INTERNAL REVIEW BOARD

Requirements and Responsibilities

OCTOBR 9, 2017
NATIVIDAD MEDICAL CENTER

Contents

Overview

NMC acknowledges the ethical and legal burden involved in research. To this end NMC is seeking to establish a Program for the Protection of Human Subjects. The component parts of this program should include:

1. Establishment of an Institutional Review Board (IRB)
2. A program of education of IRB members and NMC staff
3. A compliance program

An institution or organization that has not registered an Institutional Review Board or been assigned an Institutional Organization (IORG) number must complete an initial IRB registration application. Before obtaining Federal-wide Assurance (FWA), an institution must either register its own IRB or designate an already registered IRB operated by another organization.

The FWA is the only type of assurance currently accepted and approved by Office for Human Research Protections (OHRP). Through the FWA and the Terms of the FWA, an institution commits to Health and Human Services (HHS) that it will comply with the requirements in the HHS Protection of Human Subjects regulations at 45 CFR part 46.

IRB Objectives

The primary objective of an IRB, is to assess projects to determine that it is likely that the rights and the welfare of the human subjects will be protected.

Protection of the investigator and the institution are secondary objectives that are best assured by protection of the subjects.

Protection of the rights and welfare of human subjects involved in research projects includes but is not limited to:

1. The protection of the rights and welfare of patients and/or volunteers who participate in research and the assurance that patients and/or volunteers are provided with enough information about a study so that they can give effective informed consent prior to their participation.
2. A determination that the risks are reasonable in relation to the benefits, if any, to subjects and the importance of the knowledge that may be expected to result.
3. Providing a consent document that not only complies with the regulations but also is likely to be understood by the population being sought.
4. Providing continuing review at a frequency determined by potential risks, the speed at which the field of study is changing, and events occurring in the conduct of the study, but at a minimum of one review per year.
5. To provide objective and timely review services for the investigators.
6. To provide educational opportunities related to human research protections for IRB members and staff.

IRB Policies & Procedures

1. Policies and procedures governing and guiding the IRB would be working documents intended to facilitate the effective and efficient operation of the IRB.
2. HHS regulations at 45 CFR 46.103(b)(4) and (5) require that institutions have written IRB procedures for each of the following:
    a. The procedures which the IRB will follow for conducting its initial review of research;
    b. The procedures which the IRB will follow for conducting its continuing review of research;
    c. The procedures which the IRB will follow for reporting its findings and actions to investigators and the institution;
    d. The procedures which the IRB will follow for determining which projects require review more often than annually;
    e. The procedures which the IRB will follow for determining which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review;
    f. The procedures which the IRB will follow for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject; and
    g. The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, any Department or Agency head, and OHRP of:
    h. Any unanticipated problems involving risks to subjects or others (hereinafter referred to as unanticipated problems);
    i. Any serious or continuing noncompliance with 45 CFR Part 46 or the requirements or determinations of the IRB; and
    j. Any suspension or termination of IRB approval.

IRB Jurisdiction

The following studies shall be subject to IRB review:

1. Studies either conducted by or participated in by staff members of NMC, medical or non-medical, when they are representing NMC.
2. Studies conducted within NMC facilities or property.
3. Studies conducted using private information under the jurisdiction of NMC
4. Studies conducted in a private practice or by community investigators but using NMC facilities or services for standard, non-investigational procedures.
5. The following studies may be reviewed by the IRB:
    a. Studies conducted by part time staff members outside the scope of their employment and the confines of the institution, and
    b. Studies conducted by community investigators with or without access to an institutionally based IRB.

Duties and Responsibilities

While no regulation requires assignment of duties to specific parties, it is useful to understand who has primary responsibility for some duties.

NMC Administration

1. Provide meeting space, office space, supplies, and secretarial support as necessary to accomplish the tasks of the IRB.
2. Provide sufficient budget to meet IRB operational, educational and instructional needs.
3. Appoint an Institutional Review Board Coordinator to serve as an "Institutional Officer" as described in the National Institute of Health (NIH) and FDA regulations. This person is the lead contact person for OHRP.
4. As needed, provide direction, guidance, information and support to the IRB.
5. Work to assure that IRB opinions are trusted and respected.
6. Appoint the IRB members from recommendations submitted by the established Board so as to provide
    a. A board with sufficient expertise, diversity, and independence to impartially review protocols, and
    b. A board that will offer diverse opinions about local conditions.
7. Appoint the IRB chair from recommendations submitted by the established Board.
8. Hear appeals from IRB decisions and complaints filed against it. IRB disapproval cannot be overturned by any other institutional entity.

NMC IRB Coordinator

1. Is not a member of the IRB.
2. Supports and facilitates all IRB processes and will, at the least:
    a. Provide protocol materials to IRB members for review prior to a scheduled meeting;
    b. Generate minutes from each meeting for approval of the IRB and signature of the chair;
    c. Structure monthly "Standing Reports" for dissemination of information to the Board regarding activities that do not require full board action (e.g. Expedited Reviews; Facilitated Reviews);
    d. Generate correspondence from each meeting and, as necessary, obtain the chair’s signature, and
    e. Provide courtesy notice to approved investigators regarding the impending expiration of IRB approval.
3. Provides for communication(s) between researchers and members.
4. Receives inquiries from research participants regarding participation in the study and/or with complaints and has the authority to appropriately support the subjects.
5. Maintains IRB files in conformance with regulatory requirements.

5. Report, via monthly Standing Reports, information related to IRB: continuing reviews; and/or, amendment/modification reviews.
6. In consultation with the IRB Chair, prepares the IRB annual report.
7. Provides interpretation and application of federal regulations.
8. Develops, implements and interprets policies and procedures.
9. At least annually, reviews the materials sent to investigators (i.e. guidelines, forms, letters, etc.) for compliance with the Policies and Procedures and new regulatory or societal needs.
10. Oversees compliance with federal regulations, state/local laws, institutional policy, and IRB procedures.
11. Responds to regulatory agencies' audits.

IRB

1. Conducts an objective and timely review of each study presented to it by making a decision to approve, request modifications, or disapprove each study presented.
2. Uses the Operating Procedures, the criteria for review required by the FDA and HHS, as well as, the ethical principles of the Belmont Report and the World Medical Association in considering decisions.
3. Determines if expert advice, not available among members, is required.
4. Determines the date of continuing review at intervals appropriate to the degree of risk, but not to exceed an interval greater than once per year.

IRB Chair

The Chair should be a known leader and a respected member of the community. The chair need not be a physician or an active member of the staff. The person appointed as chair should have time available to carry out the duties of the chair.

Responsibilities include, but are not limited to:

1. Presides at all meetings and conducts meetings in an orderly manner.
2. Votes as an IRB member.
3. Authorizes 'Called Meetings' as needed.
4. Suspends studies when issues of non-compliance appear to place participants at risk.
5. Conducts expedited and facilitated reviews, as defined in federal regulations, and exercises all of the authority of the IRB except disapproval.
6. Designates one or more experienced reviewers, from among members of the IRB, to assist with expedited and facilitated reviews.
7. Meets and communicates with the IRB Coordinator on a regular basis to review/discuss reports, concerns, and activities; and, as necessary, to sign correspondence and reports of IRB action.

IRB Member

1. Regularly attends meetings. Should a member anticipate his/her absence, it is the member's responsibility to provide the IRB Coordinator with longest possible notice of inability to attend.
2. Using all of one's area of expertise, contributes to a thorough discussion of each agenda item.
3. Considers the approval criteria offered in the regulations and the Belmont report.
4. As designated by IRB Chair, conducts expedited and facilitated reviews, as defined in federal regulations, and exercises all of the authority of the IRB except disapproval.
5. Maintains confidentiality regarding any information contained in any review. Members of the IRB should not communicate directly (outside the meeting situation) with sponsors or investigators about IRB deliberations except with the express permission of the chair.
6. Reveals any potential conflict of interest as soon as it is recognized. No member of the IRB may participate in an initial or continuing review of any project in which the member has conflict of interest, except to provide information to the IRB. A member with a conflict of interest must abstain from participation in deliberation and voting on that protocol.

Researchers/Investigators

The Researcher/Investigator is the ultimate protector of the participant's rights and safety. The investigator's responsibility for the study may not be delegated with impunity. Although duties may be delegated, the investigator is responsible for the conduct of the study.

Researchers/Investigators, at a minimum:

1. Assume responsibility for compliance with all federal, state and institutional rules and regulations related to research involving human subjects and human subject-derived information and materials.
2. Review and are very familiar with the content of each protocol submitted to the IRB; and, instruct the study staff and sub-investigators about it.
3. When acting as Principal Investigator (PI) for a study, assure compliance with IRB requirements for attendance of IRB meeting at which the study is on the agenda for "Initial Review".
4. Clarify billing/charging components of the study with the participant in the study and with the appropriate department(s).
5. Obtain approval from other departments/committees that may be impacted/involved in a study prior to submission of a "Review Application" to the IRB Office.
6. Provide the IRB with all of the information requested on all "Review Applications" (e.g. Initial Review; Continuing Review).
7. Conduct studies in conformance with the approved protocol.
8. Provide timely information to the IRB regarding:
    a. Adverse events;

b. All changes/modifications in research activity/protocol for IRB approval prior to implementation;
c. Upon completion of a study, a final summary of the study,
d. Continuing review, and
e. Significant new information related to research activity.

9. Accept responsibility for actions of sub-investigators and staff with regard to research related activities.
10. Discuss issues of consent with the prospective participant in a manner so as to allow the person time and circumstances in which to reach as informed a position as possible.
11. Carefully weigh the welfare of individual participant's needs against the needs of the protocol and places individual participant's needs before the needs of the protocol.

IRB Composition and Membership

Selection

The membership shall be chosen for their expertise, diversity, and knowledge of institutional and community requirements and attitudes so as to promote respect for its decisions.

IRB Membership

1. The IRB will be comprised of at least seven (7) voting members.
2. Both racial and cultural diversity among members will be considered when making appointments.
3. Both men and women will be on the IRB.
4. Both scientific and non-scientific areas will be represented.
5. The IRB will include at least one member who is not otherwise affiliated with NMC.
6. Physicians will account for at least two (2) members of the IRB.

Alternate Members

At the time members for the IRB are appointed, alternate members are appointed for each type (Scientific and Non-Scientific) of IRB member. Prior to appointment, evaluations of the individual's qualifications should be comparable to that conducted for board members. The alternate member will be expected to participate in orientation activities and to be familiar with IRB policies/procedures and processes.

Ad Hoc Members

Ad hoc members are non-voting participants and are appointed as institutional representatives to "interface" with other institutional units or to provide institutional information.

Tenure

1. The term of appointment for each member will be for two fiscal years. Renewals of the two-year terms are staggered so as to give greater continuity to the IRB.
2. Members appointed to complete the term of another are appointed for the duration of that member's term. Membership may also terminate on any of the following events:
    a. Upon voluntary resignation of the member from the IRB;
    b. Upon continuing failure to be prepared for meetings;
    c. Upon failure to attend three consecutive meetings without notice to the IRB Coordinator or failure to maintain and attendance rate of 75% of scheduled meetings, and,
    d. Upon a 2/3 vote of the IRB for any reason not listed above.

Member Privacy

The names and occupations of members will be available upon request.

Meetings

1. Regular Meetings
   The IRB will meet on a monthly basis.
2. Called Meetings
   When necessary, the IRB Chair may call additional meetings. To schedule a "called meeting" a written agenda, when possible, should be provided to IRB members at least 24 hours in advance.
    a. Quorum & Voting Convened Meetings:
       A majority of members or their alternates, including at least one physician and one nonscientific member, will constitutes a quorum and will be necessary to conduct business.
    b. Approval will require a majority of the quorum. An alternate has the same voting rights and responsibility as the member being replaced. The number of votes will be recorded but names will not be used unless so requested by the member.
    c. Failure of Quorum during Meeting:
       Should the quorum fail during a meeting (i.e., those with conflicts being excused, early departures) the meeting should be terminated from further votes until the quorum can be restored.

Conflict Of Interest

Members cannot vote if they have a conflict of interest. Members are required to abstain for studies in which they have some conflict of interest. If the member is also the principal investigator, the member may contribute to the discussion but must leave once the vote has been called.

Members are deemed to have a conflict of interest if:

1. They are receiving financial backing from the same Institute of the NIH or sponsoring corporation or organization or a competing corporation, or if
2. They have a "significant" equity position in the sponsoring company or a direct competitor of that company, or if
3. They are the principal investigator or sub-investigator or are involved in the study under discussion.

Telephonic Participation

1. Whenever possible, IRB meetings should take place with all participating IRB members physically present. However, circumstances sometimes warrant conducting meetings via telephone conference call. Official Board actions may be taken at a meeting in which members participate via telephone provided that each:
    a. Has received all pertinent material prior to the meeting, and
    b. Can actively and equally participate in the discussion of all protocols
    c. Minutes of such meetings should document that these two conditions have been satisfied in addition to the usual regulatory requirements (i.e. attendance; initial and continued presence of a majority of members, etc.).

Informed Consent

Informed consent consists of both a verbal process and a document covering the main points of information necessary for consent. The IRB will look for evidence that both the process and the documentation of the process have been considered. Questions of literacy and language generally will be considered as well as privacy and timing.

Informed consent will be sought from each prospective participant or the participant's legally authorized representative. Likewise, waiver from the obligation to gain consent may be approved.

1. Interpretation - Oral

    NMC approved interpreters are available through organizational services. Approved interpreters are required for review of the informed consent document with the potential participant. Languages spoken by 5% or more of the local population will be translated.

2. Assessing Comprehension

    Though it is difficult for an IRB to assess assurances of comprehension, the researcher should provide for some means of assessing comprehension.

3. Recruitment and Advertisements

    Recruitment activities are considered to be part of the process leading to consent. The information obtained during this time is information that will be used by a subject when agreeing to participate.

All efforts to advertise a trial must have prior IRB approval. Advertisements are defined as recruitment activities designed to alert potential subjects about the existence of a study. The IRB will review those advertisements that are locally generated as well as national advertising by the research sponsor.

a. Advertisements might include:
    i. Display or classified print advertising
    ii. Videotaped "infomercials"
b. Recruitment materials for which IRB approval is not required include:
    i. Listings in databases that include only objective descriptions
    ii. Interviews on broad medical topics (investigators should make every effort to label investigational activities as investigational.)
c. The requirements for all advertising are that it be fair, unbiased and not misleading. It should never stress any inducements. While it is not a 'mini-consent" it should be a very brief introduction. No claims can be made about safety or effectiveness. A positive outcome should not be presumed.

    At a minimum an advertisement should include:

    i. A brief summary of the eligibility criteria,
    ii. A brief statement of the objective and the major procedures and, if lengthy, the time involvement, and
    iii. A method for contacting the sites.

Consent Documentation Review

1. It is recommended that the Informed Consent Document (ICD) be provided at the 5th – 7th grade reading level in at least a 12-point font size.
2. Additionally, technical and scientific terms should be adequately explained using common or lay terminology. Provisions must be made for subjects who have difficulty reading due to visual or educational impairments.
3. Informed consent will be appropriately documented, in accordance with the following options:
    a. Option One: Written Consent Form Signed by Subject or legally authorized Representative.

    The basic elements to be included in every informed consent document are:

    i. A statement that the study involves "research".
    ii. An explanation of the purpose of the research.
    iii. The expected duration of the subject's participation.
    iv. A description of the procedures to be followed, and identification of any procedures that are experimental.
    v. A description of any reasonably foreseeable risks or discomforts to the subject.

    This section will include information on physical risks and may include

information on legal, financial, social risks and risks to loss of privacy/confidentiality. Each sub-section will be identified.

vi. A description of any benefits to the subject or to others that may reasonably be expected from the research.
This section will include information on personal physical benefits and may include information on social legal, financial or social benefit.

vii. Descriptions of appropriate alternative procedures or courses of treatment, if any that might be advantageous to the subjects.

viii. Any costs to the patient or third party payers that may result from participation in the study.

ix. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
Access by the IRB, the funding agency and any sponsor must be mentioned. Harm from a breach of privacy is occasionally the only risk and, as such, this information is often found in the risk section.

x. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of or where further information may be obtained.

xi. "Minimal risk means the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests."

xii. An explanation of who to contact for answers to pertinent questions about the research and research subjects' rights, and who to contact in the event of a research related injury to the subject.
This person will be involved with the IRB rather than with any of the research bases. The consent form will not name a specific person but will give a title and phone number.

xiii. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subjects may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Additional Consent Elements, these elements are to be included only if they are pertinent to the circumstances of the protocol:

i. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently unforeseeable.

ii. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
Such circumstances can include emergence of adverse events, failure to gain FDA clearance, or failure to adhere to protocol.

iii. Any additional costs to the subject that may result from participation in the research.

iv. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

v. A statement that significant new findings developed during the course of the research which may relate to the subjects willingness to continue participation will be provided to the subject.
New findings are not likely to emerge during a 2-hour interview or a venipuncture; they are likely to emerge during a multi-year treatment.

vi. The approximate number of subjects involved in the study.

b. Option Two: Oral Presentation Using Short Form. As an alternative to standard written informed consent documents, an oral presentation of informed consent information may be used for non-English speaking participant provided:
   i. The witness/interpreter is fluent in both English and the language of the participant.
   ii. A written summary of what is presented orally (i.e. the IRB approved English language informed consent document) is prepared. At the time of consent, the person obtaining the consent and the witness/interpreter signs the summary.
   iii. A short form written consent document, stating that the elements of consent have been presented orally, is in a language understandable to the participant. At the time of consent, the participant and the witness/interpreter should sign the short form.

c. Option Three: Waiver of Documentation. The IRB may waive the requirement to obtain a signed consent form for some or all subjects if the IRB finds either:
   i. That the only record linking the participant and the research would be the ICD and the principal risk would be potential harm resulting from a breach of confidentiality; or
   ii. That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the PI to provide participants with a written statement regarding the research.

Waiver of Informed Consent

Research is considered to be a planned activity and emergency consent is not often an issue. Thus, waiver requirements are intentionally strict. Waivers are prospective for the study rather than individual to any particular subject.

The FDA and the HHS rules differ significantly. As NMC accepts the Common Rule as the minimum standard, all studies will need to meet this standard first.

1. Circumstances For Consent Waiver
   The IRB may approve a consent process that does not include some or all of the elements of informed consent or may waive the process. Generally, there are three sets of circumstances under which the regulations give the IRB authority to waive the required informed consent, provided the IRB finds and documents that the study/research meets criteria identified by regulations:
   a. Public Benefit or Service Programs Research
      The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate or otherwise examine:
      i. Public benefit or service programs,
      ii. Procedures for obtaining benefits or services under those programs,
      iii. Possible changes in or alternatives to those programs or procedures, or
      iv. Possible changes in methods or levels of payment for benefits or services under those programs, and
      v. The research could not practicably be carried out without the waiver or alteration.
   b. Waiver for Minimal Risk Studies
      i. The research involves no more than minimal risk to subjects, and
      ii. The waiver or alteration will not adversely affect the rights and welfare of the subjects, and
      iii. The research could not practicably be carried out without the waiver or alteration, and
      iv. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

      Unless all four conditions are met, informed consent shall be deemed feasible. If time permits, the investigator and an uninvolved physician must certify to the above in writing before processing. Certification must be sent to the NMC IRB within 5 working days.

Special Participant Populations

Informed consent requirements presume that the person being considered as a potential subject is autonomous: he or she has the legal capacity and emotional and mental capability to consider the proposition and is not feeling coerced or unfairly induced to agree. This is not always the case. There are many potential subjects whose ability to exercise their free will is limited in some way. Informed consent procedures used in any protocol should be sufficient to compensate for the individual's limits of understanding.

IRB members should consider whether there is any reason for the protocol to include subjects in any special subject population and, if so, if the protocol provides any special consent process.

When special populations are involved, the duty of the IRB is increased. It is suggested that provision should be made to have the informed consent process monitored either by an IRB member or by an appropriate subject advocate. It is also suggested that the IRB should consider more frequent continuing review or periodic reports.

Five subject populations have been designated by various regulators as "special subject populations" because, as a group, all members show limits to their ability to give their own consent. These populations are: pregnant women, fetuses, children, prisoners, and the mentally or emotionally disabled. Regulations have been developed for only a few of these groups. Generally, common sense and a conservative application of the usual criteria for approval will accomplish the spirit of the regulation.

The regulations often depend on a "legally authorized representative." This is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject.

Privacy Rule Authorization

A Privacy Rule Authorization is an individual's signed permission to allow a covered entity to use or disclose the individual's protected health information (PHI) that is described in the Authorization for the purpose(s) and to the recipient(s) stated in the Authorization.

In contrast, an informed consent document is an individual's agreement to participate in the research study and includes a description of the study, anticipated risks and/or benefits, and how the confidentiality of records will be protected, among other things. An Authorization can be combined with an informed consent document or other permission to participate in research. If a covered entity obtains or receives a valid Authorization for its use or disclosure of PHI for research, it may use or disclose the PHI for the research, but the use or disclosure must be consistent with the Authorization.

The Authorization must be written in plain language. A copy of the signed Authorization must be provided to the individual signing it if the covered entity itself is seeking the Authorization.

The Privacy Rule specifies core elements and required statements that must be included in an Authorization. An Authorization is not valid unless it contains all of the required elements and statements. An Authorization, must include the following core elements and required statements:

Authorization Core Elements

1. Description of PHI to be used or disclosed (identifying the information in a specific and meaningful manner).
2. The name(s) or other specific identification of person(s) or class of persons authorized to make the requested use or disclosure.
3. The name(s) or other specific identification of the person(s) or class of persons who may use the PHI or to whom the covered entity may make the requested disclosure.
4. Description of each purpose of the requested use or disclosure. Researchers should note that this element must be research study specific, not for future unspecified research.
5. Authorization expiration date or event that relates to the individual or to the purpose of the use or disclosure (the terms "end of the research study" or "none" may be used for research, including for the creation and maintenance of a research database or repository).
6. Signature of the individual and date. If the Authorization is signed by an individual's personal representative, a description of the representative's authority to act for the individual.

Authorization Required Statements

1. The individual's right to revoke his/her Authorization in writing and either (1) the exceptions to the right to revoke and a description of how the individual may revoke Authorization or (2) reference to the corresponding section(s) of the covered entity's Notice of Privacy Practices.
2. Notice of the covered entity's ability or inability to condition treatment, payment, enrollment, or eligibility for benefits on the Authorization, including research-related treatment, and, if applicable, consequences of refusing to sign the Authorization.
3. The potential for the PHI to be re-disclosed by the recipient and no longer protected by the Privacy Rule. This statement does not require an analysis of risk for re-disclosure but may be a general statement that the Privacy Rule may no longer protect health information.

A research subject may revoke his/her Authorization at any time. However, a covered entity may continue to use and disclose PHI that was obtained before the individual revoked Authorization to the extent that the entity has taken action in reliance on the Authorization. In cases where the research is conducted by the covered entity, this would permit the covered entity to continue using or disclosing the PHI as necessary to maintain the integrity of the research, as, for

example, to account for a subject's withdrawal from the research study, to conduct investigations of scientific misconduct, or to report adverse events.

Post Approval

Approval is not the end of the relationship with the IRB. The IRB presumes that the protocol is being implemented exactly as approved and without any problems. It is the investigator's responsibility to keep the IRB informed of significant problems or violations of protocol.

1. Continuing Review

The person listed as the Principal Investigator is responsible for submitting a renewal request prior to the stated expiration date. The designated investigator will be sent a courtesy renewal reminder notice approximately 60 days prior to the expiration date.

The major question asked during continuing review is whether, in light of the information gathered since the last review, the members would again conclude that approval is appropriate.

The type of information sought is:

a. A summary of the activity during the approval period
b. The status of the study
    i. Open to enrollment,
    ii. Closed to enrollment, treatment continuing, or
    iii. Follow-up monitoring only.
c. The number of participants
    i. Number enrolled,
    ii. Number still in study,
    iii. Number withdrawn,
    iv. Number lost to follow-up
d. A summary of adverse events and safety reports and whether the risk assessment has changed.
    i. Number and type of adverse events at this location.
e. Whether the expectation of benefit from the study to society or to subjects has changed.
f. Whether the alternatives to participation have changed and
g. Whether there is any new information about qualification of the investigator or the site
    i. FDA audit reports
    ii. Sponsor monitoring reports
h. Information about the consent process.
    i. The most frequent question raised

ii. The person most often giving information and gaining consent

Adverse Event Reports

Adverse Events (AEs) are new findings or unexpected problems whose nature, severity, and frequency are not described in the information provided to the IRB or to study participants. AEs may cause or increase the risk of physical or psychological harm to the research participant or others.

1. AE information is generated from two sources:

    a. Adverse Event Reports (Internal Events): Events that occur locally within studies approved by this IRB, and
    b. Safety Reports (External Events): Adverse events reported from other sites that are sent to the sponsor and are then forwarded to the NMC investigator for transmission to the IRB. Ideally the data center provides useful evaluative information.
2. A report summarizing information provided to the investigator via SRs will be submitted as a part of the materials required for continuing review. However, if at any time, prior to a study's expiration date, the study's sponsor and/or the FDA issues an "Action Letter" related to any experimental and / or investigational component of a study requiring:
    a. A change in the study's protocol and/or Informed Consent Document; and/or,
    b. Notification of the study's participants of new information or insights necessitating changes, the investigator is required to submit the SR(s) and the modification(s) to the IRB for review and approval prior to implementation.
3. Reporting Adverse Events:
    a. Unexpected AEs and SAEs must be reported in writing within five (5) working days using the AE Report Form. This form must be completed and signed by the Principal Investigator. Although an electronic submission is acceptable, a signed, hard-copy is required as follow-up to the electronic submission.
    b. AEs will be reviewed by the IRB Chair or his/her designee and will be reported to the full IRB at the next scheduled meeting via the 'Standing Report' provided at IRB Meetings.
    c. Action will be taken if the new information changes the risk/benefit evaluation or if the new information should be conveyed to currently enrolled subjects and should be included in a modified consent form. The IRB chair shall have the authority to temporarily stop the study until the IRB can be convened if there is a reasonable risk of a previously unanticipated harm to other subjects.
    d. Following review of the AE report, a copy of the report, reflecting the action(s) of the IRB, will be provided to the investigator and/or the investigator's research staff.

Reports and Records
IRB will Report to the NMC Board of Trustees

Annual Report (for activity from October, 1 to September, 30)
The IRB will issue an annual report that will summarize the activity. The minimum data reported will include:

1. Initial Reviews by Full Board
2. Approved As Submitted
3. Approved Contingent
4. Returned With Questions
5. Disapproved
6. Expedited Reviews
    a. Approved As Submitted
    b. Approved Contingent
    c. Referred For Full Board Review
    d. Facilitated Reviews
        i. Approved As Submitted
        ii. Approved Contingent
        iii. Referred For Full Board Review
    e. Contingencies Removed
    f. Continuing Review
        i. Approved As Submitted
        ii. Approved Contingent
        iii. Returned For Clarification
        iv. Disapproved
    g. Occasional Reports
        The IRB will report any problems with the current policies and procedures, forms, relationships, etc.
7. Other Reports
    a. Minutes
        The minutes will be in sufficient detail to summarize the major points of discussion and resultant actions. Every detail is not necessary if documentation is available in documentation linked to the minutes such as letters or file summaries.
    b. Drug Report
        The IRB will generate a list of investigational drugs and devices receiving IRB approval for the information of the Pharmacy and the Pharmacy & Therapeutics Committee

Records of NMC IRB

IRB records will be in the possession of and handled by NMC IRB Coordinator, an employee of NMC.

Records will include:

1. Study files including the description of the study and of the test article, correspondence, the approved consent form and proposed advertising,
2. Minutes of all meeting(s),
3. Lists of the board members, their degrees and areas of expertise and their statements about conflict of interest.
4. Organizational files including guidelines, policies and procedures, bylaws, etc.

All records will be considered confidential and will not be released except with the express permission of the subject or under court order. Inspectors from the FDA will be allowed to review and copy files.

Record Retention

All IRB records, hard copies and/or electronic copies, will be accessible to staff of the IRB Office.

Records of closed studies will be retained in hard copy for 3 years after the study has been closed to enrollment and there are no participants remaining in follow-up. After 3 years the records will be converted to electronic files for retention.