications requested in the interim memo. The IRB retains the option of sending its written correspondence by mail, fax, or e-mail.

Incomplete applications can result in significant delays in the review and processing of research protocols. In an effort to prevent this dilemma, the IRB will hold incomplete submission packets for 60 days. If the submission packet is not completed within 60 days, the packet will be returned to the primary investigator unprocessed, unless the primary investigator requests an extension. If the submission packet is still incomplete after the extension period, the packet will be returned to the primary investigator as “INCOMPLETE-NOT PROCESSED.” If the investigator wishes to resume the research project they will have to re-submit the entire application packet to the IRB.

This process does not preclude the investigator from resubmitting nor does it adversely effect any submissions the investigator may currently have under IRB review. A preliminary outline of the results of IRB deliberations is generally available for the investigator to review within 72 hours after the IRB meeting, with final documentation sent to the principal investigator shortly thereafter. If the IRB tables or rejects a protocol, rationale for this decision shall be provided to the primary investigator and he/she retains the right to respond to the IRB in person or in writing [21 CFR 56.109(d)].

Conflict of Interest
Conflict of interest, whether actual or perceived can affect the integrity of scientific research. Due to the possible complex and varying relationships investigators may have with sponsors, it is difficult to create a boilerplate informed consent form statement that will universally and adequately inform subjects of the relationship. As a result, the IRB request that investigators manipulate the boilerplate provided on the consent form for their own disclosure statements.

All informed consents should contain a “Conflict of Interest Statement.” This is an absolute requirement when the project is funded. If the research project is not funded please contact the OR&SP to request the deletion of the statement from the informed consent. However, if the investigator falls into any of the following categories a statement is required:
1. The investigator is responsible for the healthcare of the subject,
2. The investigator has a financial interest with the sponsor of the study. This could mean a
significant interest in the company, interest in the development of the product and/or any other potential conflict of interest or commitment.

If the investigator or any of the key personnel fall into this category they must disclose this information to the IRB and to the potential research subjects. The investigator with a potential conflict of interest or commitment must also report this issue to the “Conflict of Interest Committee” at NEO MED. To assist the investigator the IRB will also report this conflict to the “Conflict of Interest Committee” at NEO MED.

**Role of IRB Chair:**
The IRB Chair is ultimately responsible for setting the agenda for each meeting, determining what applications will be exempt, expedited, or require full IRB review. The Chair is officially authorized to represent the IRB in communicating with investigators, administrators, legal advisors, and community representatives. It is the IRB Chair who will consider applicant’s appeal of an IRB decision as to whether further information warrants the IRB’s review of its decision. The IRB Chair may approve applications that qualify for expedited review; disapproval requires full IRB review. The Chair is also a mentor for the IRB members and OR&SP staff.

**Responsibility of the Human Protection/IRB Administrator:**
The Human Protections/IRB Administrator is responsible for coordinating the functions of the IRB with other activities relating to sponsored research and oversee the staff support to the IRB.

The HPA/IRB Administrator may review and approve applications that qualify for exempted approval. The HPA/IRB Administrator will review every submission for classification of exempted review, expedited review, or full board review. The HPA may also approve applications that qualify for expedited approval in the absence or at the discretion of the IRB Chair. The HPA will also assist IRB members and Investigators with questions or concerns regarding human subjects research.

The IRB Administrator is responsible for developing and maintaining those systems relating to IRB applications, written procedures, meeting notices, agenda, minutes, approval notices, and on-going review. The IRB Administrator assures that the IRB Chair is provided staff support, and upon request to fulfill the Chair’s responsibilities. He or she is also responsible for seeing that the computerized sponsored research database which contains timely and appropriate information regarding IRB activities and Institution's research projects is maintained.

**Responsibility of IRB Coordinator:**
Prior to each meeting, the IRB Coordinator will receive applications from faculty, review each application for completeness, and distribute the packet of applications to the necessary individuals. In this process, the IRB Coordinator works with the HPA/IRB Administrator in identifying those applications requiring full IRB review, prepares a written agenda for the
meeting, and assigns primary reviewers if needed. The IRB Coordinator is responsible for all logistics of the meeting room, preparation of any additional meeting handouts, introducing visitors into the meeting, and assisting the IRB Chair as needed. The IRB Coordinator prepares the official IRB minutes and the Interim Report on behalf of the Chair.

**Role of Investigators**
It is requested that the principal investigator attend the IRB meeting in which his/her protocol is to be reviewed. At the meeting, investigators are asked to wait in the hall until the IRB staff member invites them in at the appropriate time. Once the IRB members have acquainted themselves with a specific protocol, the investigator is invited into the room in order to answer questions and clarify concerns. In lieu of attending the meeting, the investigator may be asked to provide supplementary information for review by the IRB.

**Role of Primary Reviewer**
Many IRB members are selected to serve on the IRB because of their technical expertise. In this capacity, they will frequently be asked to serve as a primary reviewer. The responsibility of a primary reviewer is to present at the IRB meeting his/her evaluation of the application with regard to:

1) The appropriateness of scientific design as it pertains to the involvement of human subjects;  
2) Level of risk to the subjects;  
3) Risk/benefit ratio;  
4) Suitability of the consent form;  
5) The equitable selection of research subjects;  
6) Provisions for confidentiality;  
7) Qualifications of the investigators;  
8) Suitability of equipment and facilities for management of the subjects’ rights and welfare.

This permits the IRB to focus its discussion on the appropriate issues based on the motion on the floor and make its conclusion in a productive manner. A worksheet for the primary reviewer is available on-line at the OR&SP web site [http://www.neoucom.edu/DEPTS/GRAN/forms.html](http://www.neoucom.edu/DEPTS/GRAN/forms.html)

**Guidelines for the primary reviewer:**  
The primary reviewer may remain anonymous to the investigator unless the reviewer chooses otherwise. Under no circumstance will the name of the primary reviewer be disclosed in the minutes of the IRB’s meeting.

1. Review the protocol early enough to inquire about specific questions with investigator(s). Delays in approval can be avoided if potential conflicts are dealt with prior to decision of the IRB.  
2. Make an organized list of concerns, questions or corrections to be brought up with the board. This helps speed up the time required to review the projects without overlooking significant details.
3. Briefly review the purpose(s) of the potential ethical problems and how these are dealt with in the proposal.
4. Differentiate between points of ethics (including science) and style. The investigators must address concerns regarding ethical issues, while those of style are more logically handled as suggestions (unless the style interferes with an ethical point).
5. The primary reviewer may contact the investigator in advance in order to clarify an issue of concern, to ask the investigator to provide supplementary information, or to invite the investigator to attend the IRB meeting.
6. If the application does not adequately address the above concerns, you should consult with the IRB chair as to the advisability of withdrawing the application from the agenda. Then prepare a brief outline of the substantive questions to be addressed before the investigator can re-submit.
7. Most changes deal with the consent form. Pencil in minor modifications and corrections on your copy of the consent form and give to the IRB secretary, to help speed up handling the changes.
8. After your review of the project, make a motion whether to approve or disapprove, including suggested risk assignment and any requests for clarification or changes to be made.

**Role of IRB Members**

All IRB members are provided a set of resource materials plus access to a variety of supplementary resources and tools on-line at many web sites (please contact OR&SP for a complete listing). Members are expected to reference these materials when evaluating applications and participating in IRB discussions at meetings.

The IRB’s role is best served when each individual feels free to speak to any observations or concerns on all protocols under review. Each member is expected to have reviewed the agenda material provided in advance, with particular attention to the rights and best interests of subjects, potential for risk, and the quality of informed consent.

Because the IRB cannot function without certain representation present, in addition to having a quorum, a substantial commitment falls on individual members to attend all IRB meetings. If an IRB member is unable to attend a specific meeting, it is that individual’s responsibility to notify the IRB staff.

If a committee member has a conflict of interest in a given application, such as serving as investigator or consultant, the member must make this known at the outset of the discussion and must be absent during the final discussion and vote on the application.

IRB members are reminded of the confidential nature of information discussed during the evaluation of applications, especially those sponsored by commercial organizations. At the conclusion of each meeting, IRB members are to take care to personally shred all application materials or provide them to the IRB secretary for confidential disposal.
**Role of Institution:**
NEOMED is committed to complying with ethical standards, as well as State and federal regulations as needed to support its research community. The College will provide resources such as staff support, facilities, faculty/staff training, publications and supplies, as needed to implement such standards and regulations.

*Neither the Dean nor the College is able to override negative or restrictive IRB decisions, however the Dean of the College may impose more restrictive sanctions on the IRB’s approval of a given research project.*

**Informed Consent**
Informed consent is a process that requires more than the signing of an “official” form. The most important part of the informed consent is not the signature of the research subject but the complete understanding and willingness of the subject to participate in the research. Two key components of informed consent are:

1. Participation must be voluntary
2. Adequate information must be provided at a level commensurate with the individual’s level of understanding.

The autonomy and welfare of participants and the integrity of science as a profession rely on both components of informed consent. Additionally, informed consent is not necessarily a one-time procedure. Protocol changes, adverse events, beneficent discoveries, and such must be related to enrolled subjects. Investigators are required to work with the IRB to ensure re-consent is obtained as appropriate.

The IRB ensures that legally effective informed consent is obtained and documented in a manner that meets College policy and Federal regulations. The IRB has the authority to observe or have a third party observe the consent process. The IRB reserves the right to conduct unannounced audits of research activities to assure that the informed consent document conforms to the authorized version.

**Basic Elements of Informed Consent:**
*NEOMED Guidelines for Written Consent* provides specific requirements for informed consent at NEOMED. These guidelines are based on Federal regulations (45 CFR 46.116), which stipulate that, in seeking informed consent, the following fourteen informational components shall be provided to each subject:

1) Statement that the study involves research,
2) Explanation of the purposes of the research
3) Statement of the expected duration of the subject’s participation in the research
4) Description of the procedures to be followed,
   a) Identification of any procedures that are experimental.
5) Description of any reasonably foreseeable risks or discomforts to the subject.
6) Description of any benefits to the subject or to others that may reasonably be expected from the research.
7) Disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
8) Statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
9) For research involving more than minimal risk or more than loss of confidentiality, 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.
10) Explanation of whom to contact for answers to pertinent questions about the research and research subjects’ rights,
11) Explanation of whom to contact in the event of a research-related injury to the subject; and
12) Statement that the subject will be told in a timely manner of any significant new information that may affect their willingness to stay in the study.
13) 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.
14) Statement regarding the investigators “Conflict of Interest.” This statement should be included even if the investigator does not have a conflict of interest.

Please Insert the Following Statements if Applicable to the Research Project:
1) Statement that a research subject’s tissues or other biological specimens might be used in a commercial product or a cell line that could be shared with other institutions.
   a) Subjects should be informed that they will not be entitled to financial royalties or other payments as a result of the use of their specimens
2) Participants should be informed that participation in research studies should not viewed as a replacement for routine health care.
3) Participants should be informed that their health insurance provider(s) may not cover experimental treatment. They should be informed whether or not these providers will be billed for the experimental therapy.

Informational Sheets:
NEOMED IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects. If the NEOMED IRB determines that the research project is eligible for a waiver of informed consent the IRB may require the use of an “Informational Sheet.” The “Informational Sheet” does not require the research subject’s signature. However, Investigator’s must present and explain the informational sheet exactly as they would the informed consent. The research project must meet ALL of the following criteria to qualify:

1) The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.
2) The research presents no more than minimal risk of harm to subjects
3) The research involves no procedures for which written consent is normally required outside of the research context.
4) The waiver or alteration will not adversely affect the rights and welfare of the subjects
5) The research could not practicably be carried out without the waiver or alteration
6) Whenever appropriate, the subjects will be provided with additional pertinent information
   after participation.

If the NEOMED IRB determines that a study qualifies for an “Informational Sheet” in place of
an “Informed Consent” this document must meet the requirements set forth for the “Informed
Consent.” The only sections that may be excluded are the signature and, if necessary, the
significant new findings statement.

**Documentation of informed consent.**

In most cases, informed consent is documented by the use of a written consent form approved by
the IRB and signed by the subject or the subject’s legally authorized representative. The subject
or their representative must be given ample time to read the form and contemplate its contents
before signing. A copy should be given to the person signing the form; another kept in the
investigator’s research records, and (if medical research) one in the patient medical record.

The consent form must be written in language considered appropriate at the *eighth grade reading
level* regardless of the subject population. Novel tools to assist the informed consent process
include videos, question and answer workbooks, photos, sketches and diagrams. The use of bold
face font, underlined font, and simple paragraph structures are highly recommended as an aid to
calibrate informed consent to a participant’s level of educational sophistication. A glossary of lay
terms is provided on-line at the NEOMED's web site
(http://www.neoucom.edu/DEPTS/GRAN/index.html) to assist in preparing “reader-friendly”
consent forms.

The IRB recognizes that certain populations may require additional protections because they are
经济发展ally or educationally disadvantaged. Every subject’s rights and welfare should be
safeguarded by making sure that any possible coercion or undue influence is eliminated (e.g.,
compensation that is not commensurate with risk, discomfort, or inconvenience involved;
recruiting in settings where voluntary participation might be compromised). Investigators should
address these issues specifically when submitting their protocol to the IRB.

Federal regulations require the translation of consent documents into the language that is most
easily understood by research subjects. The possibility of illiteracy should be accounted for, as
should the need for communicating in non-English languages. Non-English speaking subjects
must have informed consent documentation presented in a written language that they understand
(21 CFR 50.20 -27 and FDA Information Sheet, October 1, 1995, page 49). The inability to read
or to read English is not an appropriate basis for exclusion from most research.

If the research protocol proposes to use non-English language consent documents, quality
assurance procedures should be developed such as translation of the consent document from
English to the second language and then back to English, by a certified translator, to ensure that
the information is correctly conveyed. The IRB is required to review and approve all non-
English consent forms and recruitment tools. The role of cultural values and norms of subjects
should also be addressed. This information should be provided in a clearly identifiable form to
the IRB for review.
**Deception in Research:**

Deception or Withholding Information from Subjects: There are times, especially in behavioral research, when investigators plan to withhold information about the real purpose of the study or purposely give subjects false information about some aspect of the research. As a result, the subject will not give prospective fully informed consent. The use of deception or incomplete disclosure imposes special responsibilities on the investigator and the IRB. Incomplete disclosure or the use of deception cannot be used as a means to secure the participation of subjects in research.

Minor deception, such as withholding specific points of interest in an attempt to prevent a bias in the results, can be acceptable, provided the subject is fully debriefed after participation. Risks stemming from major deception, such as leading a subject to believe that s/he has committed a crime or has a disease, must be clearly counterbalanced by the benefits of the research. Federal regulations do not allow the IRB to waive some or all of the elements of informed consent, including a fair and comprehensive description of all elements of the research, if the study is more than minimal risk.

In addition, the waiver of the elements of consent must not adversely affect the rights and welfare of subjects, and must be essential to the ability to carry out the research. The IRB will consider whether the withheld information would influence the decision of potential subjects to participate in the research. The IRB will NOT approve a study that presents more than minimal risk where subjects are deceived or not given complete information that they would consider material to the decision to participate.

Investigators should justify, in detail, in the protocol, the reasons for deceiving or withholding information from subjects, including an explanation of: a) the necessity for deceiving subjects; b) how the potential benefits of the research justify the use of deception; and c) how the investigators will conduct the debriefing. In addition, investigators should include a debriefing script or statement that indicates the information subjects will receive regarding their participation in the research.

The IRB in collaboration with the investigator will determine whether subjects should be debriefed either after unwittingly participating in research or after knowingly participating in research that involved deception. The IRB may require debriefing when it contributes to the subject’s welfare, i.e., when it corrects painful or stressful misperceptions, or when it reduces pain, stress, or anxiety concerning the subject’s performance. For example, if a subject is lead to believe through participation in deceptive research that s/he has committed a crime or has a disease, a debriefing session may correct the induced stress, pain, anxiety, etc.

**IRB Decisions/Actions:**

The IRB reviews, and has the authority to approve, require modification of, or disapprove all human subject research activities, including proposed changes in previously approved projects. The following describes the most common classes of review and decisions made by the IRB:
**Categories of IRB Decisions/Actions.**
Following review of the application, the IRB will take one of the following actions:

1. **Approved.** The protocol is approved as submitted.
2. **Conditionally Approved:** The problems regarding the protocol are not of a serious nature and consist of minor changes needed in the consent document or clarification regarding an item in the protocol that need to be documented in the application or protocol. Generally the IRB Chair is authorized by the IRB to review and approve the investigators’ resolution of these problems. If more significant problems are identified, the IRB may stipulate how such issues will be resolved. If the investigator does not accept such amendments, he/she must resubmit a justification to the full IRB for review and approval.
3. **Tabled.** The changes proposed or the questions asked by the IRB are significant enough to warrant additional review and clarification.
4. **Disapproved.** The protocol is deemed so lacking in scientific merit or raises such serious ethical questions as to be totally unacceptable.

**Categories of IRB Review**
There are several types of review processes used by the IRB. All are governed by Federal regulations as cited below:

**Exempted Research:** Whether or not a study is exempt will be determined by the OR&SP in accord with Federal policy and verified by the IRB Chair or designee. Federal policy states that investigators do not have the authority to make an independent determination that research involving human subjects is exempt. (An institution may elect to review all research under the auspices of the institution even if the research qualifies for exemption.)

Research activities considered as EXEMPT from IRB review are those in which the only involvement of human subjects will be in one or more of the following categories [45 CFR 46.101(b)]:

1) Research conducted in established or commonly accepted education settings, involving normal education practices, such as research on regular and special education instructional strategies, or research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2) Research involving the use of education tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless

   a) Information obtained is recorded in such a manner that human subjects cannot be identified, directly or through identifiers linked to the subjects; and
   
   b) 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 study of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior.

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 subjects information cannot be identified, directly or through identifiers linked to the subjects.
   a) Our note: identifiers are understood to be codes, symbols or other methods of labeling data for traceability. Research that has identifiers at any point in the research does not qualify for an exemption from IRB continuing review.

5) Research and demonstration projects which are designed to study, evaluate, or otherwise examine
   a) Public benefit or service programs;
   b) Procedures for obtaining benefits or services under those programs;
   c) Possible changes in or alternatives to those programs or procedures; or
   d) Possible changes in methods or services under those programs.

6) Taste and food quality evaluation and consumer acceptance studies, if
   a) Wholesome foods without additives are consumed, or
   b) 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 FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

This policy does not affect any foreign laws or regulations which may otherwise be applicable and which provide additional protections to human subjects of research.

The following types of studies are NOT exempt from IRB review:

1. Research involving deception
2. Sensitive behavioral research (e.g., sexual activity, substance abuse)
3. Research involving vulnerable populations
4. Research involving children
5. Research involving human ova (fertilized or not, identified or not)
6. Research involving human biological material that is identifiable to its donor

Investigators should not assume that protocols exempt from IRB review are exempt from informed consent requirements. Investigators are responsible for having on file documentation from OR&SP referring to the appropriate category of Federal exemption. To obtain documentation that one’s project is exempt from IRB review and approval, investigators should complete the IRB application form as much as applies. The completed form together with a one-page summary of the protocol (objectives, methods, involvement of human subjects) must be submitted to the OR&SP. Investigators are advised to allow at least ten working days for exempt review to take place. The project will be entered in the OR&SP database but is not subject to annual reporting requirements.
**Expedited Review**

Projects posing no more than minimal risk may receive “expedited review” by Federal policy (also called “administrative review”). However, the IRB Chair may identify reasons otherwise that warrant full IRB review instead (e.g., research involving vulnerable populations).

The IRB Chair along with a designee of the Chair will review protocols which qualify for expedited review. Consultants may assist the IRB in making decisions in expedited review. Further, expedited review cannot be performed solely by persons who are not members of the IRB.

In conducting expedited review, the IRB reviewers may exercise all of the authorities of the IRB except that they may not disapprove the research. A research activity may be disapproved only after review in accordance with review by the convened full IRB. Per Federal regulations, the full IRB shall be notified of all approvals under expedited review.

The following activities may be reviewed through expedited review procedures (as of 11/9/98):

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, 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:
   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 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.
   a) Where medical devices are employed, they must be cleared/approved for marketing.
   b) 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.
   c) Examples:
      i) 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;
      ii) Weighing or testing sensory acuity;
      iii) Magnetic resonance imaging;
      iv) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
      v) 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.

**Full Review**
Procedures described in both FDA and DHHS regulations require a convened meeting.
NEOMED’s IRB normally holds its meetings on a bi-monthly basis. The only acceptable
alternative to a convened meeting is a conference call in which interaction is possible, a critical
aspect of the review process. A majority of the IRB members must be present, including at least
one member whose primary concerns are in nonscientific areas.

If an investigator listed on the protocol is also an IRB member, he or she must absent
himself/herself from the review except to answer questions pertaining directly to the research.

When the protocol is approved, the IRB also determines the frequency that the project will be
reviewed, not to exceed one year. Under no circumstances can retroactive approval be granted.

**Research Conducted at the Consortium Hospitals.**
Due to federal requirements, the NEOMED IRB must issue approval of human research:
regardless of sponsorship, if one or more of the following apply:

1) The conduct or recruitment of the research involves institutional resources (property, facility
   or funding, including extramural funds administered by the institution), or
2) The research is conducted by or under the direction of any employee, student or agent of this
   institution in connection with his or her institutional responsibilities, or
3) The research is conducted by or under the direction of any employee, student or agent of this
   institution using any property or facility of this institution, or
4) The research involves the use of this institution's non-public information to identify or
   contact human research subjects or prospective subjects.

NEOMED IRB approval is required even if all of the research is being conducted at the
Consortium Hospitals and has been approved by the Consortium Hospital’s IRB. Please contact
the office of Research and Sponsored Programs for further information.
Federal Wide Assurance & Cooperative Research Agreements

For an institution to accept research funding from the federal government they must have an assurance filed with the Office of Human Research Protections (hereinafter OHRP). A Federal Wide Assurance (hereinafter FWA) is an agreement between NEOMED and OHRP. This agreement stipulates that NEOMED will ensure that all research is conducted according to federal regulations, regardless of funding sources.

Federal Regulations also permit institutions that possess a Federal Wide Assurance to accept IRB approvals from other institutions that also possess a FWA. This is considered a “Cooperative Research Agreement (hereinafter CRA).” To obtain a CRA please follow the steps listed below:

1) Obtain IRB Approval from the PI’s primary institution.
2) Submit the following documents to the secondary IRB.
   a) Initial application to the primary institution
   b) All correspondence between the PI and the IRB for the primary institution.
   c) All approvals from the primary institution.
3) After the above-mentioned documentation is submitted the secondary IRB will then review the complete file.
4) If the secondary institution approves of the research the PI will receive a letter stating that the primary IRB approval has been accepted. A letter and agreement will also be sent to the primary IRB.

However, the secondary IRB is not required to accept the other institutions IRB.

Please note that it is the responsibility of the PI to submit copies of changes to both IRB’s!
This study will be terminated if the PI is not complaint with submission to both IRB’s.

Other Types of Review

Federal regulations provide guidance for IRB review in unique and rare situations as described below:

**Emergency Use** Although FDA regulations require that in general, clinical investigations of test articles (investigational drug, device, or biologic) be reviewed and approved by the IRB before they are conducted, the regulations provide for an exception of this rule in the case of an emergency. This type of exception can be made for emergency use of an investigational drug or device on a one-time, one patient basis only, per institution.

Please note that an Emergency Use exemption does not apply to research studies about Emergency Medicine. Studies of this nature must be submitted to the IRB using the standard protocol submission procedure previously described in this Manual.

The following conditions must be met for the “emergency use of a test article on human subjects” [21 CFR 56.102(d)]:

Even for emergency use of an investigational drug, an Investigational New Drug (IND) exemption is necessary (21 CFR 312.36). The FDA requires notification for the emergency use of an unapproved investigational device.

**Procedure.** For the emergency use of an unapproved investigational drug, device or biologic, the following procedure has been established:

1. The treating physician should call and advise the IRB Chair that he/she is requesting permission for the emergency use of a research therapy. The IRB Chair will ensure that the requests meet the requirements of emergency use; will check whether the drug or device has already been used on an emergency basis at NEOMED; will advise the treating physician of any other restrictions that may apply.

2. Informed consent must be obtained before the use of the test article unless this is not feasible and is certified in writing by both the investigator and a physician who is not otherwise participating in the clinical investigation (21 CFR 50.23).

3. Once the IRB Chair has been notified and it has been verified that the therapy in question has not been given an emergency use exemption in the past, the therapy may be used on an emergency basis, for one time, one patient only.

4. A written report must be submitted to the IRB within 5 days of emergency use of the test article [21CFR56.104(c)]. The report should include the following:
   a. Name, address and telephone number of dispensing physicians and department.
   b. Name of investigational drug or device
   c. Name of sponsor
   d. Date of request for permission
   e. Date of actual use of drug or device
   f. Name of patient
   g. Description of rationale for use
   h. Description of the patient’s response to the therapy.

The treating physician should advise the IRB Chair if documentation is needed informing the manufacturer of IRB approval. The IRB Chair will notify OR&SP to issue such a notice ONLY after review and approval of the full IRB.

Notifying the IRB does not equate to an IRB approval, nor does it mean that the IRB has reviewed the specific use of the test article in the emergency setting. Any subsequent use of the test article at the institution is subject to IRB review. If emergency medical care is initiated without prior IRB review and approval, the patient may not be considered a subject in research, nor may the outcome of such care be included in any report of research activity.
Once a drug, device, or biologic has been used on an emergency basis, a protocol should be developed for future use as further “Emergency Use” exemptions cannot be granted. Compare with “Treatment IND” and “Single-Patient Use”

**Single-Patient Use**

Often referred to as "compassionate use," this policy allows a physician to obtain access to an investigational therapy for the treatment of a single patient. Unlike “Emergency Use” exemptions, each “single patient use” must be reviewed and approved by the IRB as well as by the FDA, and all requirements for informed consent must be met. Usually the patient is in a desperate situation and unresponsive to other therapies, or in a situation where no approved or generally recognized treatment is available. Further there is usually little evidence that the proposed therapy is useful, but may be plausible on theoretical grounds or anecdotes of success. Access to investigational drugs for use by a single, identified patient may be gained either through the sponsor under a treatment protocol, or through the FDA, by first obtaining the drug from the sponsor, and then submitting a treatment IND to the FDA requesting authorization to use the investigational drug for treatment use. Compare with Emergency Use and Treatment IND.

**Treatment IND**

This is a treatment protocol that is added to an existing investigational new drug application (IND) which allows physicians to treat qualifying patients according to the protocol, and which provides additional data on the drug’s safety and effectiveness. Treatment INDs are available for patients with life threatening or other serious diseases for which no satisfactory alternative drug or other therapy exists. Treatment INDs require standard IRB submission and approval. The treatment IND must comply with all regulations governing informed consent. Compare with Emergency Use and Single-Patient Use.

Investigators should be aware that in response to concerns regarding the effect of treatment INDs on the ability of investigators to attract subject into clinical trials for phase three testing, treatment INDs can be placed on clinical hold if they are "impeding enrollment in, or otherwise interfering with the conduct or completion of a study that is designed to be an adequate and well-controlled investigation of the same or another investigational drug." Any clinical hold placed on a Treatment IND should be reported immediately to the IRB.

**Risk/Benefit Analysis**

Risks to research subjects who participate in research must be justified by the expected benefits to the subjects or to society. One of the major responsibilities of the IRB is to assess the risks and benefits of the proposed research.

“Risk” is defined as probability of harm or injury, whether physical, psychological, social, or economic, occurring as a result of participation in a research study. Both the probability and magnitude of possible harm vary from minimal to significant. Federal regulations define only “minimal risk”:

*A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed 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. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination.

“Benefit” is defined as a valued or desired outcome to the research participant or society. Payment for participation is not considered a benefit but rather a recruitment incentive. The IRB must:

1. Identify the risks associated with the research as distinguished from the risks of therapies the subjects would receive even if not participating in research;
2. Determine that the risks will be minimized to the extent possible;
3. Identify the probable benefits to be derived from the research;
4. Determine that the risks are reasonable in relation to the benefits to the subjects, if any, and the importance of the knowledge to be gained;
5. Assure that potential subjects will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits;
6. Determine intervals of periodic review, and where appropriate, determine that adequate provisions are in place for monitoring the data collected, and where the subjects are likely to be members of a vulnerable population, determine that appropriate additional safeguards are in place to protect the rights and welfare of these subjects.

Once the risks have been identified, the IRB must assess whether the research presents greater than minimal risk.

FDA Guidance on Significant and Non-significant Risk Device Studies.

FDA regulations on human research state that for studies involving use of an investigational device, the investigator (or sponsor) must obtain either a "significant risk" (SR) Investigational Device Exemption (IDE) from the FDA, or a "non-significant risk" (NSR) IDE from the IRB. The FDA’s document titled, "Guidance on Significant and Non-Significant Risk Device Studies" (available on-line at www.fda.gov) provides a discussion of criteria for the investigator and IRBs to use in making these decisions, and lists examples of non-significant and significant risk device studies.

The IRB will make two separate decisions, based on different criteria. First: Is the investigation approvable or not? Second: Does the proposed investigation result in significant or non-significant risk? (If NSR, an IDE can be given by the IRB. If not, the investigator must be advised to seek a SR IDE from the FDA).

Risk determination is based on the proposed use of a device in an investigation, not on the device alone. If a device being investigated might cause significant harm to any of the subjects, the study should be considered "significant risk." Also, if the subject must undergo a procedure as part of the study, e.g., a surgical procedure to implant the device, the IRB must consider the potential harm caused by the procedure as well as the potential harm caused by the device. The following are examples of studies that are significant risk: investigations in which the potential harm to subjects could be life-threatening, could result in permanent impairment of a body
function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure.

While the IRB is serving as FDA's surrogate with respect to review and approval of non-significant risk device studies, the ultimate decision in determining if a device study is SR or NSR is the FDA's. On some occasions, FDA may overrule an IRB's decision that a device study presents non-significant or significant risk. When FDA overrules an IRB's non-significant risk determination, an IDE application must be submitted to FDA. On the other hand, when FDA considers the device study to be non-significant risk, FDA may return an IDE application to the investigator or sponsor, and the IRB will then determine if it wants the study to take place as a non-significant risk investigation.

**Record Keeping – IRB**

Minutes will be recorded and maintained for each meeting and will containing the following:

1) Date of meeting
2) List of members present or absent
3) List of guests attending the meeting
4) Approval of minutes
5) Report of proposals reviewed administratively
6) Report of addenda/corrections/adverse events for on-going projects
7) New Research Proposals Reviewed: review of new proposals, including the following information:
   a) Title of proposal
   b) Name of all investigators
   c) A brief, administrative introduction to the project
   d) A summary of key issues discussed
   e) Questions, changes, corrections needing attention by applicant
   f) Vote to approve, disapprove, or table
   g) Level of risk assigned
   h) Length of approval period (up to one year maximum)
8) On-going review: as needed, to review amendments requiring full board consideration, and follow up on discussion of proposals previously tabled or other business relating to proposals submitted or approved.
9) Continuing Review (See Approval Period/Continuing Review)

OR&SP is responsible for preparing and maintaining documentation of IRB activities including:

1) Copies of all research proposals reviewed, scientific evaluations (if any), approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.
2) Minutes of IRB meetings.
3) Records of continuing review activities.
4) Copies of all correspondence between the IRB and investigators.
5) A list of IRB members.
6) Written procedures for the IRB.
7) Statements of significant new findings provided to subjects.

The IRB’s official files of all projects reviewed are retained for at least 3 years after completion of the research. Such records will be accessible for inspection and copying by authorized representatives of NEOMED, DHHS, OHRP and the FDA. In addition, OR&SP maintains a computerized database profiling on-going research approved by the IRB, which supports administrative activities of the research community relating to the IRB and funded research.

**Record Keeping – Investigators**

Investigators are notified in writing of the IRB’s decisions, including results of expedited review. This notice includes the approval date, risk classification, and approved project period, and is accompanied by the authorized version of the consent form (indicated by a stamp on behalf of the IRB). A 5-digit reference number is assigned to each application and provided to the investigator at the time of IRB review. This number must appear on all communications between the investigator and the IRB to assure that all related documents are correctly associated with a given project.

Investigators will maintain documentation and record keeping in accord with good academic process and as required by applicable University policy. Research investigators are responsible for retaining the records of all IRB-approved projects in a specified location for at least 3 years after completion of the research. This responsibility includes storage of confidential data in a secure manner that assures only authorized personnel will have access. While this timeline applies to Federal requirements, investigators are advised to ascertain the retention requirements of their certification, licensing, and/or professional bodies, as appropriate.

**Approval Period/Continuing Review**

The IRB approval process is not a one-time event in the life of a research project. As studies progress, safety and effectiveness data that has been accruing may warrant revision to the protocol, key contact personnel may have changed, research regulations may have changed, or there may be other pertinent information that needs to be assimilated into future protocol approvals. Continuing review and approval is necessary even if recruitment of subjects stops but previously enrolled subjects continue to participate in the research or the study is in data analysis. Federal regulations require re-evaluation of approved research at intervals that are appropriate to the degree of risk. All research must be reviewed within the anniversary date of the previous IRB review. IRB approval is a temporary authority that may be withdrawn at any time if warranted by the conduct of the research.

Annual Progress Report: The Office of the Research and Sponsored Programs (ORSP) will send investigators a reminder e-mail to provide a progress report (A Continuation Form or a Closure Form) near the close of the study’s approval period. It is the PI’s responsibility to return a progress report to the ORSP prior to the study’s expiration date. (unless ceasing study procedures would in any way increase the risks to current study participants).

In an effort to assist investigators with this process, within one month of the expiration of the current approval period, OR&SP will send a Continuing Review and Study Completion Report Form to the principal investigator requesting information needed by the IRB for on-going review of the project. (It can also be downloaded from the “Research” web site.)
Office of Research and Sponsored Programs:
OR&SP supports a process by which completed progress report forms are routed for review according to the IRB’s classification of each project’s most recent review status. These reviews proceed as follows:

**Continuation Form or Closure Form – Expedited Review:**
IRB staff at OR&SP reviews the progress report forms and attachments, working with the investigator as needed to assure that the informed consent document(s) reflect the status of the protocol in progress and current NEOMED Consent Guidelines. Once this step is completed, OR&SP will forward the continuation or closure request for final review and approval by the IRB chair or Vice-Chair. *(For further procedural details, see Expedited Review.)* Along with all administrative actions, a report of studies given expedited approval for continuation is reported to the full board.

**Continuation requests – Full Board:**
OR&SP will assign two primary reviewers and place the continuation request on the next available agenda of a convened IRB meeting. At that meeting, the first primary reviewer leads the discussion about the renewal request. Material accompanying the Research Report Form include a summary of the study, an outline of all amendments and adverse effects occurring during the approval period, the most recently used informed consent, and any reports of other findings relating to subject safety. During this review, the IRB will make a determination whether any new findings, new knowledge, or adverse effects should be communicated to subjects. Discussion will focus on any substantive issue resulting from this review. Final approval will include stipulated changes to the informed consent document(s), whether the risk classification is altered, and the length of the new approval period, not to exceed one year.

**NEOMED Investigators:**
All University investigators, including students, are responsible for abiding by the protocol approved by the IRB, coordinating any communications regarding IRB approval through the principal investigator (including reporting of adverse events), and implementing the authorized informed consent process. The latter includes not only the consent form, but also recruitment materials and the manner in which prospective subjects are approached and consent is obtained. Research investigators must promptly report proposed changes in previously approved human subject research activities to the IRB. The proposed changes must not be initiated without IRB review and approval, except where necessary to eliminate immediate hazards to the subjects. Investigators are expected to report adverse effects and other problems to the IRB, sponsors, designated institutional representatives, and the FDA.

The principal investigator is also responsible for assuring that annual progress report forms (the Continuation or the Completion Form) are completed as requested by OR&SP and filed in a timely manner so as to obtain IRB review prior to the project’s expiration date. While the OR&SP sends courtesy reminders close to a project’s expiration date, it is the responsibility of the principal investigator to submit a continuation application before the expiration of his/her current approval. If a progress report is not received prior to the study’s expiration date, the study will be administratively closed by the IRB. All enrollment, study procedures and data analysis must stop immediately until approval is re-established. The IRB may also prohibit the principal investigator from opening any additional studies or from continuing any ongoing studies until the required progress report is received and the study in question has been brought into compliance.
The information requested in a progress report pertains to the approved project and includes the following:

1. A description of adverse events or unanticipated problems involving risks to subjects,
2. Number of subjects enrolled during the approval period,
3. A summary of any recent literature, findings obtained thus far, reports on multi-center trials,
4. Amendments or modifications to the protocol,
5. Verification that the approved consent form was used,
6. An indication of the project’s status.

Complete instructions for requesting extension approval appear on the Continuation Review Report Form. The continuation of research after expiration of IRB approval is a violation of Federal regulations [21 CFR 56.103(a)]. If the IRB has not reviewed and approved a research study by the study's current expiration date, i.e., IRB approval has expired research activities must stop. No new subjects may be enrolled in the study. However, if the investigator is actively pursuing renewal with the IRB and the IRB believes that an over-riding safety concern or ethical issue is not involved, the IRB may permit the study to continue for the brief time required to complete the review process.

If a research study has been formally completed or terminated, the principal investigator must notify the IRB in writing by filing a Study Completion Report Form. The investigator is responsible for reporting data in a completely accurate manner when publishing results of a study.

**Adverse Events**
Adverse events are defined as undesirable and unintended, although not necessarily unexpected, result of therapy or other intervention. Adverse events do not necessarily have to have a causal relationship with a specific investigative drug or device. An adverse event may or may not be serious and may or may not be expected.

Investigators are responsible for reporting two types of adverse events (AE):
1) Any subject injuries or adverse reactions associated with the study procedures, and/or problems involving the conduct of the study that may occur during the course of the research project;
2) Any possible breach of human subject protection in any research activities of which the investigator may become aware. This includes loss of confidentiality and/or emotional harm.

The IRB Chair is responsible for the appropriate and timely presenting of such events to the full IRB for the purpose of evaluating risk assignment, consent information, and approval period.

**Serious Adverse Events (SAE)**
A serious adverse event is any untoward medical occurrence that occurs during the research and is life threatening requires hospitalization or prolongs existing hospitalization, results in persistent or significant disability or incapacity, or results in a congenital anomaly or birth defect.
Failure to report an AE or SAE is a breach of the conditions in which the IRB granted protocol approval. This breach can result in the suspension or termination of the research study. Unreported AE’s or SAE’s can affect the safety and welfare of current and future research participants thus it is essential that these events/incidents be reported in a thorough and timely manner.

There are situations where a serious or unexpected adverse event requires an immediate change to a protocol in order to relieve an apparent immediate hazard to research subjects. In these situations, the principal investigator may implement a change necessary to protect the welfare of the research subjects. Investigators are encouraged to contact the IRB if this type of situation arises prior to implementation of the protocol change. Investigators are required to notify the IRB in writing of the change, within 72 hours, and include a description of the change and events that necessitated immediate implementation.

**Drugs and Biologics:**
Per 21 CFR 312.64, an investigator shall promptly report to the sponsor any adverse event that may reasonably be regarded as caused by, or probably caused by, the therapy. If the adverse effect is alarming, the investigator shall report the adverse effect immediately. The investigator shall simultaneously notify the IRB of these events.

**Radioactive Drugs:**
Per 21 CFR 361, the investigator shall immediately report to the IRB and Radioactive Drug Research Committee all adverse effects associated with the use of the radioactive drug in the research study. All adverse events (reactions) probably attributable to the use of the radioactive drug in the research study shall be immediately reported by the Radioactive Drug Research Committee to the FDA, Center for Drug Evaluation and Research, HFD-160, 5600 Fishers Lane, Rockville, MD 20857. The IRB must also receive a copy of this report.

**Medical Devices:**
Per 21 CFR 812.150, an investigator shall submit to the sponsor and to the reviewing IRB a report of any associated unanticipated adverse event occurring during an investigation as soon as possible, but no later than 10 working days after the investigator first learns of the event. Fatal or life-threatening events must be reported to the IRB immediately.
**Gene Therapy:**
Investigators who have received approval from the FDA to initiate a human gene transfer protocol must report any serious adverse event immediately to the NEOMED IRB, Office of Hazardous Materials Safety, the NIH Office for Human Research Protections (OHRP), NIH/OBA, and FDA, followed by the submission of a written report filed with each group. Reports submitted to NIH/OBA shall be sent to:

Office of Biotechnology Activities  
National Institutes of Health  
6705 Rockledge Drive, Suite 750, MSC 7985  
Bethesda, MD 20892-7985  
Phone: 301-496-9838  
Fax: 301-496-9839  
[www.od.nih.gov/oba](http://www.od.nih.gov/oba)

Please use the Serious Adverse Event Reporting Form found on the NIH/OBA web site: [http://www.od.nih.gov/oba/rac/documents1.htm](http://www.od.nih.gov/oba/rac/documents1.htm) when reporting serious gene transfer adverse events to the agency.

**Noncompliance:**
Failure to obtain IRB approval prior to the involvement of human subjects constitutes violation of College policy, which is subject to disciplinary action and/or legal action by the College in accord with standard academic practice.

**Suspension/Termination**
The IRB has the authority to suspend or terminate previously approved research that is not being conducted in accordance with the IRB’s requirements or that has been associated with unexpected harm to subjects (21 CFR 56.113).

The IRB may suspend or terminate approval for any of the following reasons:
1. The investigator fails to  
   a. Obtain informed consent  
   b. Retain completed consent form(s)  
   c. Make required revisions prior to starting the study  
   d. Make requested changes in the study  
   e. Provide accurate progress reports regarding the conduct of the study, i.e., number of subjects, adverse reactions, etc.  
   f. Inform the IRB that the sponsoring agency has discontinued the study for reasons of safety
2. The investigator shows lack of propriety or deceit through:  
   a. Evidence the original study has been altered  
   b. Unauthorized modification of the study or consent form  
   c. Scientific misconduct involving risks to human subject or others  
   d. Evidence that the rights of subjects have been violated
3. Careful review of reports of adverse events show that unexpected or serious harm occurred to subjects.
4. Significant new findings developed during the course of the research, which alter the feasibility of the study.

This suspension or termination may occur during the progress of a study or prior to the onset of a study. The investigator will be informed in writing of the suspension or termination, and a copy of the letter will be sent to the appropriate affiliated institutions, the sponsor, and the FDA.

Special Conditions

Advertising.
The IRB is responsible for ensuring the equitable selection of research subjects. Additionally, OHRP and the FDA considers direct advertising for study subjects to be the start of the informed consent and subject selection process. Thus, in fulfilling this responsibility the IRB reviews the materials and methods that investigators use to recruit subjects. Since advertising (classified, display, posters, videos, television/radio commercials, etc.) is a method of recruitment and an extension of the informed consent process, the IRB reviews the information contained in the ad to determine that adequate protection is afforded in recruiting subjects.

In general, advertising to recruit subjects should be limited to:
1. The purpose of the research
2. Briefly stated eligibility requirements
3. Straightforward and truthful description of benefits to subjects (e.g., payment or free treatment)
4. Location of the research and how to obtain further information.
5. Name and address of principal investigator.

No claims should be made, either explicitly or implicitly, that the study treatment is safe, effective, or superior. Advertising should not use terms such as "new treatment," "new medication," or "new drug" without explaining that the test article is investigational. Advertisements should not promise "free medical treatment," when the intent is only to say subjects will not be charged for taking part in the investigation.

Remuneration: Research Subjects.
Payment to research subjects for participation in studies is not considered a benefit, it is a recruitment incentive. Financial incentives are often used when health benefits to subjects are remote or non-existent. Remuneration for participation in research must be described in the Consent Form and approved by the IRB. The amount of remuneration should be reasonable and commensurate with the expected contribution of the subject and should not constitute undue pressure to volunteer for the research project. Quantification of the remuneration should include consideration of travel and parking expenses, time commitment, etc. Just as the size of payment can put inappropriate pressure on subjects, so can the schedule of payment. Holding payment until the subject has completed every procedure in a long, multi-week, multi-visit study is
inappropriate. For studies with more than two or three visits, payment should be prorated, that is, based on the amount of time subjects have spent participating so far. Any departure from this guideline should be justified to the IRB.

**Remuneration: Investigators.**

It is not uncommon for research investigators to receive financial compensation (e.g., cash, stock, options) from study sponsors. The principal investigator’s spouse or dependant children may also have equity interest in the study sponsor. These dualities of interest have the potential to affect study integrity, thus the principal investigator must inform the IRB of such dualities during the protocol application process. The FDA requires that the study sponsor disclose these financial relationships to the FDA when their clinical studies are submitted in support of product marketing [63 Federal Register 5233 (1998)]. Additionally, the IRB may require that these financial interests be disclosed to research participants during the informed consent process as described below:

[name of investigator] has a personal financial interest in [name of sponsoring company or other interested entity]. The nature of this interest has been reviewed by the NEOMED IRB and determined that this interest will not compromise the quality or integrity of the research study. Further, the IRB has determined that the interest will not compromise the safety or welfare of research participants.

**Medical Record Review**

Use of medical records information for purposes of individual patient treatment, or in-house or program evaluation (e.g., Grand Rounds presentations) is not considered to be "research" and IRB approval need not be obtained. However, if the medical record information will be gathered with the intent of research, publication or presentation to an outside group, this is considered to be within IRB jurisdiction and requires review.

**Critical Care Research.**

The medical status of prospective subjects in a critical care setting may preclude his/her ability to provide informed consent. However, when the research presents no more than minimal risk and involves no procedures for which written consent is normally required outside the research context, the IRB may waive the requirement for written consent (see [Waivers to signed consent form](#)).

**Genetic Research.**

Genetics is concerned with the study of genes and their alleles; however, the relationship between this information and the health of an individual is frequently unclear. Biological relatives share genetic material and may be affected by the same conditions, thus, the information gained from a study may have implications beyond the individual subject. Matters of privacy and confidentiality take on special importance because misunderstanding or misuse of genetic data can have profound implications for families, society and science. Only investigators with competence in genetic counseling should provide subjects with the results of genetic tests obtained for research purposes. A clear understanding should be conveyed concerning the limitations in interpreting genetic tests due to technical variability and the limited knowledge about the clinical implications of specific polymorphisms.
The IRB offers the following guidance with regards to human genetics research:

1. Genetics research subjects or, when appropriate, their guardians are required to provide voluntary, informed written consent.

2. Participants should have the option of selecting whether or not they want access to the genetic information generated by the study. Their decision should be recorded in the informed consent form.

3. Participants should be informed that in pedigree analysis and family linkage studies, the investigation might determine that some members of their family are not genetic relatives. However, those results will not be disseminated. Furthermore, it is sometimes possible that other family members may learn private genetic information about the participant.

4. Where genetic research may generate information important to the relative of a research subject, the subject's consent should be sought prior to approaching relevant family members. If there is a threat to a family member's health and the participant refuses permission to disclose his or her genetic information, the investigator must consider whether the threat is of a sufficiently serious nature so as to warrant disclosure without the participant's consent. In these cases, ethics committees are available for guidance.

5. Researchers should be aware of the pressure that may be applied by other family members to participate in studies. They should be particularly sensitive to the issue in the context of research that is burdensome or carries risks, such as the possibility of revealing information that might be predictive of future illness. The recruitment of family members identified by a participant should only be undertaken if the participant agrees, and with the participant's assistance if possible.

6. There are many levels of confidence in science and in the uses of information, making it difficult to propose universal standards for consent for unspecified future genetic research. Therefore, the IRB proposes three (3) tiers of consent for unspecified future genetic research.

   a. Unidentified. The sample source is completely unidentified: a) only the sex and age of the source are identified; and b) the donor has no possibility of receiving individual results or rewards. This does not require prior consent but does require IRB approval.

   b. Coded or potentially identifiable. If the sample source has the possibility of identifying a number of characteristics, such as, age, sex, dates of exposure or general health habits, but not individuals, the donor may receive general information, if desired, regarding research results. There will be no attempt to personalize the research results. To prevent the possibility of access to the information by others, the researcher will ensure all information of pertinence to individuals will be protected. Clinically relevant information can be given to the
participant on request. This requires informed consent for the overall study but not for each specific use of the genetic materials. Researchers are obligated to consider how to deal with informing sample donors of clinically relevant results should they be discovered. IRB approval is required.

c. Identifiable. If the sample source is to have open-ended identification, the researcher can obtain as much coded information as necessary for the study. The subjects must be re-consented in advance and they may, if they desire, receive their individual research results.

**Genetic Research Involving Children**

Genetic research with children involves special ethical obligations. Children may be at particular risk of perceived adverse consequences, both within and outside their families, as a result of genetic testing. The protocol should include a formal discussion with parents about the decision where and when to reveal genetic information to children. If the child is over seven (7) years of age, s/he should be given age-appropriate genetic counseling and where appropriate, consent forms for assent to the testing.

The IRB will consider the inclusion of children in research who are wards of the state or any other agency or institution. For research that involves more than minimal risk with no prospect of direct benefit to the child, or for research that requires approval of the Health and Human Services Secretary, the study must either be 1) related to the child’s status as a ward, or 2) be conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards. [45 CFR 46.406-409]. The IRB is required to appoint an advocate for each child who is a ward. The advocate is required to have the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child’s participation in the research and who is not associated in any way with the research, the investigator, or the guardian organization. The requirement for an advocate is in addition to gaining permission from any other person acting on behalf of the child as guardian or in loco parentis.

**Human Stem Cell Research:**

The IRB supports the NIH guidelines on the use of stem cells for research purposes. The IRB also supports the report and recommendations of the National Bioethics Advisory Committee (NBAC) regarding human stem cell research. Research utilizing human pluripotent stem cells for both basic knowledge and for clinical applications is subject to IRB review and current Federal regulations.

**Special Populations:**

**Children** Research involving children should only be conducted when it is not contrary to the best interests of the child, where consent has been obtained by the child's parents, guardians, or others as required by law. Where appropriate, assent should also be obtained from the child. Social or peer pressure to participate should be minimized. Punishment or other negative actions
should not follow a child’s refusal to participate in a research study. Further, all clinical investigators must be familiar with State laws requiring reports of suspected child abuse or neglect. *Investigators are responsible for all relevant regulations within 45 CFR 46 Subpart D.*

**Research not involving greater than minimal risk.**  
NEOMED will conduct research in which the IRB finds that no greater than minimal risk to children is presented, only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 45 CFR §46.408.

**Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.**  
1) NEOMED will conduct research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, only if the IRB finds that:  
   a) The risk is justified by the anticipated benefit to the subjects;  
   b) 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  
   c) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 45 CFR §46.408.

**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 condition.**  
1) NEOMED will conduct research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, only if the IRB finds that:  
   a) The risk represents a minor increase over minimal risk;  
   b) 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;  
   c) 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  
   d) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in 45 CFR §46.408.
**Employees of NEOMED and its Affiliates:**
Employees, such as office staff, lab technicians, and post-doctoral fellows, are similar to students in that they are vulnerable to perceived, even if not intended, pressures to appear cooperative and supportive of their supervisor’s work. Accordingly, many of the same procedures employed to reduce the likelihood of coercion in recruiting student volunteers apply equally to employees. The IRB will not approve recruitment procedures that include employees from the investigator’s own lab or office as research subjects.

**NEOMED Students.**
Students traditionally have served as subjects for academic research, biomedical research and behavioral research. The obvious concern is that their participation may not be truly voluntary because of a desire to appear particularly cooperative or highly motivated, or because participation in research is a course requirement. The IRB suggests several procedures to reduce the possibility of unintended coercion, while still permitting students to participate as subjects in research.

These include:
1. Design study advertisements so that they recruit subjects from a broad base of students;
2. Avoid personal solicitations of students by faculty, graduate assistants, or fellow students;
3. Provide a number of research projects from which to chose, if participating as a subject in research can be used as a course requirement;
4. Provide alternative and equal methods for meeting course credit (or extra credit) requirements, such as attending a series of research presentations by faculty, writing a brief paper, conducting one’s own research.

**Minorities.**
Federal regulations require the equitable selection of minorities as research subjects [45 CFR 46.111. (a)(3)]. The inclusion of minorities in research is important both to ensure that they are eligible for an equal share of the benefits of research, and to ensure that they do not bear a disproportionate burden. Sometimes minorities are subject to different clinical conditions compared to other populations. For example, sickle cell anemia and Tay Sachs disease only affect a few minority groups. Other research focuses on characteristics of diseases or effectiveness of therapies in particular populations (e.g., HIV transmission, treatment for hypertension), and may also concern conditions or disorders that disproportionately affect a certain racial or ethnic group. Exclusion or inappropriate representation of these groups, by design or inadvertence is unjust. Considering that participation in research could potentially offer direct benefits to the subjects (e.g. HIV/AIDS research), under-representation of minorities denies them, in a systematic fashion, the opportunity for direct benefit.

**Prisoners:**
Prisoners are considered vulnerable because they are in a restrictive, institutional environment that affords little opportunity for voluntary choices, earning wages, interaction with the community, and obtaining medical care. Studies have shown that prisoners often volunteer for
medical research as a means of access to a competent medical examination, because health care may be woefully inadequate in prison.

Because a prisoner’s autonomy is limited, they may participate only in certain categories of research, and special precautions are needed to assure that their consent to participate in the research is both knowing and voluntary [45 CFR 46.302].

The IRB will only allow research studies involving prisoners when the research involves the following methods and goals:

1. Studies of the possible causes, effects, and process of incarceration and criminal behavior, if these studies present no more than minimal risk or inconvenience to the subjects;
2. Studies of prisons as institutions, or of prisoners as incarcerated persons, if those studies present no more than minimal risk or inconvenience to the subjects;
3. Research on conditions affecting prisoners as a class (e.g., research on hepatitis, drug addiction, sexual assaults, and other conditions more prevalent in a prison population than elsewhere), but only after the Secretary of Health and Human Services has consulted with experts in medicine, ethics, and penology and published a notice approving the proposed research in the Federal Register; and
4. Research on practices that are intended, and reasonably likely, to enhance the well being of the subjects. However, if some of the prisoners will be assigned to control groups, which will not benefit from the research, then the study must first be approved by the Secretary of Health and Human Services, after consultation with appropriate experts, as described above.

Additionally, the IRB will review each submitted protocol to verify that:

1. Any advantages that prisoners will realize as a result of participating in the research, when compared to the general living conditions within the prison, are not so great as to impair prisoners’ ability to weigh the risks and benefits of participation and freely choose whether or not to participate;
2. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers (usually demonstrated by enrolling non-prisoner subjects from the community, as well);
3. Procedures for selecting subjects within the prison are fair, and free from arbitrary manipulation by prison authorities or prisoners;
4. Control subjects will be selected randomly from among the group of eligible volunteers, unless the principal investigator justifies a different procedure;
5. The information presented during recruitment and consent procedures is in a language, and level of complexity, understandable to the subject population;
6. The IRB must be assured that the parole board will not take research participation into account in making decisions about parole, and each prisoner is informed in advance that participation will have no effect on the possibility of parole;

7. If medical follow-up is necessary to protect the health and welfare of the subjects, adequate provision is made for such care, taking into account the varying length of prisoners’ sentences.

8. The IRB that reviews research involving prisoners is required to have at least one member who is either a prisoner, or a prisoner representative. The majority of the IRB members cannot be in any way associated with the prison(s) involved.

**Terminally Ill Patients:**
Terminal patients (generally recognized as those with six months or less to live) are a vulnerable research population. Out of desperation, these patients may be willing to "try anything" that might offer hope of either a cure or a slowing of the disease process. Others, aware that nothing further can be done to cure their disease, might fear abandonment by the medical establishment or their family, and agree to participate in research as a means of maintaining contact with physicians expert in treating their condition or to prevent alienation from their relatives.

Knowing this, the classification as “terminally ill” should not necessarily be an exclusion criterion for participating in research. Many terminally ill individuals are willing to submit to considerable discomfort and risk for the possible benefit of future patients suffering from the same condition, and will volunteer for research about their particular condition in hopes of helping other, similarly situated patients in the future.

Investigators should be sensitive to these matters and remind potential research subjects that in general, they will likely not experience any personal medical benefit from their participation in a particular study, rather the benefit is anticipated for future patients as data is generated and analyzed. This is especially important because in some research studies, the dosage subjects will be given is not expected to produce a therapeutic result. At the same time, it is important not to automatically treat terminally ill patients as incompetent or incapable of autonomous decision-making. This needs to be assessed on an individual basis, with the help of a psychiatrist, if needed.

**Women.**
The primary aim of clinical trials is to provide scientific evidence leading to a change in health policy or a standard of care; therefore it is imperative to determine if the intervention or therapy being studied affects men and women differently. NIH has concluded that the inclusion of women in research is sufficiently important that the only justifiable reason to exclude non-pregnant women of child-bearing potential from research is compelling evidence that the proposed project would be inappropriate with respect to the health of the subject or the purpose of the research. A discussion of this determination can be found in their guideline: NIH Outreach Notebook of the Inclusion of Women and Minorities in Biomedical and Behavioral Research (1994).
Research on pregnant women
This is regulated by the following Federal Codes: 45 CFR 46, Subpart B; 45 CFR 46.207 (a); 45 CFR 46.207(b).

Research on women with childbearing potential
This population is also regulated by the following Federal Codes: Federal Register, Vol. 58, No. 139, p 39411, Sections G and H, Thursday, July 22, 1993; Federal Register, Vol. 58, No. 139, p 39409, Section G, Thursday, July 22, 1993.

Prior to the initiation of a trial, investigators should discuss with the participants known or theoretical risks as a result of becoming pregnant during the trial period. The following is suggested language for use in informed consent documentation for a trial of a potentially toxic drug substance in women of childbearing potential:

If you are a woman who is able to become pregnant, it is expected that you will use a medically accepted method of birth control [outline the recommended forms of birth control] to prevent exposing a fetus to a potentially dangerous agent with unknown risk. If you are pregnant or currently breast feeding, you may not participate in this drug study. If you are pregnant, if you become pregnant, or if you are breast-feeding during this study, you or your child may be exposed to an unknown risk. There are also known risks to you or your unborn baby, including [state specific risks].

To confirm to the extent medically possible that you are not pregnant, you are required to agree [to have a pregnancy test done before beginning this research study] [to begin the study after the onset of your next menstrual period] [choose one]. You must agree to avoid sexual intercourse or use a birth control method judged to be effective by the investigator and which will not interfere with the proposed investigation. Pregnancy could still result despite the responsible use of a reliable method of birth control while participating in this research study. You agree to notify the investigator as soon as possible of any failure of your birth control method, or if you become pregnant, either of which may result in your being withdrawn from the study.

Fetuses
Per 45 CFR 46.208, no fetus in utero may be involved as a subject in any activity covered by this subpart unless: (1) the purpose of the activity is to meet the health needs of the particular fetus and the fetus will be placed at risk only to the minimum extent necessary to meet such needs, or (2) the risk to the fetus imposed by the research is minimal and the purpose of the activity is the development of important biomedical knowledge which cannot be obtained by other means. The research activity may be conducted only if the mother and father are legally competent and have given their informed consent [see full regulations for exceptions regarding the father's informed consent.]
Until it has been ascertained whether or not a fetus \textit{ex utero} is viable, a fetus \textit{ex utero} may not be involved as a subject in an activity covered by this subpart unless:

1. There will be no added risk to the fetus resulting from the activity, and the purpose of the activity is the development of important biomedical knowledge which cannot be obtained by other means, or
2. The purpose of the activity is to enhance the possibility of survival of the particular fetus to the point of viability.

No nonviable fetus may be involved as a subject in an activity covered by this subpart unless:

1. Vital functions of the fetus will not be artificially maintained,
2. Experimental activities which of themselves would terminate the heartbeat or respiration of the fetus will not be employed, and
3. The purpose of the activity is the development of important biomedical knowledge, which cannot be obtained by other means. In the event the fetus \textit{ex utero} is found to be viable, it may be included as a subject in the activity only to the extent permitted by and in accordance with the requirements of other subparts of this part.

The research activity may be conducted only if the mother and father are legally competent and have given their informed consent [see full regulations for exceptions regarding the father's informed consent.]

Activities involving the dead fetus, macerated fetal material, or cells, tissue, or organs excised from a dead fetus shall be conducted only in accordance with any applicable State or local laws regarding such activities.
Glossary of Lay Terms

**Adjuvant Therapy:** Therapy provided to enhance the effect of a primary therapy; auxiliary therapy.

**Adverse Effects** An unintended, but not necessarily unexpected, result of therapy or other intervention that is unpleasant or dangerous (e.g., headache following spinal tap).

**Assent Agreement** by an individual not competent to give legally valid informed consent to participate in research.

**Assurance** A formal, written statement submitted to a federal agency that an institution promises to comply with applicable rules governing research with human subjects.

**Autonomy** Personal capacity to consider alternatives, to make choices, and to act with undue influence or interference of others.

**Belmont Report** A statement of basic ethical principles governing research within human subjects issued in 1978 by the National Commission for the Protection of Human Subjects.

**Beneficence** An ethical principle discussed in The Belmont Report that is expressed in two general rules (1) do not harm, and (2) maximize possible benefits and minimize possible harm.

**Benefit** Something that promotes or protects well being; an advantage.

**Case-Controlled Study** A study comparing persons with a given disease and persons without the given disease (controls) with respect to antecedent factors.

**CFR** Code of Federal Regulations: a compendium of rules issued by federal agencies for conducting biomedical research.

**Class I, II, III Devices** Classifications of medical devices by the FDA according to potential risks or hazards.

**Clinical Trials** Research on human subjects designed to evaluate prospectively the safety and efficacy of diagnostic, therapeutic, or preventive intervention.

**Cohort** A group of subjects initially identified as having one or more characteristics in common, who are followed up over time.

**Compensation** Payment or medical care provided to subjects injured in research; does not refer to payment (remuneration) for participation in research.
**Competence** A legal term used to denote capacity to act on one’s own behalf; the ability to understand information presented; to appreciate the consequences of acting (or not acting) on that information, and to make a choice.

**Confidentiality** Pertains to the treatment of information that an individual has disclosed in a relationship of trust, and with the expectation that it will be divulged to others only in ways that are consistent with the understanding of the original disclosure without permission.

**Contract** An agreement that a specific research activity will be performed at the request and under the direction of the agency providing the funds. Research performed under a contract is more closely controlled by the agency than research performed under a grant.

**Controls (subjects)** Subjects used for comparison who are not given a treatment under study or do not have a given disorder, background, or risk factor that is the object of the study.

**Device (medical)** Therapeutic, diagnostic, or prosthetic articles that do not interact chemically with the body.

**Double-blind design** A study design in which neither the investigators nor the subjects know to which treatment group individual subjects are assigned.

**Emergency Use** The use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval.

**Equitable** Fair or just; used in the context of selection of subjects to indicate that the benefits and burdens of research are fairly distributed.

**Expedited Review** Review of proposed research by a designated individual rather than by the entire IRB. Federal rules permit expedited review for certain types of low-risk research. Also called “administrative review.”

**Experimental** Term often used to denote a therapy that is unproven or scientifically invalidated with respect to safety and efficacy. A procedure may be considered “experimental” with out necessarily being part of a formal study(research) to evaluate its usefulness. [Procedures and tests that are considered routine or non-experimental may be used as part of the procedures in a experimental study.]

**False-Negative** When a test wrongly shows an effect or condition to be absent.

**False-Positive** When a test wrongly shows an effect or condition to be present.
**FDA** Food and Drug Administration, an agency of the U.S. Government, established by the Congress in 1912, and presently part of the Department of Health and Human Services. When referenced in documents such as consent forms, the agency should be referred to as the U.S. Food and Drug Administration initially, and subsequently my be abbreviated to FDA.

**General Assurance** Term used to denote an institutional assurance covering multiple research projects.

**Grant** Financial support provided for research study designed and proposed by an investigator (principal investigator). The granting agency exercises no direct control over the conduct of approved research supported by a grant.

**Informed Consent** A person’s voluntary agreement, based on adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure.

**Investigational (New Drug or Device)** A drug or device permitted by the FDA to be tested in humans but no yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing.

**Longitudinal Study** A study designed to follow subjects forward through time.

**Minimal Risk** Probability and magnitude of physical or psychological harm that does not exceed those encountered in ordinary everyday life or in the performance of routine medical and psychological examination.

**Null Hypothesis** The proposition to be tested statistically that the experimental intervention has “no effect,” meaning that the treatment and control groups would show no difference as a result of the intervention.

**Nuremberg Code** A code of research ethics developed during the trials of Nazi war criminals following World War II and widely adopted as a standard during the 1950s and 1960s.

**Open Design** An experimental design in which both the investigator(s) and the subject(s) know the treatment to which the subjects are assigned.

**OHRP** Office of Human Research Protections at the U.S. Department of Health and Human Services, responsible for implementing DHHS regulations governing research with human subjects.

**Phase 1, 2, 3 Drug Trials** Different stages of testing drugs in humans, from first application in humans (Phase 1) through limited (Phase 2) and broad clinical tests (Phase 3).

**Placebo** A chemically inert substance given in the guise of medicine for its psychologically suggestive effect; used in controlled clinical trials to determine whether improvement and side effects may reflect imagination or anticipation rather than the actual power of the drug.
**Preclinical Investigations** Laboratory and/or animal studies designed to test the mechanisms, safety, and efficacy of an intervention prior to its application in humans.

**Principal Investigator** The scientist, clinician, or scholar with primary responsibility for the design and conduct of a research project.

**Prospective Study** Study designed to observe outcome or events that occur subsequent to identification of the group of subjects to be studied. They need not involve manipulation or intervention but may be purely observational or involve only the collection of data.

**Protocol** The formal design or plan of an experiment or research activity; specifically, the plan submitted to an IRB for review and to an agency for research support.

**Randomization (Randomized)** Assignment of subjects to different treatments, interventions, or conditions according to chance rather than as dictated by the standard or usual response to their condition, history, or prognosis.

**Remuneration** Payment for participation in research.

**Research** Careful or diligent search, studious inquiry, or examination; especially investigation or experimentation aimed at the discovery and interpretation of facts, revision of accepted theories or laws in the light of new facts, or practical application of such new or revised theories or laws.

**Respect for Persons** An ethical principle discussed in The Belmont Report requiring that individual autonomy be protected.

**Retrospective Studies** Research conducted by reviewing records from the past and information about past events elicited through interviews with persons who have and who do not have (controls) the condition under investigation.

**Risk** The probability that harm may occur. In IRB review, probability and severity of possible pain or discomfort should be included in the concept of risk.

**Single-Blind Design** A study design in which the investigator, but not the subject, knows the identity of the treatment assignment. Sometimes it is the subject and not the investigator who knows.

**Sponsor** The developer of a new drug who distributes it to investigators and physicians for clinical trials and who is responsible for securing FDA clearance for trials and for reporting the results of those trials to the FDA. A sponsor may be either a private pharmaceutical manufacturer, a research institution, a clinical investigator, or a federal agency.

**Statistical Significance** The probability that two treatments or conditions under study are really different as opposed to the likelihood that any observed variations have resulted by chance. By consensus, if there is less than a 1 in 20 possibility that observed differences occurred by chance,
the results are said to be statistically significant (at the .05 level of confidence). If the possibility that the difference resulted by chance, and is 1 in 100, the results are said to be statistically significant at the .01 level of confidence.

**Subjects (Human)** Individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project. Under DHHS regulations, human subjects are defined as “living human beings.”

**Therapy** Treatment intended and expected to alleviate a disease or disorder.

**Voluntary** Free of coercion, duress, or undue inducement. Used in a research context to refer to a subject’s decision to participate.