Notre Dame of Maryland University

Institutional Review Board

Policies & Procedures for
Human Subjects Research Protection

Institutional Review Board
Human Research Protection Program

Version 2.0 (2022)

1. Revision History

Prepared by Notre Dame of Maryland University Institutional Review Board (IRB)
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2. Mission

Notre Dame of Maryland University (NDMU) fosters a research environment that promotes respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of NDMU. In the review and conduct of research, actions by NDMU will be guided by the Principles set forth in the *Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (often referred to as the "*Belmont Report*"), and will be performed in accordance with the Department of Health and Human Services ("DHHS") policies and regulations at 45 CFR 46 (also known as the "Common Rule"). All of these principles stress such factors as, *inter* alia, respect for persons, beneficence and justice. The actions of NDMU will also conform to all other applicable federal, state, and local laws and regulations.

In order to effectively conduct research, NDMU maintains a Human Research Protection Program ("HRPP") which includes one Institutional Review Board ("IRB"), which not only reviews research protocols involving human subjects, but also evaluates both risk against and protection for those subjects.

The mission of the IRB is to:

- safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected
- determine and certify that all projects reviewed by the IRB conform to the policies and procedures set forth in this document, including all applicable regulations regarding the health, welfare, safety, rights, and privileges of human subjects
- provide timely and high quality education, review and monitoring of human research projects
- facilitate excellence in human subjects research

The IRB includes mechanisms to:

- establish a formal process to monitor, evaluate and continually improve the protection of human research participants
- dedicate resources sufficient to do so
- exercise oversight of research protection
- educate investigators and research staff about their ethical responsibility to protect research participants
- assist the investigators in complying with federal and state regulations.
- when appropriate, intervene in research and respond directly to concerns of research participants

2.1. Introduction

The *NDMU Policies and Procedures for Human Subjects Research Protection* details not only the policies and regulations governing research with human subjects, but also the procedures for submitting research proposals for review by the NDMU IRB. These policies and procedures apply to all research involving human subjects if NDMU faculty, staff, students, or facilities are involved, regardless of sponsorship and/or performance site, whether domestic or foreign.

NDMU is guided by the ethical principles regarding all research involving humans, as set forth in the Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research: *Ethical Principles and Guidelines for the Protection of Human Subjects of Research,*

(*National Commissions for the Protection of Human Subjects of Biomedical and Behavioral Research*, April 1979).

2.2. Ethical Principles: The Belmont Report

It is the duty of NDMU IRB to review and make decisions on all protocols for research involving human subjects. The two principal responsibilities of the IRB are (1) the protection of research subjects from undue risk and (2) the protection of research subjects from deprivation of personal rights and dignity. This protection is best assured by consideration of three principles as set forth in the Belmont Report, which are the touchstones of ethical research that:

- voluntary participation by the subjects, indicated by free and informed consent, is assured;
- an appropriate balance exists between the potential benefits of the research to the subject or to society and the risks assumed by the subject; and
- there are fair procedures and outcomes in the selection of research subjects.

These principles are referred to as Respect for Persons, Beneficence, and Justice.

Respect for Persons: Voluntary Participation and Informed Consent

One of the most important elements in any research involving human research subjects is the assurance of voluntary informed consent. Any person who is to be a research participant whether designed for his/her own direct benefit or for the advancement of scientific knowledge in general, must understand as completely as possible what the study entails and the potential risks and benefits of the study. The person must give his/her consent freely, without pressure or inappropriate inducement. The IRB at NDMU strives to ensure voluntary informed consent of research subjects through a careful review of the recruitment and consent process, and a further review of the details of the consent form and/or any other materials to be viewed by subjects.

The informed consent concept is further extended to those studies in which the subjects are not able to give personal consent for themselves. In this situation, the consent document is addressed to those who have been designated responsible for the research subject's wellbeing (e.g., parent of a child). The IRB's concern is to verify that the consent process and document are likely to assist these persons in making an informed decision as to the best interests of the research subject. The capacity for truly informed and voluntary participation in research varies widely among study populations. At one extreme there may be ample understanding and manifest freedom from coercion; at the other, there may be degrees of understanding and freedom that affect the consent of potential subjects. The IRB must exercise special care when considering subjects whose ability to give free and informed consent may be compromised in any way.

Beneficence: The Risk-Benefit Ratio

The IRB is charged with deciding, for any proposed activity that falls under its jurisdiction, whether:

> "The risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept (those) risks."
> *(Federal Register, May 30, 1974)*

The assessment of the risk/benefit relation is a complex task. There are risks of injury or discomfort to the individual that can be physical, psychological, financial, and/ or social. Conversely, there may be potential benefits to the individual, to a group to which the individual belongs, and/or to society. During the review of applications, the IRB must carefully assess the types and degrees of both risks and

benefits for a given subject population, as well as the investigator's communication of these risks and benefits to the subject in the consent process and consent form. While the IRB is not charged with reviewing scientific design per se, it must occasionally do so in order to assess the risk/benefit ratio. If a study design seems inadequate in attainment of the stated aim of the investigation, then no benefit can be anticipated from conducting the study. Thus, there would be no justification for placing any research subject at risk, however minimal. Therefore, the design of the study must be sound, and the nature and likelihood of all risks and benefits must be made clear in any application to the IRB.

Justice: The Fair Selection of Research Subjects

Both the risks and the potential benefits of research should be spread fairly among potential research subjects and research subject groups. Study design and selection of subjects should avoid bias for or against a particular group based on such factors a gender, sexual orientation, socioeconomic status, immigration status, race, or social group.

Sharing Research Risks

The guiding principle in the ethical selection of research subject groups is that any risks of the research should fall upon the groups who might benefit from the research. If the results of a risky protocol might benefit the general population, it would be unethical to focus subject recruitment on vulnerable or disadvantaged groups (e.g., institutionalized people or prisoners; patients at free clinics primarily patronized by people unable to afford other medical care) simply because this population is easily accessible or can be persuaded to participate. Further, an undue share of research risks should not burden groups already burdened by other factors. Rather, attempts should be made to include a fair sampling of the populations who might benefit from the study. When research involves persons whose autonomy is compromised, it is expected that the research bear some direct relationship to the conditions or circumstances of the research subject population. In addition, groups fully able to consider the research risks and informed consent process should be considered for selection in a study prior to involvement of the more vulnerable populations. For example, investigational drugs are typically tested in adults prior to being tested in children. Certain investigational drugs and procedures may be tested in healthy volunteers prior to being tested in patients.

Sharing Research Benefits

In recent years, increasing attention has been paid to the rights of various groups to be included in research. Through advocacy groups, many individuals have come to insist on having access to experimental treatments, as these experimental treatments may potentially provide the best medical care available. In addition, researchers, ethicists and public officials have recognized that because many clinical trials focus primarily on white middle-class research subject groups, the results of certain trials were of questionable value for members of other social, racial, sexual, and ethnic groups. As a result, both the National Institutes of Health and the FDA now require that a study design include as broad a range of research subjects as feasible, and further that the data be analyzed to uncover responses that differ between groups. For example, where women of child-bearing potential, pregnant and nursing women were previously routinely excluded from new drug trials, it is now required that, whenever possible, these women be asked to make their own choices after being fully informed of the risks of the research.

3. Definitions

Agent
Agents include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility.

Common Rule
The Common Rule refers to the "Federal Policy for the Protection of Human Subjects" adopted by several federal agencies. Although the Common Rule is codified by each agency separately, the text is identical to DHHS regulations in 45 CFR 46 Subpart A. For the purposes of this document, references to the Common Rule will cite the DHHS regulations.

Human subjects research
For the purposes of this policy "human subjects research" is defined as any activity that either

- Meets the DHHS definition of "research" and involves "human subjects" as defined by DHHS;

Research
(as defined by DHHS regulations)—a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. "Generalizable knowledge" means that (1) conclusions are drawn from particular instances and (2) the information from the investigation is to be disseminated. A "systematic investigation" is defined as a methodical planned inquiry to obtain or ascertain facts.

Activities that meet this definition of "research" may be funded or unfunded, or may be conducted as a component of another program not usually considered research. For example, demonstration and service programs may include evaluation components, which constitute research activities under this definition.

Human Subject
(as defined by DHHS regulations) a living individual about whom an investigator (whether professional or student) conducting research obtains:

- data through intervention* or interaction** with the individual, or
- identifiable*** private information

**Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.*

***Interaction includes communication or interpersonal contact between investigator and subject.*

****Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.*

Engagement
Institutions are considered "engaged" in a research project when the involvement of their employees or agents in that project includes any of the following:

- Intervention for research purposes with any human subjects of the research by performing invasive or noninvasive procedures.

- Intervention for research purposes with any human subject of the research by manipulating the environment.
- Interaction for research purposes with any human subject of the research.
- Obtaining the informed consent of human subjects for the research.
- Obtaining for research purposes identifiable private information or identifiable biological specimens from any source for the research. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to:
    - observing or recording private behavior;
    - using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; and
    - using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

Institutional Official (IO)

The IO (Vice President for Academic Affairs [VPAA) at NDMU] is responsible for ensuring that the NDMU IRB has the resources and support necessary to comply with all federal regulations and guidelines that govern human subjects research. The IO is legally authorized to represent the institution, is the signatory official for all assurances regarding the conduct of human subjects research on behalf of NDMU, and oversees all obligations of all such assurances.

IRB

An Institutional Review Board established in accord with and for the purposes expressed in this policy.

IRB Approval

The determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and legal requirements.

Minimal Risk

Risk for which the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Research under the Auspices of the Organization

Research under the auspices of the organization means research conducted at this institution, conducted by or under the direction of any employee or agent of this institution (including students) in connection with his or her institutional responsibilities, conducted by or under the direction of any employee or agent of this institution using any property or facility of this institution, or involving the use of this institution's non-public information to identify or contact human subjects. If NDMU faculty or students are conducting research at another university, NDMU's IRB must review the protocol and approval must be granted in order for the faculty member or student to participate. If the research is being conducted by a student, the faculty member responsible for supervising the research is the principal investigator of record and must sign any student protocol. The protocol must be reviewed and signed by the department chair in SASB or the dean of SON, SOE, or SOP, relative to where the faculty member's appointment resides before being submitted to the IRB.

4. Institutional Authority

The operating procedures in this document govern the conduct and review of all human research conducted under the auspices of the institution. This policy is made available to all investigators and research staff by being posted on the IRB website (http://www.ndm.edu/academics/office-of-academic-affairs/research-and-development/research-policies/institutional-review-board/).

The VPAA for NDMU designates the individual who serves as the Institutional Official ("IO") for the purpose of carrying out NDMU HRPP. Further, the VPAA identifies, as necessary, other individuals to whom responsibility is delegated for administrative oversight of the individual components of the HRPP.

The NDMU IRB, which reports to the VPAA or his/her delegate, has jurisdiction over all human subjects research conducted under the auspices of the institution.

All human subjects research at the following institutions or components are considered research activity of NDMU and are subject to these policies: The NDMU IRB may also review human subjects research at other institutions in accordance the Common Rule guidance on reviewing proposals approved by other institutional IRBs which are registered with HHS or have an assurance with HHS and are considered clinical practice sites for faculty where an agreement/contract has been approved by both NDMU and the other institutions' administration (reciprocity approval).

4.1. Assurance of Compliance

NDMU does hold a HHS assurance, and is registered with the US Department of Health and Human Services (IORG0009012, IRB00010753, and FWA 00024826). The registration and assurance can be located at: http://ohrp.cit.nih.gov/search/search.aspx?styp=bsc The IO is responsible to maintain the assurance of compliance.

4.2. Regulatory Compliance

The IRB is responsible for ensuring compliance with institutional policies and applicable law in its review and oversight of human subjects research. All human subjects research under the auspices of NDMU must be conducted in accordance with this policy, the Common Rule, 45 CFR 46 (as applicable), and applicable state and local law in the jurisdiction where the research is conducted. The IO is responsible to maintain regulatory compliance.

5. NDMU Institutional Review Board

The NDMU IRB is an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of this institution. The IO, the Chair of the IRB, and current IRB members review the activity of the IRB on at least an annual basis and make a determination as to the appropriate number of IRB members and meetings that are needed for the institution.

5.1. Authority of the IRB

NDMU IRB reviews and has the authority to approve, require modifications in, or disapprove all research activities conducted under the auspices of NDMU including faculty and students who are conducting research through NDMU or through another entity. The IRB also has the authority to suspend, place restrictions on, or terminate approvals of research activities that fall within its jurisdiction that are not being conducted in accordance with IRB requirements, or that have been associated with unexpected serious harm to subjects.

The IRB ensures that appropriate safeguards exist to protect the rights and welfare of research subjects [45 CFR 46.111]. In fulfilling these responsibilities, the IRB reviews all research documents and activities that bear directly on the rights and welfare of the subjects of proposed research. Examples of IRB review documentation include, *inter alia:* protocols, consent/assent document(s), the

investigator's brochure(s), tests, surveys, questionnaires and similar measures, and recruiting documents.

Before any human subject becomes involved in research at NDMU, an IRB will properly consider:

- risks to the subject and others
- anticipated benefits to the subject and others
- importance of the knowledge that may reasonably be expected to result from the study
- informed consent process to be employed

The IRB has the authority to suspend, place restrictions upon, or terminate approval of research activities that fall within its jurisdiction that:

- are not being conducted in accordance with IRB requirements, or
- that have been associated with serious harm to subjects

The IRB has the authority to observe (or delegate a third party to observe) the consent process and the research if the IRB deems this necessary.

5.2. Jurisdiction of the IRB

The IRB jurisdiction extends to all research (funded and unfunded) involving human subjects conducted at NDMU, as well as research conducted elsewhere by NDMU faculty, staff, and students.

If an IRB chair, member, or staff person believes the IRB to have been unduly influenced by any party, a confidential report shall be made to the Institutional Official (Vice-President of Academic Affairs) who can investigate and determine appropriate action.

5.3. IRB Relationship with Other HRPP Units

The IRB makes independent determinations regarding approval or disapproval of a protocol based upon whether or not human subjects are adequately protected. The IRB retains review jurisdiction over all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency that adopted the human subjects' regulations.

Research previously reviewed and approved by the IRB may be subject to review and disapproval by officials of the institution. However, officials of the institution have no authority to approve research previously disapproved by the IRB.

5.4. Relationships with Other Institutions

All NDMU faculty members and students must submit a proposal to the NDMU IRB for any research for which they plan to participate, including participation in research at other institutions or external sites. NDMU may choose, on a case-by-case basis, to cede or share its IRB oversight responsibilities to an external IRB. A formal relationship between NDMU and the external IRB must be established through a written agreement. When NDMU relies on another IRB, the IRB Chair will review the policies and procedures of the IRB to ensure that they meet NDMU standards. If the other IRB is accredited by The Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP), then it will be assumed that the NDMU standards are being met provided all local context and institutional requirements are considered. The NDMU faculty member would need to provide documentation to the NDMU IRB of approval of the study from the external IRB.

In the conduct of cooperative research projects, NDMU acknowledges that each institution is responsible for safeguarding the rights and welfare of human subjects, and further for ensuring

compliance with the applicable federal regulations. When a cooperative agreement exists, NDMU may enter into a joint review arrangement, rely on the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

When an investigator plans to conduct research at sites external to the NDMU and the site's IRB plans to defer review to the NDMU IRB, arrangements must be made for the NDMU IRB to be the IRB of record for the project and arrangements must be made for communication between the IRB and the site.

When NDMU is the coordinating center for a multi-center protocol, the IRB will require that NDMU ensure that IRB approval has been obtained at each participating site prior to initiation of the research at that site. At the time of initial review, the IRB will assess the procedures for dissemination of protocol information to all participating sites. Assessment of protocol information includes, *inter alia*, unanticipated problems involving risks to participants, protocol modifications and interim findings.

5.5. Roles and Responsibilities

Institutional Official

The ultimate responsibility of the IRB resides with the Institutional Official (IO). The IO is responsible for ensuring the IRB has the resources and support necessary to comply with all institutional policies and with regulations and guidelines that govern human subjects research. The IO signs all assurances regarding human subjects research to governmental oversight agencies.

The IO also holds ultimate responsibility for oversight over the:

- Institutional Review Board (IRB);
- Conduct of research conducted by all IRB investigators;
- Compliance with all assurances and regulations and maintaining current registrations, such as with Office of Human Research Protections

Institutional Review Board (IRB)

The IRB currently has five Board members appointed by the Institutional Official (IO). These Board members prospectively review and make decisions concerning all human subjects research conducted at NDMU facilities by its employees or agents, or under its auspices. The IRB is responsible for the protection of rights and welfare of human research subjects under the auspices of the organization. It discharges this duty by complying with all applicable requirements of law, the Federal Wide Assurance (FWA) and institutional policies.

Office of Legal Counsel

The IRB relies on the counsel of the NDMU legal team for the interpretation of applicable law in the jurisdiction(s) where the research is conducted. When there are any conflicts between legal requirements, the Office of Legal Counsel will determine the appropriate resolution.

Chairpersons of the IRB

The VPAA is responsible for appointing a Chair for the IRB for a specified term. All other IRB members are appointed by the VPAA for renewable three-year terms. Any change in appointment, including reappointment or removal, requires written notification.

The IRB Chair should be a highly respected individual who is an accomplished researcher, fully capable of managing the IRB given previous research experience, and the matters brought before it

with fairness and impartiality. Moreover, the IRB Chair must endeavor to be immune to pressure from the institution's administration and as such should be a tenured member of the faculty, the investigators whose protocols are brought before him/ her, and other professional and nonprofessional sources. The IRB Chair is responsible for conducting convened IRB meetings. The IRB Chair may designate other IRB members to perform duties, as appropriate, for review, signature authority, and other functions of the IRB Chair. The IRB Chair will advise the IO about IRB member performance and competence.

The Chair of the IRB reports to the VPAA or his/her delegate, and is responsible for:

- developing, managing and evaluating policies and procedures that ensure compliance with all regulations governing human subjects research. This includes monitoring changes in regulations and policies that relate to human research protection and overseeing all aspects of the IRB program
- advising the IO on matters regarding research at IRB
- implementing the institution's IRB policy
- assuring the IRB members are appropriately knowledgeable to review research in accordance with ethical standards and applicable regulations
- assuring that all investigators are appropriately knowledgeable to conduct research in accordance with ethical standards and applicable regulations
- the development and implementation of an educational plan for IRB members, staff and investigators
- submitting, implementing and maintaining an approved IRB registration of FWA with HHS through the IO to the Department of Health and Human Services Office of Human Research Protection (OHRP)
- assisting investigators in their efforts to carry out NDMU research mission.
- developing and implementing needed improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the research program
- developing training requirements as required and as appropriate for investigators, subcommittee members and research staff, and ensuring that training is completed on a timely basis
- serving as the primary contact at IRB for the Office for Human Research Protections (OHRP) of the U.S. Department of Health and Human Services and other federal regulatory agencies
- day-to-day responsibility for the operation of the IRB office
- responding to faculty, student and staff questions
- working closely with the IRB members on the development of policy and procedures, as well as organizing and documenting the review process

The IRB Chair is a voting member of the IRB.

Vice Chairs of the IRB

A Vice Chair serves as the Chair of the IRB in the absence of the Chair, and maintains the same qualifications, authority, and duties as the IRB Chair in the IRB Chair's absence. The Vice-Chair of the IRB is appointed by the IO while considering recommendations from the IRB Chair and nominations from IRB members.

Subcommittees of the IRB

The IRB Chairs, in coordination with the IO may establish subcommittees consisting of one or more IRB members.

Duties of a subcommittee may include the following:

- Serve as designees by an IRB Chair for the expedited review of new or continuing protocols, and/ or modifications of continuing protocols. The subcommittee must be experienced (in terms of seniority on the IRB), and must be matched as closely as possible with their field of expertise to the study.
- Review and approve revisions of protocols previously given provisional approval ("Conditional Approval") by the convened IRB.
- Conduct an inquiry into allegations of non-compliance. The subcommittee is given a charge by the IRB, which can include any or all of the following:

- review of protocol(s) in question
- review of any relevant documentation, including, *inter alia*, consent documents, case report forms, and a subject's investigational and/ or medical files, as the documentation relates to the investigator's execution of her/ his study involving human subjects
- interview of appropriate personnel if necessary
- preparation of either a written or oral report of the findings, which is presented to the full IRB at its next meeting
- recommend actions if appropriate

- Determination of the review interval and the need for additional supervision and/ or participation is made by the IRB on a protocol-by-protocol basis. For example, an on-site review by an IRB subcommittee might occur in a particularly risky research study, or approval might be subject to an audit of study performance where an investigator recently had a protocol suspended by the IRB due to regulatory concerns.

The Principal Investigator

The Principal Investigator is the ultimate protector of the human subjects who participate in research, and is ultimately responsible for all research conducted under his/her oversight. The Principal Investigator is expected to abide by the highest ethical standards and for developing a protocol that incorporates the principles of the Belmont Report. He/she/they is/are expected to conduct research in accordance with the approved research protocol and to oversee all aspects of the research by providing appropriate training and supervision of study staff, including but not limited to oversight of the informed consent process.

All subjects must give informed consent and the Principal Investigator must establish and maintain an open line of communication with all research subjects within his/her responsibility. In addition to complying with all the policies and standards of the governing regulatory bodies, the Principal Investigator must comply with institutional and administrative requirements, including but not limited to that of the IRB, for conducting research. The Principal Investigator is responsible for ensuring that all research staff completes appropriate training and must obtain all required approvals prior to initiating research.

The Principal Investigator must be qualified, licensed and credentialed for all aspects of the research under his oversight, or otherwise delegate such responsibilities to a member of the study team with the requisite qualifications, licenses or credentials. A faculty member needs to be the co-principal investigator for any student research projects, including master’s theses and doctoral dissertations. The faculty member bears full responsibility for the conduct of research by students and the management of data.

Department Chairs and Deans

Department chairs or Deans are responsible for ensuring that the Principal Investigator (PI) is qualified by training and experience to conduct the proposed research. In addition, department chairs or Deans are responsible for ensuring that the Principal Investigator has sufficient resources and facilities to conduct the proposed research. For each protocol submitted to the IRB for approval, the department chair or Dean must certify that s/he accepts responsibility for assuring adherence to the federal and state regulations and institutional policies governing the protection of human subjects of research, including applicable institutional credentialing requirements.

Department chairs or Deans are required to review all proposals before they are submitted to the IRB for review. The signatures of the Department chair or Dean indicate that the study is found to be scientifically sound, can reasonably be expected to answer the proposed question, and that the department will commit resources required to conduct the research in a way that will protect the right and welfare of participants. Such resources include but are not necessarily limited to personnel, space, equipment and time.

Institutional Biosafety Committee (IBC)

All research that involves rDNA molecules must be in compliance with the NIH Guidelines for Research Involving rDNA Molecules (NIH Guidelines). The NIH Guidelines set forth principles and standards for safe and ethical conduct of recombinant DNA research and apply to both basic and clinical research studies.

The Institutional NDMU Biosafety Committee (IBC) is responsible for approving risk assessment and the biosafety containment levels for such experiments.

Resources for the IRB

The VPAA is responsible for providing resources to the IRB including adequate meeting and office space, administrative support and staff for conducting IRB business. Office equipment and supplies, including technical support, file cabinets, computers, printer, internet access, and copy machines (etc.) will be made available to the IRB. On an annual basis, the IRB Chair will review the activity, workload and resources of the IRB and will make a recommendation about resources to the VPAA.

5.6. Conduct of Quality Assurance/Quality Improvement Activities for IRB Operations

The IRB may conduct investigations and audits of ongoing research in the following instances: (1) when the IRB directs an audit be conducted, and/or (2) when a complaint or allegation of non-compliance is received. (3) “not for cause” audits of research.

6. IRB Membership

The IRB Chair, in coordination with the IO, will identify potential candidates in consideration of IRB membership. Department Chairs and/or Deans may also be requested to identify potential candidates for appointment to the IRB board. On an ongoing basis, the IRB Chair will monitor the membership and composition of the IRB and make recommendations on the appointment of members to the IO in order to meet regulatory and organizational requirements.

Appointments are made by the IO for terms between one and three years. There needs to be an appropriate representation on the board.

IRB members are selected based on appropriate diversity, including consideration of race, gender, cultural backgrounds, specific community concerns in addition to representation by multiple, diverse professions, knowledge and experience with vulnerable subjects, and inclusion of both scientific and non-scientific members. Every effort is made to have member representation with an understanding of the areas of specialty that encompasses most of the research performed at the IRB. The IRB has procedures that specifically outline the requirements of protocol review by individuals with appropriate scientific or scholarly expertise. In addition, the IRB will include members who are knowledgeable about and experienced working with vulnerable populations that typically participate in IRB research when applicable.

The IRB must promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects; and possess the professional competence necessary to review specific research activities. A member of the IRB may fill multiple membership position requirements for the IRB.

6.1. Composition of the IRB

The IRB will always consist of at least five members with its guiding principal to promote complete and adequate review of research activities commonly conducted by the institution.

The IRB will be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

In addition to possessing the professional competence necessary to review specific research activities, the IRB will be able to ascertain the acceptability of proposed research in terms of institutional policies and regulations, applicable law, and standards of professional conduct and practice. The IRB will therefore include persons knowledgeable in these areas.

When protocols involve vulnerable populations, the review process will include one or more individuals who are knowledgeable about or experienced in working with these participants, either as members of the IRB or as consultants. Prior to the meeting, the IRB Chair shall review the agenda to ensure that the membership present for the meeting has the appropriate expertise and experience with any vulnerable populations that are included in the protocols being reviewed.

Every nondiscriminatory effort will be made to ensure that the IRB does not consist entirely of men or entirely of women, including the institution's consideration of qualified persons of both gender, so long as no selection is made to the IRB based on gender. The IRB shall not consist entirely or mostly of members of one profession.

The IRB includes at least one member whose principal concerns are in scientific areas and at least one member whose Principal concerns are in nonscientific areas.

The IRB includes at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

One member may satisfy more than one membership category.

IRB members are appointed for renewable one to three year terms. On an ongoing basis, the IRB Chair will monitor the membership and composition of the IRB and make recommendations on the appointment of members to the IO in order to meet regulatory and organizational requirements.

Officers or members of various committees/boards such as biosafety, IACUC or future offices/committees which may be created such as an Office of Sponsored Programs, Office of Development or Office of Technology Transfer are prohibited from serving as members of the IRB. Individuals from these offices may provide information to the IRB and attend IRB meetings as guests.

6.2. Appointment of Members to the IRB

The IRB Chair identifies a need for a new or replacement member, or alternate member. The IRB membership may nominate candidates and forward the names of the nominees to the IO. Department Chairs, Deans, and others may forward nominations to the IO and the IRB Chair.

For faculty membership appointments, the IO will contact the nominee. If there are no nominees, the appropriate Department Chairs or Program Directors will be contacted in writing by the IO or the IRB Chair concerning the vacancies and solicit nominees from the Department Chairs or Deans.

The final decision in selecting a new member is made by the IO who may consult the IRB Chair.

Appointments are made for renewable one to three-year periods of service. Any change in appointment, including reappointment or removal, requires notification. Members may resign by written notification to the Chair and/ or the IO.

On a periodic basis, the IRB Chair and the IO will review the membership and composition of the IRB to determine whether the IRB continues to meet regulatory and institutional requirements. Required changes in IRB membership will be reported to the OHRP.

Resignation and Termination of IRB Members

Resignation of IRB membership status, based on the wishes of the IRB member, will be submitted, in writing, to the Institutional Official and copied to the IRB Chair and, where applicable, the member's department chair or center/institute director. IRB Membership status may be terminated by the IRB Chair due to failure to attend and/or otherwise actively participate in IRB functions. Termination of any individual from IRB membership will be reported to the Institutional Official to include a written justification for the termination. Affiliated and unaffiliated IRB Committee members do not receive any direct monetary compensation for participation on the board.

6.3. Alternate Members

The appointment and function of alternate members is the same as that for Principal IRB members, and the alternate's expertise and perspective are comparable to those of the Principal member. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting. When an alternate member substitutes for a Principal member, the alternate member will receive and review the same materials prior to the IRB meeting that the Principal member received or would have received.

The IRB roster identifies the Principal member(s) for whom each alternate member may substitute. The alternate member will not be counted as a voting member unless the Principal member is absent. The IRB minutes will document when an alternate member replaces a Principal member.

6.4. Use of Consultants (Outside Reviewers)

When necessary, the IRB Chair may solicit individuals from other Universities and/or the community with competence in specialized areas to assist in the review of issues or protocols requiring scientific or scholarly expertise beyond, or in addition to, that available on the IRB. The need for an outside reviewer is determined in advance of the IRB meeting by the IRB Chair or may be recommended by the primary reviewer. The IRB Chair will ensure that all relevant materials are provided to the outside reviewer prior to the convened meeting.

Written statements of outside reviewers will be kept in IRB records and filed with the relevant protocol. Key information provided by outside reviewers at convened meetings will be documented in the meeting minutes.

The IRB Chair reviews the conflict of interest policy for IRB members with consultant(s). The consultant(s) must verbally or in writing confirm to the IRB Chair that no conflicts of interest exist prior to review. Individuals who have a conflicting interest or whose spouse or family members have a conflicting interest with the sponsor of the research will not be invited to provide consultation.

The consultant's findings will be presented to the full board for consideration either in person, via telephone or in writing. If in attendance, these individuals will provide consultation but may not participate in or observe the vote.

Ad hoc or informal consultations requested by individual members (rather than the full board) will be requested in a manner that protects the researcher's confidentiality and complies with the IRB conflict of interest policy (unless the question raised is generic enough to protect the identity of the particular Principal Investigator and research protocol).

6.5. Duties of IRB Members

The agenda, submission materials, protocols, proposed informed consent forms and other appropriate documents are distributed to members prior to the convened meetings at which the research is scheduled to be discussed. Members review the materials at least one week prior to the convened meeting to ensure full participation in the review of each proposed project. IRB members will treat the research proposals, protocols, and supporting data confidentially. All copies of the protocols and supporting data are returned to the IRB staff after the review for professional document destruction.

6.6. Attendance Requirements

Members must attend all IRB scheduled meetings, and should attend all meetings for which they are scheduled to participate. If a member is unable to attend a scheduled meeting, that member should inform the IRB Chair. If the inability to attend will be prolonged, a request for an alternate to be assigned may be submitted to the IRB Chair. If an IRB member is to be absent for an extended period, such as for a sabbatical, he or she must notify the IRB at least 30 days in advance so that an appropriate replacement can be obtained. The replacement can be temporary, for the period of absence, or permanent if the member is not returning to the IRB. If the member has a designated alternate, the alternate can serve during the Principal member's absence, when the IRB receives advance notice.

6.7. Training / Ongoing Education of Chair and IRB Members in Regulations, Procedures

A vital component of a comprehensive human research protection program is an education program for the IRB Chair and the IRB members. NDMU is committed to providing training and an on-going educational process for IRB members and the staff of the IRB Office, related to ethical concerns and regulatory and institutional requirements for the protection of human subjects. All IRB members are required to complete the CITI training module titled "IRB Member (ID: 10022)" which is located at http://www.CITIProgram.org. IRB members are required to retake the module every 5-years in accordance with the CITI training requirements at NDMU. IRB members who have successfully completed other CITI courses in the past 5-years but have not completed the specific module for IRB members listed above, will be required to complete the IRB Member (ID: 10022) course within 30 days of being on the IRB. Members of the IRB who have completed their term or have stepped down from the IRB for any reason and who have completed the IRB Member course (ID:10022) within the past 5-years, will be required to complete appropriate module for Health Information Privacy and Security (ID: 10046, 10047, 10048, 10048, 10049, or 10050) in addition to one or more of the following modules: Biomedical Research (ID: 10023), Social/Behavioral Research Course (ID: 10024), and Research with data or laboratory specimens- ONLY (ID: 10026) if the individual is considering initiating research following IRB appointment. All investigators applying to IRB approval for any proposed research studies need to complete CITI training, including students and faculty advisors of research.

Orientation

New IRB members, including alternate members, will meet with an IRB Chair for an informal orientation session. After the initial session, all new IRB members will meet with the full IRB committee. At this session, the new members will be given an IRB Handbook that includes:

- Common Rule (45 CFR 46)
- IRB Policies and Procedures
- Guidance on Reviewing Protocols
- IRB Member Directory
- Access to the on-line IRB Folder
- IRB Review forms (hard copy or digital copy)

New members are required to complete the Initial Education requirement (discussed in the next section) prior to serving as Primary Reviewer.

Initial Education

IRB members will complete the following web based training:

- CITI Training Course for IRB Members (ID: 10022) or IRB Member Refresher (49578) if IRB Member module (ID: 10022) has been previously completed while employed by NDMU
- CITI Good Clinical Practice Course (ID: 10031)
- CITI Health Information Privacy and Security (HIPS) for Clinical Investigators (ID: 10046)
- One of the following courses based on area of expertise: Biomedical Research (ID: 10023), Social/Behavioral Research Course (ID: 10024), Research with data or laboratory specimens- ONLY (ID: 10026).

To ensure that oversight of human research is ethically grounded and that the decisions made by the IRB are consistent with current regulatory and policy requirements, training is continuous for IRB members throughout their service on the IRB. Educational activities include, but are not limited to:

- in-service training at IRB meetings
- bi-annual training workshops
- review of appropriate publications
- identification and dissemination by the IRB Director of new information that might affect the human research protection program, including emerging laws, regulations, policies, procedures, and ethical and scientific issues to IRB members via email, mail, or during IRB meetings
- unlimited access to the IRB Office resource library

6.8. Liability Coverage for IRB Members

The NDMU insurance coverage applies to employees, any person authorized to act on behalf of the NDMU IRB, and any person who acts within the scope of their employment or authorized activity.

6.9. Review of IRB Member Performance

IRB Members' performance will be reviewed on an annual basis by the IRB Chair and IO. Formal feedback based upon this evaluation will be provided to IRB members in writing with an opportunity to discuss in person. Members who are not acting in accordance with the IRB mission or policies and procedures, or IRB members who have an undue number of absences, will be removed.

6.10. Reporting and Investigation of Allegations of Undue Influence

If an IRB chair, member, or staff person feels that the IRB has been unduly influenced by any party, they shall make a confidential report to the Institutional Official (IO), depending on the circumstances. The official receiving the report will conduct a thorough investigation and corrective action will be taken to prevent additional occurrences.

7. IRB Records

The IRB must prepare and maintain adequate documentation of the IRB's activities including: copies of all items reviewed, including, but not limited to research proposals; investigators' brochures and recruitment materials; scientific evaluations (if any) that accompany the proposals; approved consent documents including DHHS-approved sample consent documents, if any; DHHS-approved protocols, if any; HIPAA Authorization documents, if separate from the informed sample consent documents; any proposed amendments and the IRB action on each amendment; reports of injuries to subjects and serious and unexpected adverse events; documentation of protocol violations, and documentation of non-compliance with applicable regulations.

IRB records must also include continuing review activities and copies of all correspondence between the IRB and investigators. Statements of significant new findings provided to subjects must be maintained with the related research proposal and, when reviewed at an IRB meeting, such statements must be documented in the minutes.

Documentation of verified exemptions consists of the reviewer's written concurrence that the activity described in the investigator's request satisfies the conditions of the cited exemption category.

IRB records for initial and continuing review by the expedited procedure must include: the specific permissible category; a description of action taken by the reviewer, and any determinations required by the regulations and protocol-specific findings supporting those determinations.

IRB records must document any determinations required by the regulations and protocol-specific findings supporting those determinations.

All records must be accessible for inspection and copying by authorized representatives of the FDA, OHRP, sponsors, and other authorized entities at reasonable times and in a reasonable manner.

All IRB records and documents will be kept for 5 years or the length of the approved study whichever is longer as per the Common Rule (45 CFR 46.115(b))

7.1. IRB Records

IRB records include, but are not limited to:

- Written operating procedures
- IRB membership rosters
- Training records (the IRB Education Coordinator maintains accurate records listing research investigators, IRB members, and IRB staff that have fulfilled the facility's human subject training requirements. Electronic copies of documentation are maintained in the official IRB records located in the IRB Office.)
- IRB correspondence (other than protocol related)
- IRB Study Files
- Documentation of Emergency Exemption from Prospective IRB Approval. (21 CFR 56.104(c))

- Documentation of Exceptions from Informed Consent Requirements for Emergency Use of a Test Article ((21 CFR 50.23)
- Documentation of exemptions
- Documentation of convened IRB meetings minutes
- Documentation of review by another institution's IRB when appropriate
- Documentation of cooperative review agreements, e.g. Memoranda of Understanding (MOUs)
- Federal Wide Assurances
- Protocol violations submitted to the IRB
- Quality assurance reviews

Documentation for off-site IRBs include:

- On-line access to all applicable protocol documents
- MOU/Agreements of IRB Services
- Workflow/SOPs
- Notes/documents pertaining to administrative reviews

7.2. IRB Study Files

The IRB will maintain a separate IRB study file for each research application (protocol) that it receives for review. Protocols will be assigned a unique identification number by the IRB Chair, and entered into the IRB tracking system. Tracking Numbers will be in the following format based on date the proposal is received by the IRB Chair: letter for school/department followed by 2-digits for the year, 2 digits for the month, 2 digits for the day, 2 digits based on order it was received starting with 01 up to 99, followed by review type (01 for full review, 02 for expedited, and 03 for exempt) then the initial of the last name of the primary investigator. An example of a protocol number in which the protocol was received by the chair on September 15th, 2016 from the education department (Dr. Smith) and is determined to qualify for an expedited review would be as follows: E1609150102S.

Accurate records are maintained of all communications to and from the IRB. Copies are filed in the Principal Investigator's project file. The IRB maintains a separate file for each research protocol that includes, but is not limited to:

- Protocol and all other documents submitted as part of a new protocol application
- Protocol and all other documents submitted as part of a request for continuing review/termination of research application. This also includes progress reports, statements of significant new findings provided to participants, reports of injuries to patients
- Documents submitted and reviewed after the study has been approved, including reports of modifications to research/amendments and adverse event reports
- Copy of IRB-approved Consent Form
- IRB reviewer forms (when expedited review procedures are used) and scientific reviewer forms (where applicable)
- Documentation of type of IRB review
- For expedited review, documentation of any determinations required by the regulations and protocol-specific findings supporting those determinations, including:
    - waiver or alteration of the consent process
    - research involving pregnant women, fetuses, and neonates
    - research involving prisoners
    - research involving children
    - research involving persons with impaired cognitive function
- Documentation of all IRB review actions
- Notification of expiration of IRB approval to the Principal Investigator and instructions for submitting relevant continuing review materials
- Notification of suspension of research

- Correspondence pertaining to appeals
- Copies of approval letters and forms that describe what Principal Investigator must have before beginning the study
- IRB correspondence to and from research investigators
- All other IRB correspondence related to the research
- For devices, a report of prior investigations
- Reports of unanticipated problems involving risk to subjects or others and adverse events.

7.3. Minutes of an IRB Meeting

Proceedings must be written and available for review by the next regularly scheduled IRB meeting date. After ratification of the minutes by the Board members, if it is determined that revisions/corrections are necessary, the Minutes will be amended and presented at the following IRB meeting.

Minutes of IRB meetings must contain sufficient detail to show:

- The basis for requiring changes in research
- The basis for disapproving research
- Justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document
- The presence of a quorum throughout the meeting, including the presence of one member whose primary concern is in a non-scientific area
- Attendance at the meetings, including documentation of those members or alternate members who are participating through videoconference or teleconference, including documentation that those attending through videoconferencing or teleconferencing received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions
- Alternate members attending the meeting and for whom they are substituting
- Names of consultants present
- Name of investigators present
- Names of guests present
- The initial attendance list shall include those members present at the beginning of the meeting. The minutes will indicate, by name, those members who enter or leave the meeting. The vote on each action will reflect those members present for the vote on that item
- Business items discussed
- Continuing education
- Actions taken by the IRB including those involving full review. The IRB must use the minutes to notify IRB members of actions taken through expedited review and those studies that have been determined to be exempt from IRB review
- Separate deliberations, actions, and votes for each protocol undergoing initial review, continuing review, or review of modifications by the convened IRB
- Documentation that the research meets each of the required criteria [45 CFR 46.116(d)] along with protocol-specific information containing justification as to why the IRB considers the research to meet each criterion when approving a consent procedure that does not include or that alters some or all of the required elements of informed consent, or when waiving the requirement to obtain informed consent
- Documentation that the research meets each of the required criteria [45 CFR 46.117(c)] along with protocol-specific information justifying why the IRB considers the research to meet each criterion when the requirements for written documentation of consent are waived
- When approving research that involves populations covered by Subparts B, C, or D of 45 CFR 46, the minutes will document the IRB's protocol-specific justifications and findings regarding the determinations stated in the Subparts or the IRB's agreement with the findings and justifications as presented by the investigator on IRB forms
- The vote on actions, including the number of members voting for, against, and abstaining. Number of those excused, Number of those recused
- Notations indicating an IRB member's conflicting interest with the research under review

and further that the conflicted IRB member was not present during the deliberations or voting on the proposal (and that the quorum was maintained)
- A written summary of the discussion of controversial issues and their resolution
- Review of additional safeguards to protect vulnerable populations if entered as study subjects when this is not otherwise documented in IRB records
- For initial and continuing review, the frequency of continuing review of each proposal, as determined by the IRB, including identification of research that warrants review more often than annually and the basis for that determination
- Risk level of initial and continuing approved protocols
- Review of interim reports, e.g. unanticipated problems or safety reports; amendments; report of violation/deviations; serious or continuing non-compliance; suspensions/terminations, etc.
- Review of Plans for Data and Safety Monitoring
- Documentation, as required by 45 CFR 164(i)(2), indicating the approval of a waiver or alteration of the HIPAA Authorization
- Relevant information provided by consultants will be documented in the minutes or in a report provided by the consultant
- The rationale for significant risk/non-significant risk device determinations
- Determinations of conflict of interest management plans and that the IRB found it acceptable.
- Identification of any research for which there is need for verification from sources other than the investigator that no material changes are made in the research
- A list of research approved since the last meeting utilizing expedited review procedures

7.4. Membership Rosters

A membership list of IRB members must be maintained and must identify members sufficiently to describe each member's chief anticipated contributions to IRB deliberations. The list must contain the following information about members (IRB Membership Roster)

- Name
- Earned degrees
- Affiliated or non-affiliated status (neither the member him/ herself nor an immediate family member of the member may be affiliated with NDMU)
- Status as scientist (biomedical scientist, behavioral health scientist, other scientist, non-scientist). For purposes of this roster, IRB members with research experience are designated as scientists. Research experience includes training in research (e.g., doctoral degrees with a research-based thesis) and previous or current conduct of research.
- Indications of experience, such as board certifications or licenses sufficient to describe each member's chief anticipated contributions to IRB deliberations
- Representative capacities of each IRB member; including naming the IRB members knowledgeable about or experienced in working with children, pregnant women, cognitively impaired individuals, and other vulnerable populations locally involved in research
- Role within the IRB (Chair, Co-Chair, etc.)
- Voting status (Any *ex officio* members are non-voting members)
- Alternate status, including the name of the member he/ she alternates with
- Relationship (e.g., employment) between the individual IRB member and the organization

The IRB Office must keep the IRB membership list current. The IRB Chair must promptly report changes in IRB membership to the Office for Human Research Protections, DHHS.

7.5. Documentation of Exemptions

Documentation of verified exemptions consists of the reviewer’s citation of a specific exemption category and written concurrence that the activity described in the investigator’s request for satisfies the

conditions of the cited exemption category. The exempt determination is reported at the next convened IRB meeting and documented in the Minutes.

7.6. Documentation of Expedited Reviews

IRB records for initial and continuing review by the expedited procedure must include: the specific permissible category; that the activity described by the investigator satisfies all of the criteria for approval under expedited review; the approval period and any determinations required by the regulations including protocol-specific findings supporting those determinations.

7.7. Access to IRB Records

The IRB has policies and procedures to protect the confidentiality of research information:

- Physical IRB records are kept secure in locked filing cabinets, locked storage rooms.
- Digital IRB records are maintained on password-protected, secure hardware.
- Ordinarily, access to IRB records is limited to the IRB Chair, IRB members, authorized institutional officials, and officials of federal and state regulatory agencies (OHRP, FDA, etc.). Research investigators are provided reasonable access to files related to their research. Appropriate accreditation bodies are provided access and may recommend additional procedures for maintaining security of IRB records. All other access to IRB records is limited to those who have legitimate need for them, as determined by the IO and Director.
- Records are accessible for inspection and copying by authorized representatives of regulatory agencies during regular business hours.
- Records may not be removed from the IRB Chair's office or a secure location where records are kept (given the approval of the OI); however, the IRB staff will provide copies of records for authorized personnel if requested.
- All other access to IRB study files is prohibited.

7.8. Records Retention Requirements

"Retention" refers to the storage of records of inactive/closed/terminated/exempt/not-human-subjects-research studies and past board meeting minutes.

IRB records are stored as described above.

Records pertaining to conducted research must be retained for at least three years after completion of the research. IRB records not associated with research or for protocols cancelled without participant enrollment will be retained at the facility for at least three years after closure.

Physical records associated with closed or terminated studies shall, after the five year retention period expires, be electronically scanned and thereafter shredded or otherwise destroyed in accordance with institutional policy.

Electronic records must be retained for at least 3 years on the IRB's current production systems.

7.9. Written Policies and Procedures

This document details the policies and regulations governing research with human subjects, and further set forth the requirements for submitting research proposals for review by the NDMU IRB.

These *Policies and Procedures* are frequently updated. The IRB Chair will keep the NDMU research community apprised of any new information that may affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues. Such notification may be given via electronic mail, displayed on the IRB's website and via the OSR's web-

based newsletter. The policies and procedures will be available on the NDMU IRB website and will be available for download.

8. IRB Review Process

These procedures and guidelines apply to all research involving human subjects, regardless of sponsorship and performance site, conducted under the auspices of NDMU.

8.1. Human Subjects Research Determination

The responsibility for the initial determination as to whether an activity constitutes human subjects research rests with the investigator. The investigator should make this determination based on the definitions of "human subjects research".

Investigators will be held responsible by NDMU to make the proper human subjects research determination. As such, investigators are urged to request a confirmation that an activity does not constitute human subjects research from the IRB Office. The request may be made verbally, by telephone, via electronic mail or through a formal written communication. All requests must include sufficient documentation of the research activity to support the determination.

Within the IRB, determination of human subjects research may be made by experienced members of the member of the IRB. Determinations will analyze whether the activity meets the definitions of "research" and involves "human subjects," The IRB staff will respond to investigators' formal requests for determination of human subjects research status in writing. A copy of the submitted materials and determination correspondence will be kept on file along with other IRB documentation.

8.2. Exempt Research

All research using human subjects must be approved by the IRB. However, certain categories of research (i.e., "exempt research") do not require review and approval by the convened IRB. While Exempt research is subject to institutional review, it is reviewed, determined and approved by an IRB Chair, or designee of the Chair.

Reviewers will use the *Checklist for Exempt Determination* to determine and document whether or not the protocol meets the exemption criteria.

An exemption from IRB review does not equate to an exemption from the HIPAA requirement for authorization or waiver of authorization when the research involves a covered entity's protected health information. Researchers who receive an exemption determination but whose research involves protected health information must still (1) submit a HIPAA authorization form (or a request for waiver of HIPAA authorization), or (2) if applicable, submit a HIPAA form for conducting research involving decedents' information or research using a limited data set. Researchers who wish to review protected health information (e.g., medical records) to prepare a research protocol must submit the appropriate HIPAA form for IRB approval.

Limitations on Research Subjects; Vulnerable Populations

Children

Exemption for research involving survey or interview procedures or observations of public behavior does NOT apply, except for research involving observations of public behavior when the investigator does not participate in the activities being observed (see: Child).

Prisoners
Exemptions do NOT apply; IRB review is required.

Categories of Research Permissible for Exemption

The categories of research permissible for Exemption are described on the IRB Application for Exemption. The IRB Office staff and IRB members are required to use the *Checklist for Exemption Determination* to make a determination.

Only the IRB may deem a research project to be exempt from IRB review. Research activities not regulated by the FDA in which the only involvement of human subjects will be in one or more of the following categories are exempt from federal regulations, but require IRB review*:*

1. Research conducted in established or commonly accepted educational settings, involving normal educational 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 educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
    - information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects, or
    - any disclosure of the human subjects' responses outside of the research setting could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement),survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2), if:
    - the human subjects are elected or appointed public officials or candidates for public office
    - Federal statute(s) require(s) that, without exception, the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter
4. Research involving the collection or study of existing (reviewed materials existing at the time the research is proposed) data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
5. Research and demonstration projects which are conducted by, or subject to, the approval of Federal Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:
    - public benefit or service programs;
    - procedures for obtaining benefits or services under those programs;
    - possible changes in or alternatives to programs or procedures listed in the two bullet points above
    - possible changes in methods or levels of payment for benefits or services under those programs

    Such projects must be conducted pursuant to specific federal statutory authority. There must be no statutory requirements for IRB review, the research must not involve significant physical invasions or intrusions upon the privacy of subjects, and the exemption must be invoked only with authorization or concurrence by the funding agency.
6. Taste and food quality evaluation and consumer acceptance studies:
    - if wholesome foods without additives are consumed; or
    - if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture

The IRB Chair (or designee) reviews all requests for exemptions and determines whether the request meets the criteria for exempt research. The IRB Chair may designate an IRB member to review requests for exemptions submitted to the IRB. The Chair selects designees who are qualified to review this category of submission based on their expertise of the protocol content and knowledge of regulations pertaining to research. If there is not a designated reviewer to consider requests for exemptions, the IRB Chair reviews the requests. Individuals involved in making the determination of an IRB exempt status of a proposed research project cannot be involved in the proposed research. Reviewers do not have any apparent conflict of interest.

To document the IRB reviewer's determination of the request for exempt research, he/she completes the Exemption Determination Form. The IRB reviewer verifies on the form whether the submission meets the definition for "research" or "clinical investigation". If the request meets the definitions of both human subject and research, the reviewer indicates whether the request for exemption was approved or denied, and if approved, the rationale for the determination and category under which it was permitted.

Exempt studies are communicated to the IRB at the next convened meeting after the approval of exemption.

The decision must be communicated in writing to the investigator and the IRB. Documentation must include the specific categories justifying the exemption.

Investigators will be given feedback as to the qualification of the application for exemption status either by telephone or via electronic mail. Upon the IRB's completion of the review, the IRB staff will inform the Principal Investigator of the results of the review via electronic mail.

Additional Protections

Although exempt research is not covered by the federal regulations, such research is not exempt from NDMU policies on the responsible conduct of research or the ethical guidelines of the Belmont Report. The individual making the determination of exemption will use the *Checklist for Exemption Determination* to determine whether to require additional protections for subjects (including specifics of the informed consent procedures) in keeping with the guidelines of the Belmont Report.

8.3. Expedited Review of Research

The IRB may use the expedited review procedure to review either or both of the following: (A) some or all of the research appearing on the categorical list and found by the reviewer(s) to involve no more than minimal risk, and/or (B) minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

A minor change is one which, in the judgment of the IRB reviewer, makes no substantial alteration in (i) the level of risks to subjects; (ii) the research design or methodology (e.g., an addition of a procedure which would increase risk to subjects); (iii) the number of subjects enrolled in the research (e.g., increases representing greater than 10%); (iv) the qualifications of the research team; (v) the facilities available to support safe conduct of the research, or (vi) any other change in the research that would otherwise warrant review of the proposed changes by the convened IRB. Adding procedures that are not eligible for expedited review would not be considered a minor change.

Under an expedited review procedure, the review may be carried out by an IRB Chair or by one or more IRB reviewers designated by the Chair. The IRB Chair may appoint other designees from among the members of the IRB when a particular field of expertise is required for an expedited review. At the discretion of the reviewer, the reviewer(s) may forward expedited reviews to the IRB Chair when additional review is needed in order to evaluate minimal risk status and determine expedited status. On

an annual basis, the IRB Chairs will designate a list of IRB members eligible to conduct expedited review, and the IRB Office will select expedited reviewers from that list. IRB members eligible to conduct expedited review must have served on the IRB for at least three months.

When reviewing research under an expedited review procedure, the IRB Chair, or designees, should receive and review all documentation that would normally be submitted for a full-board review including the complete protocol, a Continuation review form summarizing the research to date (including modifications and adverse events), as applicable, notes from the pre-screening conducted by the IRB Office staff, and the current consent documentation. The IRB Chair or designees shall determine the regulatory criteria for use of such a review procedure by using the Reviewers Checklist.

If the research clearly qualifies for expedited review, the reviewer shall conduct the expedited review. If the research does not clearly qualify for expedited review, the reviewer shall refer the application to the IRB for full review at its next convened meeting.

The reviewer(s) conducting the initial or continuing review will determine whether the research meets the expedited procedure criteria and, if so, whether the research meets the regulatory criteria for approval. If the research does not meet the criteria for expedited review, then the reviewer will indicate that the research requires full review by the IRB and the protocol will be placed on the next agenda for an IRB meeting.

A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth below.

Reviewers will indicate approval, required modifications or disapproval. If modifications are required, the reviewer will inform the investigator via Research Navigator. If the modifications are minor, the reviewer(s) may determine if the investigator has sufficiently addressed the modifications. If the modifications are major and have been reviewed by the IRB Chair, the reviewer(s) may send the review back to the Chair for further review. Upon the discretion of the reviewer(s) and/ or the IRB Chair, the protocol may be submitted to the IRB for full board review.

In the event that expedited review is carried out by more than one IRB member and the expedited reviewers disagree on the resolution of the application, the IRB Chair may make a final determination. Upon the discretion of the IRB Chair, the protocol will be submitted to the IRB for review.

Categories of Research Eligible for Expedited Review

[63 FR 60364-60367, November 9, 1998]

The activities listed below should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

- The categories in this list apply regardless of the age of subjects, except as noted.
- The expedited review procedure may not be used where identification of the subjects and/ or subjects' responses would reasonably place them at risk of criminal or civil liability, or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- The expedited review procedure may not be used for classified research involving human subjects.
- The standard requirements for informed consent (or waiver, alteration, or exception) apply regardless of the type of review–expedited or convened–utilized by the IRB.

8.4. Pilot Studies

Pilot studies will not require IRB submission or approval provided that (all of the following):

- there are 10 or less subjects included,
- that data from those subjects are not used as research data, and
- that data from those subjects are not disseminated in any manner.

8.5. Secondary Data Sets

Projects using public, de-identified, secondary data sets will not require IRB submission or approval.

8.6 Training Requirements for Investigators

All study investigators including principle/primary, co-investigators, and sub/student investigators are required to complete CITI training within the past 5-years and provide proof of completion is CITI training was completed at an institution other than NDMU. CITI training is available free of charge to all NDMU faculty, staff, and students. Investigators who will access students' records in the course of research are required to complete FERPA training prior to submitting an IRB application. FERPA training is provided free of charge to NDMU faculty, staff, and students. Proof of completion of FERPA training must be submitted along with the IRB application even if the FERPA training was conducted through NDMU.

8.7. Convened IRB Meetings

Except where an expedited review procedure is followed, the IRB must review proposed research at convened meetings (also known as "Full-Board meetings") at which a quorum is present.

Schedule of IRB Meetings

In general, the IRB will be schedule for one meeting during each of the following months, unless there is a need for additional meetings in order to review a high volume of IRB applications: August, October, November, January, February, March, April, and May or June. The IRB will attempt to limit any meetings from the middle of June to the middle of August as many faculty members are 9-month employees. The IRB Chair may suspend certain meetings due holidays, weather, events, or certain time of the year where member workload is high outside of the IRB. However, the IRB will meet in person at least 4 times per year with one face to face meeting in person/remotely every quarter of the fiscal year. Meeting dates, times, and locations will be scheduled at least 1 meeting ahead with at least 2 weeks' notice unless a meeting is needed to complete the review of proposals which could not be reviewed in a normally scheduled meeting due to the large number of applications/proposals requiring full review by the IRB. IRB will work with faculty members who are mentoring student research, especially research that is conducted in the confines of a specific course and semester, to schedule a meeting to review any non-exempt protocols such that there is sufficient time for the students to complete the research and the course objectives in the confines of the semester.

Quorum

A quorum consists of a simple majority of the voting membership, including at least one member whose primary concern is in a non-scientific area. The IRB Chair will confirm that an appropriate quorum is present before calling the meeting to order. The IRB Chair will be responsible in ensuring that the IRB meetings remain appropriately convened.

Votes may only occur when a quorum is present. The IRB Chair takes note of arrivals and departures of all members and tracks whether or not quorum is not present. If a quorum is not maintained, the

proposal must be tabled or the meeting must be terminated. All members present at a convened meeting have full voting rights, except in the case of a conflict of interest where the member with the conflict of interest can be excused from the meeting during the review and voting processes.

In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.

While it is preferred that IRB members be physically present at the meeting, if physical presence is not possible, a member may be considered present if participation occurs via teleconference or videoconference. In such cases, the member must have received all pertinent material prior to the meeting and must be able to participate actively and equally in all discussions.

Opinions of absent members that are transmitted by mail, telephone, facsimile or e-mail may be considered by the attending IRB members but may not be counted as votes or to satisfy the quorum for convened meetings.

It is generally expected that at least one unaffiliated member and at least one member who represents the general perspective of participants (the same individual can serve in both capacities) will be present at all IRB meetings. Although the IRB may, on occasion, meet without this representation, individuals serving in this capacity must be present for at least 80% of the IRB meetings.

Pre-Meeting Distribution of Documents

Review and meeting materials are available electronically by email or on the Learning Management site.

Meeting Procedures

The representative of the IRB Chair in the event that the IRB Chair is absent, will call the meeting to order, once it has been determined that a quorum is in place. The appointed individual will remind IRB members to recuse themselves from the discussion and vote by leaving the room where there is a conflict. The IRB will review and discuss the IRB Minutes from the prior meeting and determine if there are any revisions/corrections to be made. If there are no changes to be made, the Minutes will be accepted as presented and considered final. If it is determined that revisions/corrections are necessary, the Minutes will be amended and presented at the following IRB meeting.

The IRB reviews all submissions for initial and continuing review, as well as requests for modifications. The Primary and Secondary Reviewer present an overview of the research and lead the IRB through the completion of the regulatory criteria for approval in the *Institutional Review Board - Protocol Review/Initial Review* checklist.

All members present at a convened meeting have full voting rights, except in the case of a conflict of interest when the member is excused for that portion of the meeting when the item is under action. In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting. Minute taking will rotate among the IRB members as the IRB Chair will be facilitating the meeting.

Guests

At the discretion of the IRB, the Principal Investigator may be invited to the IRB meeting to answer questions about their proposed or ongoing research. The Principal Investigator may not be present for the discussion or vote on their research.

Other guests may be permitted to attend IRB meetings at the discretion of the IRB Chair. Guests may not speak unless requested by the IRB and must sign the IRB's *Confidentiality Agreement*.

Primary Reviewers

The IRB Chair assigns a primary and secondary reviewer for all protocols. Assignment of reviewers will be dependent on the scientific or scholarly expertise required to review the research in addition to the previous number of protocols reviewed by a member in the same area of research and overall number of protocols reviewed in order to distribute the workload as evenly as possible among members.

If the IRB Chair cannot identify a primary reviewer with appropriate expertise, the IRB Chair will solicit consultants from the Institution or the community with competence in such specialized areas to assist in the review of the issues or protocols requiring appropriate scientific or scholarly expertise beyond or in addition to that available on the IRB.

Prior to the convened IRB meeting, each protocol application (including background information, project protocol, and informed consent) is reviewed in depth by the assigned Primary reviewer(s). All other IRB members receive all copies of aforementioned. They are expected to have reviewed all provided material in order to have a meaningful discussion of the presented information during the convened IRB meeting. The primary reviewer is responsible to entering all of the protocol submission documents and the primary reviewer form into the IRB management site.

8.8. Review Process

Submitting Electronically to the IRB

The IRB requires that the research proposal be delivered to the IRB Chair electronically via email through IRB@ndm.edu in one PDF document. Electronic submission through IRB@ndm.edu is encouraged due to faster delivery time of the information to the IRB Chair and ability to forward the information with reviewers more rapidly compared to hard copies using campus mail.

IRB Member Conflicts of Interest

IRB members and consultants will not participate in any IRB action, including the initial and continuing review of any project, in which the member has a conflicting interest, except to provide information requested by the IRB. IRB members are expected to self-identify conflicting interests. A Primary Reviewer or expedited reviewer with a conflict of interest must notify the IRB staff, and the IRB staff will, in turn, re-assign the protocol to another IRB member.

An IRB member is considered to have a conflicting interest when the IRB member or an immediate family member (defined as having a relationship to a person, whether by blood, law, or marriage, as a spouse, parent, child, grandparent, grandchild, stepchild, or sibling) of the IRB member:

- has an involvement in (or is directly supervising) a research project being reviewed by the IRB
- is the project director, or a member of the research team
- has a financial interest (for example, a financial interest in the sponsor or the product or service being tested) in the research whose value cannot be readily determined or whose value may be affected by the outcome of the research
- has a financial interest in the research with value that exceeds $10,000 or 5% ownership of any single entity when aggregated for the IRB member and their immediate family
- has received or will receive any compensation whose value may be affected by the outcome of the study
- has a proprietary interest in the research (property or other financial interest in the research including, but not limited to, a patent, trademark, copyright or licensing agreement)
- has received payments from the sponsor that exceed $10,000 in one year when aggregated for the IRB member and their immediate family

- is an executive or director of the agency or company sponsoring the research,
- any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a protocol

IRB members will be excused from the meeting room when the IRB reviews research in which the IRB member has a conflicting interest, except when otherwise requested to provide information to the IRB. The IRB Chair will allow for board discussion to commence upon the conflicted member's removal from the meeting. The conflicted member is not counted toward the quorum and his/her absence during the discussion and vote on the protocol will be noted in the IRB meeting minutes.

If the Conflict of Interest status of an IRB member changes during the course of a study, the IRB member is required to declare such conflict to the IRB Chair and/or IRB Director.

Possible IRB Actions Taken by Vote

Approved

The study is approved as submitted.

Conditionally Approved

The IRB may approve research with conditions if, given scope and nature of the conditions, the IRB is able, based on the assumption that the conditions are satisfied, to make all of the determinations required for approval (i.e., approval criteria and any applicable special determinations (e.g., waivers, alterations, vulnerable population determinations, etc.)). Any time the IRB cannot make one or more of the determinations required for approval, the IRB may not approve the study with conditions.

The IRB may require the following as conditions of approval of research:

- Confirmation of specific assumptions or understanding on the part of the IRB regarding how the research will be conducted (e.g., confirmation that research excludes children);
- Submission of additional documentation (e.g., certificate of training);
- Precise language changes to the study, consent, or other study documents; or
- Substantive changes to the study, consent, or other study documents along with clearly stated parameters that the changes must satisfy.

When the IRB approves research with conditions, the conditions will be documented in the IRB minutes.

When the convened IRB approves research with conditions, the IRB may designate the IRB Chair (and/or other qualified individual(s)) to review responsive materials from the investigator and determine that the conditions have been satisfied. If the conditions have not been satisfied, or are only partially satisfied, the responsive materials must be referred to the convened IRB for review.

After verification, the following will be documented in IRB records and written communication to the investigator:

- The date when verification was made that all IRB conditions have been satisfied (i.e., the "effective date");
- For initial approval, the date when approval becomes effective (i.e., the date on which the investigator's response has been accepted as satisfactory), and;
- The date by which continuing review must occur.

Deferred for Substantive Issues

Substantive issues regarding the protocol and /or consent form must be addressed. This action is taken if substantial modification or clarification is required, or insufficient information is provided to judge the protocol application adequately (e.g., the risks and benefits cannot be assessed with the information provided). IRB approval of the proposed research will not occur by the convened IRB until subsequent review of the material submitted for by the Principal Investigator.

If the application is deferred the following will occur:

- the IRB Office informs the investigator in writing of the IRB's decision, setting forth the IRB's questions and concerns
- the investigator's response is sent to the IRB Office
- in order to receive approval for a deferred protocol, the protocol must be submitted for full IRB review at a subsequent, convened meeting of the same IRB. The IRB Office will provide to the IRB members the investigator's response, the revised protocol and/or consent with highlighted changes, all original submission materials (inclusive of changes, if any were required), and the previous IRB written decision (relayed to the Principal Investigator by the IRB Office) signed by the Principal Investigator. The deferred protocol is then placed on the agenda for the following meeting
- the amended protocol application is given full IRB review
- the outcome of the IRB's deliberations is once again communicated to the investigator in writing
- the IRB's determination concerning the subsequent amended submission will be documented in the minutes of that meeting

Unapproved
Questions and issues are of such a magnitude that the IRB determines approval of the study is unwarranted. Approval of a previously disapproved protocol requires full IRB review

Appeals
Should the IRB make a decision the investigator believes to be unduly restrictive, the investigator may appeal to the full IRB (*see*: Appeal of IRB Decisions).

Determination of Risk
Concurrent with the initial and continuing review process, the IRB will make a determination with respect to the risks associated with the research protocols. Risks associated with the research protocols will be classified as either "minimal" or "greater than minimal" based on the "absolute" interpretation of minimal risk. The meeting minutes will reflect the IRB's determination regarding risk levels.

Period of Approval
Concurrent with the initial and continuing review process, the IRB will make a determination with respect to the frequency of review of the research protocols. All protocols will be reviewed by the IRB at intervals appropriate to the IRB's determination of the degree of risk, but no less than once per year. In certain circumstances, a shorter review interval (e.g. bi-annually, quarterly, or after accrual of a specific number of participants) may be required. The meeting minutes will reflect the IRB's determination regarding review frequency. No study shall be approved by the IRB for a duration longer than 3 years without requiring the investigator to reapply for IRB approval after 3 years.

Review More Often Than Annually
Unless specifically waived by the IRB, research that meets any of the following criteria will require review more often than annually:

- significant risk to research subjects (e.g., death, permanent or long lasting disability or morbidity, severe toxicity) without the possibility of direct benefit to the subjects;
- the involvement of especially vulnerable populations likely to be subject to coercion (e.g., institutionalized psychiatric patients, incarcerated minors); or
- a history of serious or continuing non-compliance on the part of the Principal investigator.
- the following factors will also be considered when determining which studies require review more frequently than on an annual basis:

  - The probability and magnitude of anticipated risks to subjects;
  - The likely medical condition of the proposed subjects;
  - The overall qualifications of the Principal Investigator and other members of the research team;
- the specific experience of the Responsible Investigator and other members of the research team in conducting similar research;
- the nature and frequency of adverse events observed in similar research at this and other institutions;
- the novelty of the research, thereby increasing the possibility of unanticipated adverse events, and
- any other factors that the IRB deems relevant.

In circumstances where the IRB mandates an approval period of less than one year, the IRB may define the review period (1) with a time interval, or (2) in circumstances where a specified number of subjects were studied or enrolled in the study. If a specified number of subjects were studied or enrolled in the study, it is understood that the approval period in no case may exceed 1 year. Further, the number of subjects studied or enrolled in the study will determine the approval period only when the specified number of subjects were studied or enrolled in the study for less than 1 year.

Independent Verification Regarding Material Changes

Protecting the rights and welfare of subjects often requires the IRB to independently verify information about various aspects of the study utilizing sources other than the investigator. Independent verification includes, but is not limited to:

- adverse event reporting
- information in the scientific literature
- reports of drug toxicity
- drug approval status
- confirmation that no material changes occurred during the IRB-designated approval period

The IRB will determine the need for verification from outside sources on a case-by-case basis based upon the following criteria:

- protocols where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources
- protocols conducted by Principal Investigators who have previously failed to comply with federal regulations and/or the requirements or determinations of the IRB
- protocols randomly selected for internal audit
- whenever else the IRB deems verification from outside sources is relevant

The following factors will also be considered when determining whether or not a study requires independent verification:

- the probability and magnitude of anticipated risks to subjects
- the likely medical condition of the proposed subjects
- the probable nature and frequency of changes that may ordinarily be expected in the type of research proposed

In making independent verification determinations, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period, may retrospectively require such verification at the time of continuing review, review of amendments and/or unanticipated problems, or may require such verification at any time during the approval period in the light of new information.

If any material changes have occurred without IRB review and approval, the IRB will decide the corrective action to be taken.

Consent Monitoring

In reviewing the adequacy of informed consent procedures for proposed research, the IRB may on occasion determine that special monitoring of the consent process by an impartial observer (a "consent monitor") is required in order to ensure that the approved consent process is being followed and to ensure that subjects are truly giving informed consent.

Such monitoring may be particularly warranted for:

- high risk studies
- studies that involve particularly complicated procedures or interventions
- studies involving highly vulnerable populations (e.g., Patients in high acuity units in acute care settings, children)
- studies involving study staff with minimal experience in administering consent to potential study participants
- other situations when the IRB has concerns that consent process is not being conducted appropriately

Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular investigator or a research project.

If the IRB determines that consent monitoring is required, the IRB Chair and the IRB Director will develop a monitoring plan and submit it to the IRB for approval. The consent monitoring may be conducted by IRB staff, IRB members or another party, either affiliated or not with the institution. The Principal Investigator will be notified of the IRB's determination and the reasons for the determination. Arrangements will be made with the Principal Investigator for the monitoring of the consent process for a specified number of subjects. When observing the consent process, the monitor will determine whether the:

- informed consent process was appropriately completed and documented
- participant had sufficient time to consider study participation
- consent process involved coercion or undue influence
- information was accurate and conveyed in understandable language
- subjects appeared to understand the information and gave their voluntary consent

Following the monitoring, a report of the findings will be submitted to the IRB, which will determine the appropriate action to be taken.

Significant New Findings

During the course of research, significant new knowledge or findings about the medication or test article and/or the condition under study may develop. The Principal Investigator must report any significant new findings to the IRB and the IRB will review them with regard to the impact on the subjects' rights and welfare. Since the new knowledge or findings may affect the risks or benefits to subjects or subjects' willingness to continue in the research, the IRB may require, during the ongoing review process, that the Principal Investigator contact the currently enrolled subjects to inform them of the new information. The IRB will communicate this to the Principal Investigator. The informed consent should be updated and the IRB may require that the currently enrolled subjects be re-consented, acknowledging receipt of this new information and for affirming their continued participation.

Other Committee Approvals

The investigator is required to secure the approval of other research committees (if applicable) such as FDA, etc. The Principal Investigator is responsible for submitting the required materials to the above-referenced committees and securing their approval. Prior to IRB approval, the IRB requires documentation of approval from the following committees (as applicable)

Reporting IRB Actions

All IRB actions are communicated directly to the Principal Investigator within five to seven (5-7) working days of the IRB's determination via a template letter prepared by the IRB staff and signed by the IRB Director. When approving a protocol, the IRB will forward notification of approval along with a copy of the approved consent form. The approval will contain date(s) of the protocol approval and the protocol expiration date. When deferring a protocol, the IRB notification will include the modifications required for approval along with the reasoning for requiring such modifications. When disapproving, terminating or suspending a protocol, the IRB notification will include the reasoning behind such decision.

All letters to investigators are maintained electronically by the IRB.

8.9. Continuing Review of Active Protocols

The IRB will conduct a continuing review of ongoing research at intervals that are appropriate to the level of risk for each research protocol, but not less than once per year. Continuing review must occur as long as the research remains active for long-term follow-up of participants, even when the research is permanently closed to the enrollment of new participants and all participants have completed all research-related interventions. Continuing review of research must occur, even when the remaining research activities are limited to the analysis of private identifiable information.

Approval Period

For each initial or continuing protocol approval, the IRB will indicate an approval period with an approval expiration date specified. IRB approval is considered to have lapsed at midnight on the expiration date of the approval. For a study approved by the convened IRB, the approval period starts on the date that the IRB conducts its final review of the study; that is, the date that the convened IRB approved the research or the date the convened IRB deferred the research for non-substantive issues. For a study approved under expedited review, the approval period begins on the date the IRB Chair or IRB member(s) designated by the Chair gives final approval to the protocol.

The approval date(s) and approval expiration date are clearly noted on all IRB notifications sent to the Principal Investigator and must be strictly adhered to. Investigators should allow sufficient time for development and review of renewal submissions.

Review of a change in a protocol ordinarily does not alter the date by which continuing review must occur. This is because continuing review is review of the full protocol, not simply a change to it.

No grace periods extending the conduct of research beyond the expiration date of IRB approval will be permitted. Therefore, continuing review and re-approval of research must occur by midnight of the date when IRB approval expires. It is the PI's responsibility to ensure that the continuing review of ongoing research is approved prior to the expiration date. By federal regulation, no extension past that date can be granted.

Continuing Review Process

Investigators must submit the following for continuing review:

- the current consent document
- any newly proposed consent document
- *Disclosures of Financial Interest* forms

In conducting continuing review of research ineligible for expedited review, all IRB members are provided with and review all of the above-referenced material. The Primary Reviewer and IRB Chair will also receive a copy of the most recent protocol version. At the convened IRB Board meeting, the

Primary Reviewer will lead the IRB through the completion of the regulatory criteria for approval in the *Reviewer's Checklists*.

Review of currently approved or newly proposed consent documents must occur during the scheduled continuing review of research by the IRB, but informed consent documents should be reviewed whenever new information becomes available that would require modification of information in the informed consent document.

A new protocol version that has not been previously approved by the IRB will not be accepted at the time of continuing review. Any new protocol must be submitted through a modification request with all accompanying materials and must be approved before reviewing the continuation.

Lapse in IRB Approval

The IRB and investigators must plan ahead in order to meet required continuing review dates. If the IRB has not reviewed and approved a research study by the end of the approval period specified by the IRB, all research activities must cease, including recruitment and enrollment of subjects, consent, interventions, interactions, and data collection, unless the IRB concludes that it is in the best interests of individual subjects to continue participation in the research interventions or interactions. This will occur even if the investigator has provided the continuing information before the expiration date. Therefore, investigators must allow sufficient time for IRB review before the expiration date.

An expiration letter (or electronic mail) will be sent to investigator(s) by the last date of the approval period.

Failure to submit continuing review information on time is considered non-compliance and will be handled according to the non-compliance

Once suspended, IRB review and re-approval must occur prior to re-initiation of the research.

The continuation of research after expiration of IRB approval is a violation of the regulations. 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 cease. No new subjects may be enrolled in the study. However, IRB may find that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. The procedure for obtaining approval to continue subject participation after expiration of IRB approval is as follows:

- the Principal Investigator will submit to the IRB Chair a written list of research subjects for whom stopping of the research would cause harm
- the IRB Chair will review written requests from investigators who wish to continue research with existing subjects in research procedures
- the IRB Chair will determine which subjects, if any, may continue with the study. The IRB Chair will further determine the specific procedures that may continue to be performed when ceasing such procedures will harm the subject
- the IRB Chair will either orally communicate the decision to the investigator(s) or communicate such decision via electronic mail. The IRB Chair will also provide a written response

8.10. Modification of an Approved Protocol

Investigators may wish to modify or amend their approved applications. Investigators must seek IRB approval before making any changes in approved research—even though the changes are planned for the period for which IRB approval has already been given. A change may be implemented without IRB when the change is necessary to eliminate an immediate hazard to the subject (in which case the IRB must then be notified at once).

Modifications may be approved if they are within the scope of what the IRB originally authorized. For example, if a researcher wishes to add a population to an existing study, but not alter the study procedures or purpose, a modification request is usually appropriate. Likewise, modifying a procedure without changing the study's purpose or study population may also be appropriate.

Investigators must electronically submit all necessary materials necessary to inform the IRB about the changes in the status of their study, including:

- revised Investigator's protocol application or sponsor's protocol (if applicable)
- revised approved consent/parental permission/assent documents (if applicable) or other documentation that would be provided to subjects when such information might relate to their willingness to continue to participate in the study
- revised or additional recruitment materials
- any other relevant documents provided by the investigator
- the investigator's current curriculum vitae or other documentation evidencing qualifications if applicable

The Principal Investigator must electronically submit all revised materials in Microsoft Word format, noting changes via highlight or "Track Changes".

All changes must be accompanied by a detailed summary of the changes and a rationale (as applicable).

IRB office staff will determine whether the proposed changes may be approved through an expedited review process, if the changes are minor, or whether the modification warrants full board review. The reviewer(s) using the expedited procedure has the ultimate responsibility to determine that the proposed changes may be approved through the expedited review procedure and, if not, must refer the protocol for full board review.

Expedited Review of Protocol Modifications

The IRB may use expedited review procedures to review minor changes in ongoing previously-approved research during the period for which approval is authorized. An expedited review may be carried out by the IRB Chair and/or designee(s) among the IRB Minor changes/modifications would not include the addition of procedures involving more than minimal risk to participants or changes that do not fall in categories (1)-(7) of research that could be reviewed using the expedited procedure

The reviewer(s) complete the *Checklist for Amendment Review Determination* to determine whether the modifications meet the criteria allowing review using the expedited procedure, and if so, whether the research with the proposed modifications meets the regulatory criteria for approval.

Full Board Review of Protocol Modifications

When a proposed change in a research study is not minor (e.g., procedures involving increased risk or discomfort are to be added), then the IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the subjects' continued welfare.

Major changes/modifications would include the addition of procedures involving more than minimal risk to participants or changes that do not fall in categories (1)-(7) of research that could be reviewed using the expedited procedure.

All IRB members electronically review all documents provided by the investigator.

At the meeting, the Primary Reviewer presents an overview of the modifications and leads the IRB through the completion of the regulatory criteria for approval.

When the IRB reviews modifications to previously approved research, the IRB consider whether information about those modifications might relate to participants' willingness to continue to take part in the research and if so, whether to provide that information to participants.

Closure of Studies

The completion or termination of the study is a change in activity and must be reported to the IRB. Although subjects will no longer be "at risk" under the study, a final report to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.

Investigators submit closures to the IRB electronically via IRB7. The investigator must submit a final report with the closure application. IRB staff will review the closure application for completeness and will determine how to notify the IRB. Closure applications will be reviewed, noted and the final report will be included on the next agenda.

8.11. Unanticipated Problems

Federal regulations require organizations to have written policies and procedures to ensure the prompt reporting of unanticipated problems involving risks to subjects or others to the IRB, appropriate institutional officials, and regulatory agencies and departments.

> *NOTE: For simplicity, unanticipated problems involving risks to subjects or others will be referred to as "unanticipated problems" in this policy.*

Not all unanticipated problems involve direct harm to subjects. Events can occur which are unexpected and result in new circumstances that increased the risk of harm to subjects without directly harming them. In addition, the event may have presented unanticipated risks to others (e.g., the sexual partners of the subjects, individuals the subject may come in contact with, family members, research personnel, etc.) in addition to the subjects. In each case, while the event may not have caused any detectable harm or adverse effect to subjects or others, they nevertheless represent unanticipated problems and should be promptly reported.

Events which involve direct harm to subjects are referred to as "Adverse Events". Although adverse events occur most commonly in the context of biomedical research, adverse events can occur in the context of social and behavioral research. Only unanticipated adverse events that are related to the research need to be reported. If one of your research subjects dies while participating in your study, you do not have to report the death if you're positive it was not study-related.

Definitions

Unanticipated Problem Involving Risks to Participants or Others (Unanticipated Problem)

Any event, any incident, experience, outcome, or new information that (1) was unforeseen and (2) indicates that the research procedures caused harm to participants or others or indicates that participants or others are at increased risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Adverse Event (AE)

Any physical, psychological or social harm to subjects during the course of research. An AE can be any unfavorable or unintended event including abnormal laboratory finding, symptom or disease associated with the research or the use of a medical investigational test article.

Unanticipated
An event is "unanticipated" when its specificity and severity are not accurately reflected in the informed consent document, protocol and/or Investigator's Brochure.

The incident, experience or outcome is not expected (in terms of nature, severity, or frequency) given the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent documents; and the characteristics of the subject population being studied;

Related to the Research
An event is "related to the research procedures" if in the opinion of the principal investigator, it was more likely than not to be caused by the research procedures or if it is more likely that not that the event affects the rights and welfare of current participants.

Reporting

Principal investigators must report to the IRB as soon as possible, but in all cases within 5 working days of any:

- adverse events which in the opinion of the principal investigator are both unexpected and related
- an unanticipated event related to the research that exposes individuals other than the research participants (e.g., investigators, research assistants, students, the public, etc.) to potential risk
- information that indicates a change to the risks or potential benefits of the research. For example:
    - an interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially presented to the IRB
    - a paper is published from another study that shows that the risks or potential benefits of your research may be different than initially presented to the IRB
- a breach of confidentiality, including the loss of digital storage devices
- incarceration of a participant in a protocol not approved to enroll prisoners
- change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant
- complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team
- protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) that harmed participants or others or that indicates participants or others may be at increased risk of harm
- event that requires prompt reporting to the sponsor
- sponsor imposed suspension for risk

The IRB will accept other reports when the investigator is unsure whether the event should be reported. The investigator should first contact the IRB by email or telephone to determine if the reporting is necessary.

Study staff should report the above events electronically with the form entitled *Reportable New Information*.

IRB Review

Upon receipt of a Reportable New Information (RNI) from the Investigator, the IRB Chair or a member(s) of the IRB who have appropriate expertise to review the event.

Based on the information received from the investigator and upon the advice of the RA or other reviewers, the IRB Chair or IRB Director may suspend research to ensure protection of the rights and welfare of participants. Suspension directives made by the IRB Chair or IRB Director must be reported to a meeting of the convened IRB.

The IRB chairperson (or designee) has authority to require submission of more detailed contextual information by the Principal Investigator, the sponsor, the study coordinating center, or Data Safety Monitoring Borad/Data Monitoring Committee about any adverse event occurring in a research protocol as a condition of the continuation of the IRB's approval of the research.

If the IRB considers that either (1) the problem was foreseen OR (2) no participants or others were harmed AND participants or others are not at increased risk of harm, the IRB Member indicates on the form that the problem is not an unanticipated problem. The form is filed in the protocol record, the determination is communicated to the investigator and no further action is taken.

If the IRB Member considers that the problem is an unanticipated problem, but that the risk is no more than minimal, the IRB Member will review the:

- currently approved protocol
- currently approved consent document
- previous reports of unanticipated problems involving risks to participants or others
- investigator's brochure, if one exists

The IRB Member will take appropriate action depending on the nature of the risk involved, including modification of the protocol or the consent form, if applicable, after reviewing all of the materials. The results of the IRB Member's review will be recorded in the protocol record, communicated to the investigator, reported to the IRB, and referred to the IRB Office to be handled according the reporting procedures.

All reported unanticipated problems where the risk is more than minimal will be reviewed at a convened IRB meeting. All IRB members are provided a copy of the *Reportable New Information* and supporting documents provided by the investigator. All IRB members have access to:

- the currently approved protocol
- the currently approved consent document
- previous reports of unanticipated problems involving risks to participants or others
- the investigator's brochure, if one exists

After review of the protocol and event report, the full IRB will make findings and recommendations based on the following considerations:

- whether the reported event is an unanticipated problem involving risks to participants or others according to the definition in this policy.
- what action in response to the report is appropriate.
- whether suspension or termination of approval is warranted.
- whether further reporting to Institutional and/or federal officials is required.

If the IRB considers the event to not represent an unanticipated problem the results of the review are recorded in the protocol record, the IRB minutes and communicated to the investigator; the IRB may recommend any of the following actions:

- nothing further
- requiring modifications to the protocol
- revising the continuing review timetable
- modifying the consent process
- modifying the consent document
- providing additional information to current participants (e.g. whenever the information may relate to the participant's willingness to continue participation)
- providing additional information to past participants
- requiring additional training of the investigator and/or study staff
- other actions appropriate for the local context

If the IRB considers the event to represent an unanticipated problem, the IRB will consider the following actions:

- modification of the protocol
- modification of the information disclosed during the consent process
- providing additional information to current participants (This must be done whenever the information may relate to the participant's willingness to continue participation)
- providing additional information to past participants
- requiring current participants to re-consent to participation
- alteration of the frequency of continuing review
- observation of the research or the consent process
- requiring additional training of the investigator and/or study staff
- notification of investigators at other sites
- termination or suspension of the research
- obtaining additional information
- referral to other organizational entities (e.g., legal counsel, risk management, institutional official)
- other actions appropriate for the local context

The results of the IRB review are recorded in the IRB minutes, protocol record, communicated to the investigator and referred to the IRB Office to be handled according the reporting procedures.

8.12. Appeal of IRB Decisions

The IRB will consider appeal(s) of a disapproved new protocol submission. The Principal Investigator may appeal an IRB decision in writing. All appeals must be addressed to the IRB Chair and should be accompanied by a letter from the Investigator detailing the reason for the appeal. The Investigator should be prepared to attend the IRB meeting to address issues raised by the Board.

If the IRB makes a decision that the investigator believes to be unduly restrictive on the proposed research, the investigator may appeal, in writing, for review by the convened appropriate IRB. The investigator may first discuss the matter with the IRB Chair, taking care to explain the reasons for believing that the proposed procedures are in compliance with NDMU IRB policy and with Federal regulations. If the issue cannot be resolved satisfactorily by negotiation, the investigator may appeal the decision of the IRB, in writing. In either case, the IRB will reconsider the appeal based upon the new information provided and will continue to re-review protocols as long as the investigator wishes to appeal.

9. Criteria for IRB Approval of Research

In order for the IRB to approve human subjects research it must determine that the following requirements are satisfied:

- risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes
- risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility

- selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disable persons, or economically or educationally disadvantaged persons
- informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by [45 CFR §46.116]
- informed consent will be appropriately documented, in accordance with, and to the extent required by [45 CFR §46.117]
- when appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects
- when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data
- when some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects

9.1. Risk/Benefit Assessment

The goal of the assessment is to ensure that the risks to research subjects posed by participation in the research are justified by the anticipated benefits to the subjects or society. Toward that end, the IRB must:

- judge whether the anticipated benefit, either of new knowledge or of improved health for the research subjects, justifies asking any person to undertake the risks
- disapprove research in which the risks are judged unreasonable in relation to the anticipated benefits

The assessment of the risks and benefits of proposed research—one of the major responsibilities of the IRB—involves a series of steps:

- identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research
- determine whether the risks will be minimized to the extent possible
- identify the probable benefits to be derived from the research
- determine whether the risks are reasonable in relation to the benefits to subjects, if any, and assess the importance of the knowledge to be gained
- ensure that potential subjects will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits

Risks to subjects are minimized:

- by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk
- whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes

Risks to subjects are reasonable in relation to anticipated benefits, if any, and to the importance of the knowledge that may reasonably be expected to result.

- in evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research—as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research
- the IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility

Scientific Merit

In order to assess the risks and benefits of the proposed research, the IRB must determine that the science is adequate to provide sufficient benefit to justify the risks, including:

- the research uses procedures consistent with sound research design;
- the research design is sound enough to reasonably expect the research to answer its proposed question; and
- the knowledge expected to result from this research is sufficiently important to justify the risk.

For research that is funded externally or is internally funded (such as through local research award programs) the IRB may take into account that the research will be going through a peer review process. For departments that conduct scientific merit review, departmental scientific review is documented by the signature of the administrative official responsible for the investigator's research unit on new protocol applications. In cases where the proposed research is not funded and there is no departmental scientific review, the IRB relies on the knowledge and disciplinary expertise of its members and alternates or consults with other researchers on or off campus for scientific merit review.

Documentation is required by the IRB demonstrating that the following questions where considered during the scientific review:

- does the research uses procedures consistent with sound research design?
- is the research design sound enough to reasonably expect the research to answer its proposed question;

For research subject to International Conference on Harmonization (ICH)/Good Clinical Practice (GCP)guideline (E6):

- policies and procedures include the evaluation of the available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial
- clinical trials are scientifically sound and described in a clear, detailed protocol

Other Considerations

In assessing the benefits of the research, the IRB must also review:

- the qualifications of the research team, including their technical and scientific expertise, as well as their knowledge and understanding of their obligation to protect the rights and welfare of research participants
- the adequacy of the resources necessary for human research protection, care of research participants, and safety during the conduct of the research

9.2. Selection of Subjects is Equitable

The IRB will review the inclusion/exclusion criteria for the research to ensure equitable selection of subjects. In making this assessment the IRB takes into account the purposes of the research and the setting in which the research will be conducted, and is particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, fetuses, pregnant women, human in vitro fertilization, persons who are cognitively impaired, or persons who are economically or educationally disadvantaged.

Recruitment of Subjects

The investigator will provide the IRB with all recruiting materials to be used in identifying participants including:

- the information contained in the advertisement (including web-based sites)
- the mode of its communication
- the final copy of printed advertisements
- the final audio/video taped advertisements

The IRB must approve any and all advertisements prior to posting and/or distribution. The IRB will review:

- the information contained in the advertisement
- the mode of its communication
- the final copy of printed advertisements
- the final audio/video taped advertisements

The IRB reviews advertising to ensure that advertisements do not:

- state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol
- make claims, either explicitly or implicitly, that the drug, biologic or device is safe or effective for the purposes under investigation
- make claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other drug, biologic or device
- use terms, such as “new treatment,” “new medication” or “new drug” without explaining that the test article is investigational
- promise “free medical treatment,” when the intent is only to say subjects would not be charged for taking part in the investigation
- include exculpatory language
- emphasize the payment or the amount to be paid, by such means as larger or bold type

The IRB determines that advertisements are limited to the information prospective subjects need to determine their eligibility and interest, such as:

- the name and address of the clinical investigator or research facility
- the condition under study or the purpose of the research
- in summary form, the criteria that would be used to determine eligibility for the study
- a brief list of participation benefits (if any)
- the time or other commitment required of the subjects
- the location of the research and the person or office to contact for further information
- a clear statement that this is research and not treatment
- a brief list of potential benefits (e.g. no cost of health exam)
- advertisements will not include reimbursement/compensation for participation in a trial offered by a sponsor to involve a coupon good for a discount on the purchase price of the product once it has been approved for marketing

This information should be submitted to the IRB with the initial application or as an addendum to the protocol.

The IRB reviews the material to assure that the material is accurate and is not coercive or unduly optimistic, creating undue influence to the subject to participate.

Any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest.

Once approved by the IRB, an advertisement cannot be altered or manipulated in any way without prior IRB approval.

9.3. Informed Consent

The IRB will ensure that informed consent will be sought from each prospective subject or the subject’s legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20. In addition, the Committee will ensure that informed consent will be appropriately documented in accordance with, and to the extent required by [45 CFR 46.117] and [21 CFR 50.27]. For detailed policies on informed consent.

9.4. Data Safety Monitoring

The IRB will review the data safety monitoring plan for protocols involving more than minimal risk during initial review and at continuing review. The initial plan submitted to the IRB should describe the procedures for safety monitoring, reporting of unanticipated problems involving risks to subjects or others, descriptions of interim safety reviews and the procedures planned for transmitting the results to the IRB. This description should include information regarding an independent Data and Safety Monitoring Board (DSMB), if one exists, or an explanation why an independent data safety monitor is not necessary.

The IRB determines that the safety monitoring plan makes adequate provision for monitoring the reactions of subjects and the collection of data to ensure the safety of subjects. The overall elements of the monitoring plan may vary depending on the potential risks, complexity, and nature of the research study. The method and degree of monitoring needed is related to the degree of risk involved. Monitoring may be conducted in various ways or by various individuals or groups, depending on the size and scope of the research effort. These exist on a continuum from monitoring by the principal investigator in a small, low risk study to the establishment of an independent data and safety monitoring board for a large phase III clinical trial.

The factors the IRB will consider in determining whether the safety monitoring plan is adequate for the research are as follows:

- monitoring is commensurate with the nature, complexity, size and risk involved
- monitoring is timely. Frequency should commensurate with risk. Conclusions are reported to the IRB
- for low risk studies, continuous, close monitoring by the study investigator or an independent individual may be an adequate and appropriate format for monitoring, with prompt reporting of problems to the IRB, sponsor and regulatory bodies as appropriate.
- for an individual Safety Monitor the plan must include:
    - parameters to be assessed
    - mechanism to assess the critical efficacy endpoints at intervals in order to determine when to continue, modify, or stop a study
    - frequency of monitoring
    - procedures for reporting to the IRB
- for a Data Safety Monitoring Board, the plan must include:
    - the name of the Data Safety Monitoring Board
    - where appropriate, is an independent from the sponsor
    - availability of written reports
    - Composition of the monitoring group (if a group is to be used): experts in all scientific disciplines needed to interpret the data and ensure patient safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease and treatment under study should be part of the monitoring group or be available if warranted.
    - Frequency and content of meeting reports
    - The frequency and character of monitoring meetings (e.g., open or closed, public or private).

In general, it is desirable for a Data and Safety Monitoring Board (DSMB) to be established by the study sponsor for research that is blinded, involves multiple sites, involves vulnerable subjects, or employs high-risk interventions. For some studies the National Institutes of Health (NIH) require a DSMB. The IRB has the authority to require a DSMB as a condition for approval of research where it determines that such monitoring is needed. When DSMBs are utilized, IRBs conducting continuing review of research may rely on a current statement from the DSMB indicating that it has and will continue to review study-wide AEs, interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

9.5. Privacy and Confidentiality

The IRB will determine whether adequate procedures are in place to protect the privacy of subjects and to maintain the confidentiality of the data.

Definitions

Privacy
having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.

Confidentiality
methods used to ensure that information obtained by researchers about their subjects is not improperly divulged.

Private Information
information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Identifiable Information
information where the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

Privacy

The IRB must determine whether the activities in the research constitute a violation of privacy. In order to make that determination, the IRB must obtain information regarding how the investigators obtain access to subjects or subjects' information and the subjects expectations of privacy in the situation. Investigators must have appropriate authorization to access the subjects or the subjects' information.

In developing strategies for the protection of subjects' privacy, consideration should be given to:

- methods used to identify and contact potential participants
- settings in which an individual will be interacting with an investigator
- appropriateness of all personnel present for research activities
- methods used to obtain information about participants and the nature of the requested information
- information that is obtained about individuals other than the "target participants," and whether such individuals meet the regulatory definition of "human participant" (e.g., a subject provides information about a family member for a survey)
- how to access the minimum amount of information necessary to complete the study

Confidentiality

Confidentiality and anonymity are not the same. If anyone, including the investigator, can readily ascertain the identity of the subjects from the data, then the research is not anonymous and the IRB must determine if appropriate protections are in place to minimize the likelihood that the information will be inappropriately divulged. The level of confidentiality protections should be commensurate with the potential of harm from inappropriate disclosure.

At the time of initial review, the IRB ensures that the privacy and confidentiality of research subjects is protected. The IRB assesses whether there are adequate provisions to protect subject privacy and maintain confidentiality. The IRB does this through the evaluation of the methods used to obtain information:

- about subjects
- about individuals who may be recruited to participate in studies
- the use of personally identifiable records

- the methods to protect the confidentiality of research data

The Principal Investigator will provide the information regarding the privacy and confidentiality of research subjects at the time of initial review through the completion of the application, any necessary HIPAA Forms, research protocol, and/or other submitted, applicable materials. The IRB will review all information received from the Principal Investigator and determine whether or not the privacy and confidentiality of research subjects is sufficiently protected. In some cases, the IRB may also require that a Certificate of Confidentiality be obtained to additionally protect research data. In reviewing confidentiality protections, the IRB shall consider the nature, probability, and magnitude of harms that would be likely to result from a disclosure of collected information outside the research. It shall evaluate the effectiveness of proposed de-identification techniques, coding systems, encryption methods, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections.

9.6. Vulnerable Populations

At the time of initial review, the IRB will consider the scientific and ethical reasons for including vulnerable subjects in research. The IRB determines if appropriate additional safeguards are in place to protect the rights and welfare of subjects if they are likely to be members of a vulnerable population (e.g., persons with diminished autonomy).

10. Informed Consent

10.1. Informed Consent Process

No investigator may involve a human being as a subject in research without obtaining the legally effective informed consent of the subject or the subject's legally authorized representative unless a waiver of consent has been approved by the IRB in accordance with Waiver of Documentation of Informed Consent (Waiver of Signed Consent). In general, the IRB considers individuals who are unable to consent for their own clinical care to be unable to consent for research participation. Tools or instruments such as the Mini Mental Exam can be used to determine capability to consent.

Investigators must obtain consent prior to entering a subject into a study and/or conducting any procedures required by the protocol, unless consent is waived by the IRB.

Consent must always be sought under circumstances that:

- provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate
- minimize the possibility of coercion or undue influence

The IRB will consider where the consent process will take place and the individual who will be obtaining consent (e.g. the investigator, collaborator, or qualified designee) in its determination regarding the appropriateness of the consent process. When the potential participant's understanding of the research may be impaired due to the timing, location, or individuals participating in the proposed consent process, the IRB will require an alternative process.

The information that is given to the subject or the representative must be in language understandable to the subject or the representative.

No informed consent, whether oral or written, may include exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights.

A person knowledgeable about the consenting process and the research (i.e.: a member of the project's research team) to be conducted must obtain the informed consent, and must be able to answer questions about the study.

If someone other than the investigator conducts the interview and obtains consent, the investigator needs to formally delegate this responsibility and the person so delegated must have received appropriate training to perform this activity.

10.2. Definitions

Legally Authorized Representative
See *Section 10.6. Legally Authorized Representatives*.

Legal Guardian
A person appointed by a court of appropriate jurisdiction.

10.3. Basic Requirements

The requirement to obtain the legally effective informed consent of individuals before involving them in Research is one of the central protections provided for by the Federal regulations and the IRB. Investigators are required to obtain legally effective informed consent from a subject or the subject's Legally Authorized Representative. When informed consent is required, it must be sought prospectively, and properly documented.

The informed consent process involves three key features:

- disclosing to the prospective human subject information needed to make an informed decision in addition to following the requirements pertaining to consent covered by ICH-GCP (see "ICH-GCP Guidance"
- facilitating the understanding of what has been disclosed
- promoting the voluntariness of the decision about whether or not to participate in the research

Informed consent is more than just a signature on a form. It is a process of information exchange to include reading and signing the informed consent document. The informed consent process is the critical communication link between the prospective Human Subject and an Investigator, beginning with the initial approach of an Investigator and continuing through the completion of the research study. Investigators must have received the appropriate training and be knowledgeable about the study protocol in order that they may answer questions to help provide understanding to the study participant or potential study potential study participant.

The exchange of information between the Investigator and study participant can occur via one or more of the following modes of communication, among others; face to face contact, mail; telephone; or fax.

Sample or draft consent documents may be developed by a Sponsor or cooperative study group. However, the IRB-of-record is the final authority on the content of the consent documents that is presented to the prospective study subjects.

These informed consent requirements are not intended to preempt any applicable federal, state, or local laws that require additional information to be disclosed for informed consent to be legally effective.

10.4. Basic Elements of Informed Consent

Informed consent must be sought from each potential subject or the subject's legally authorized representative, in accordance with, and to the extent required by [45 CFR 46.116] and [21 CFR 50.25].

The basic elements of informed consent are:

- a statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental; a description of any reasonably foreseeable risks or discomforts to the subject
- a description of any benefits to the subject or to others which may reasonably be expected from the research
- a statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained
- for research involving more than minimal risk, an explanation as to the availability of medical treatment in the case of research-related injury, including who will pay for the treatment and whether other financial compensation is available
- an explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject
- a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled
- for FDA-regulated studies, the possibility that the FDA may inspect the records needs to be included in the statement regarding subject confidentiality
- an explanation of whom to contact to voice concerns or complaints about the research
- contact information for the IRB to obtain answers to questions about the research; to voice concerns or complaints about the research; to obtain answers to questions about their rights as a research participant; in the event the research staff could not be reached; and in the event the subject wishes to talk to someone other than the research staff

Additional elements of informed consent to be applied, as appropriate:

- a statement that the particular treatment or procedure may involve risks to the subject, which are currently unforeseeable. (For example: Include when the research involves investigational test articles or other procedures in which the risks to subjects is not well known.)
- a statement that if the subject is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable. (For example: Include when the research involves pregnant women or women of childbearing potential and the risk to fetuses of the drugs, devices, or other procedures involved in the research is not well known.)
- anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s consent. (For example: Include when there are anticipated circumstances under which the investigator may terminate participation of a subject.)
- any additional costs to the subject that may result from participation in the research. (For example: Include when it is anticipated that subjects may have additional costs.)
- the consequences of a subject’s decision to withdraw from the research. (For example: Include when withdrawal from the research is associated with adverse consequences.
- procedures for orderly termination of participation by the subject. (For example: Include when the protocol describes such procedures.)
- a statement that significant new findings developed during the course of the research which may relate to the subject’s willingness to continue participation will be provided to the subject. (For example: Include when the research is long term and interim information is likely to be developed during the conduct of the research.)
- the approximate number of subjects involved in the study. (For example: Include when the research involves more than minimal risk.)

Additional elements of informed consent to be applied when research subject to ICH-GCP (E6):

- a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject in addition to inclusion of any benefits or risks associated with alternatives
- a statement indicating that the monitor, the auditor, the IRBs, and the regulatory authority will be granted direct access to the subject's original medical records for verification of clinical trial procedures or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the subject or the subject's legally acceptable representative is authorizing such access. (ICH-GCP)

10.5. Waiver of Informed Consent

The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement for informed consent provided the IRB finds and documents that all the following conditions are met:

- the research involves no more than minimal risk to the subjects
- the waiver or alteration will not adversely affect the rights and welfare of the subjects
- the research could not practicably be carried out without the waiver or alteration
- whenever appropriate, the subjects must be provided with additional pertinent information after participation

OR

- the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
    - public benefit or service programs;
    - procedures for obtaining benefits or services under those programs;
    - possible changes in or alternatives to those programs or procedures; or
    - possible changes in methods or levels of payment for benefits or services under those programs;
- the research could not practicably be carried out without the waiver or alteration

Note: Informed Consent cannot be waived under these criteria for FDA-regulated research. Note that some research involving FDA-regulated products is not FDA-regulated and that some research that does not involve FDA-related products is FDA-regulated. Exceptions from the FDA requirements for informed consent may be waived for emergency situations [21 CFR 50.23] or for emergency research [21 CFR 50.24].

10.6. Documentation of Informed Consent (Signed Consent)

Informed consent must be appropriately documented, in accordance with, and to the extent required by [45 CFR 46.117] or [21 CFR 50.27]. Informed consent is documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent. A copy of the signed and dated consent form must be given to the person signing the form.

The consent form may be either of the following:

- a written consent document that embodies the elements of informed consent may be read to the subject or the subject's legally authorized representative, but the subject or representative must be given adequate opportunity to read it before it is signed; or
- a short form written consent document stating that the elements of informed consent have been presented orally to the subject or the subject's legally authorized representative. When this method is used:
    - there must be a witness to the oral presentation; and

- the IRB must approve a written summary of what is to be signed by the subject or representative; and
- the witness must sign both the short form and a copy of the summary; and
- for subjects who do not speak English, the witness must be conversant in both English and the language of the subject.
- the person actually obtaining consent must sign a copy of the summary; and
- a copy of the summary must be given to the subject or representative, in addition to a copy of the short form.

10.7. Waiver of Documentation of Informed Consent (Waiver of Signed Consent)

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either that 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, and the research is not FDA-regulated, or 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, or

Note: Subjects must be asked whether they want documentation linking them with the research, and their wishes must govern. Example: domestic violence research where the Principal risk is discovery by the abuser that the subject is talking to researchers.

- 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. Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent when conducted by non-researchers.

In cases in which the documentation requirement is waived, the investigator will provide in the application materials a written summary of the information to be communicated to the subject, and the IRB will consider whether to require the investigator to provide subjects with a written statement regarding the research.

10.8. Review and Approval of the Informed Consent Form

The IRB is responsible for the review and approval of the informed consent form prepared by the investigator. The wording on the informed consent form must contain all of the required elements and meet all other requirements as described in this section. If the wording of the informed consent has been initially prepared by an external entity (e.g., a pharmaceutical company or a cooperative study group, including National Cancer Institute (NCI) groups) other than by a NDMU Principal Investigator, the Investigator must prepare the consent using the NDMU IRB Consent template.

IRB approval of the wording of the consent must be documented through the use of a certification stamp on each page that indicates the date of the most recent IRB approval of the document and the expiration date. If the consent form is amended during the protocol approval period, the form must bear the approval date of the amendment rather than the date of the approved protocol.

11. Complaints, Non-Compliance and Suspension or Termination of IRB Approval of Research

11.1. Complaints

As part of its commitment to protecting the rights and welfare of human subjects in research, the IRB reviews all complaints and allegations of non-compliance and takes any necessary action to ensure the ethical conduct of research.

Complaints reported to the IRB will be evaluated as possible unanticipated problems involving risks to participants or others under Unanticipated Problems.

A Chair of the IRB will promptly handle (or delegate staff to handle), and, if necessary, investigate all complaints, concerns, and appeals received by the IRB. This includes complaints, concerns, and appeals from investigators, research participants and others.

All complaints, written or verbal (including telephone complaints), and regardless of point of origin, are recorded and forwarded to the IRB Chair and IRB Director.

Upon receipt of the complaint, the Chair will ensure that the complaint is logged and make a preliminary assessment whether the complaint warrants immediate suspension of the research project. If a suspension is warranted, the procedures in Suspension will be followed.

If the complaint meets the definition of non-compliance, it will be considered an allegation of non-compliance according to Non-Compliance.

If the complaint meets the definition of an unanticipated problem involving risk to subjects or others, it will be handled according to Unanticipated Problems.

11.2. Non-Compliance

All members involved in human subjects research are expected to comply with the highest standards of ethical and professional conduct in accordance with federal and state regulations and institutional and IRB policies governing the conduct of research involving human subjects.

Investigators and their study staff are required to report instances of possible non-compliance. The Principal Investigator is responsible for reporting any possible non-compliance by study personnel* to the IRB. Common reports to the IRB that are not serious or continuing are typically protocol violations. However, any individual or employee may report observed or apparent instances of noncompliance to the IRB. In such cases, the reporting party is responsible for making these reports in good faith, maintaining confidentiality and cooperating with any IRB and/or institutional review of these reports.

If an individual, whether investigator, study staff or other, is uncertain whether there is cause to report noncompliance, he or she may contact the IRB Chair directly to discuss the situation informally.

Reports of non-compliance must be submitted to the IRB Office within 10 working days of discovery of this noncompliance. The report must include a complete description of the noncompliance, the personnel involved and a description of the non-compliance.

Complainants may choose to remain anonymous.

*Study personnel include the principal Investigator and any staff member directly involved with participants or the informed consent process.

Definitions

Non-Compliance
failure to comply with any of the regulations and policies described in this document and failure to follow the determinations of the IRB. Non-compliance may be minor or sporadic or it may be serious or continuing.

Serious Non-Compliance
failure to follow any of the regulations and policies described in this document or failure to follow the determinations of the IRB and which, in the judgment of either the IRB Chair or the convened IRB, increases risks to participants, decreases potential benefits, or compromises the integrity of the human research protection program. Research being conducted without prior IRB approval or participation of subjects in research activities without their prior consent (in studies where consent was not specifically waived by the IRB) is considered serious noncompliance.

Continuing Non-Compliance

a pattern of non-compliance that, in the judgment of the IRB Chair or convened IRB, suggests a likelihood that instances of non-compliance will continue without intervention. Generally, non-compliance is not considered "continuing" upon initial reports or audits identifying non-compliance but is typically found only after repeated non-compliance findings. Continuing non-compliance includes failure to respond to request to resolve an episode of non-compliance.

Allegation of Non-Compliance
an unproved assertion of non-compliance.

Finding of Non-Compliance
an allegation of non-compliance that is proven true or a report of non-compliance that is clearly true. (For example, a finding on an audit of an unsigned consent document, or an admission of an investigator of that the protocol was willfully not followed would represent reports of non-compliance that would require no further action to determine their truth and would therefore represent findings of non-compliance.) Once a finding of non-compliance is proven, it must be categorized as serious, non-serious, or continuing.

IRB Review of Allegations of Non-Compliance

All allegations of non-compliance will be reviewed by the IRB Chair and the IRB Director. They will review:

- all documents relevant to the allegation
- the last approval letter from the IRB
- the last approved IRB application and protocol
- the last approved consent document
- the last approved Investigator's Brochure, if applicable
- the grant (if applicable)
- any other pertinent information (e.g., questionnaires, DSMB reports, etc.)

The IRB Chair and an IRB Member will review the allegation and make a determination as to the truthfulness of the allegation. They may request additional information or an audit of the research in question.

When the Chair and the IRB Member determine that noncompliance did not occur because the incident was within the limits of an approved protocol for the research involved, the determination is reported in writing to the Principal Investigator and, if applicable, the reporting party. The determination letter will be copied to the Institutional Official in cases where the Institutional Official and any other parties had been notified at the outset.

If, in the judgment of the IRB Chair and IRB Member, the reported allegation of non-compliance is not true, no further action will be taken. If, in the judgment of the IRB Chair and IRB Director, the reported allegation of non-compliance is true, the non-compliance will be processed according to Review of Findings of Non-Compliance.

If, in the judgment of the IRB Chair and IRB Member, any allegation or findings of noncompliance warrants suspension of the research before completion of any review or investigation to ensure protection of the rights and welfare of participants, the IRB Chair may suspend the research as described in below in Suspension or Termination with subsequent review by the IRB.

The Chair may determine that additional expertise or assistance is required to make these determinations and may form an ad hoc committee to assist with the review and fact gathering process. When an ad hoc committee assists in the review process, the Chair is responsible for assuring that minutes of the meeting are generated and kept to help support any determinations or findings made by the ad hoc committee.

Review of Findings of Non-Compliance

If, in the judgment of the IRB Chair and IRB Member, the reported finding of non-compliance is not serious, not continuing, and the proposed corrective action plan seems adequate, no further action is required and the IRB is informed at the next convened meeting. Otherwise, the matter will be presented to the IRB at a convened meeting with a recommendation that a formal inquiry (described below) will be held.

All findings of non-compliance referred to the IRB will be reviewed at a convened meeting. All IRB members will receive:

- all documents relevant to the allegation
- the last approval letter from the IRB
- the last approved IRB application
- the last approved consent document

At this stage, the IRB may:

- find that there is no issue of non-compliance
- find that there is noncompliance that is neither serious nor continuing and an adequate corrective action plan is in place
- find that there may be serious or continuing non-compliance and direct that a formal inquiry (described below) be held
- request additional information

Inquiry Procedures

A determination may be made by the IRB that an inquiry is necessary based on several issues that may include but are not limited to:

- subjects' complaint(s) that rights were violated
- report(s) that investigator is not following the protocol as approved by the IRB;
- unusual and/or unexplained adverse events in a study
- FDA audit report of an investigator
- repeated failure of investigator to report required information to the IRB

A subcommittee is appointed consisting of IRB members, and non-members if appropriate, to ensure fairness and expertise. The subcommittee is given a charge by the IRB, which can include any or all of the following:

- review of protocol(s) in question

- review of FDA or sponsor audit report of the investigator, if appropriate
- review of any relevant documentation, including consent documents, case report forms, subject's investigational and/or medical files etc., as they relate to the investigator's execution of her/his study involving human subjects
- interview of appropriate personnel if necessary
- preparation of either a written or oral report of the findings, which is presented to the full IRB at its next meeting
- recommend actions if appropriate

Final Review

The results of the inquiry will be reviewed at a convened IRB meeting where the IRB will receive a report from the subcommittee. If the results of the inquiry substantiate the finding of serious or continuing non-compliance, the IRB's possible actions could include, but are not limited to:

- request a correction action plan from the investigator
- verification that participant selection is appropriate and observation of the actual informed consent
- an increase in data and safety monitoring of the research activity
- request a directed audit of targeted areas of concern
- request a status report after each participant receives intervention
- modify the continuing review cycle
- request additional Investigator and staff education
- notify current subjects, if the information about the non-compliance might affect their willingness to continue participation
- modification of the protocol
- modification of the information disclosed during the consent process
- requiring current participants to re-consent to participation
- suspend the study (see below)
- terminate the study (see below)

In cases where the IRB determines that the event of noncompliance also meets the definition of unanticipated problem involving risks to subjects or others, the policy and procedure for review of such events will also be followed.

The investigator is informed of the IRB determination and the basis for the determination in writing and is given a chance to respond. If the IRB determines that the non-compliance was serious or continuing, the results of the final review will be reported as described below in Reporting.

Additional Actions

A finding of serious or continuing non-compliance may also result in the following sanctions, among others:

- suspension or termination of IRB approval of specific research protocols or of all research involving human subjects in which the investigator participates
- sponsor actions: in making decisions about supporting or approving applications or proposals covered by this policy, the DHHS or Agency head may take into account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant has been subject to a termination or suspension as described above, and whether the applicant or the person or persons who would direct or has/have directed the scientific and technical aspects of an activity has/have, in the judgment of the DHHS or Agency head, materially failed to discharge responsibility for the protection of the rights and welfare of human subjects
- institutional or individual action by the OHRP and/or the FDA. The OHRP and/or the FDA may:
    - withhold approval of all new NDMU studies by the IRB
    - direct that no new subjects be added to any ongoing studies
    - terminate all ongoing studies, except when doing so would endanger the subjects

  - notify relevant state, federal and other interested parties of the violations
- individual disciplinary action of the investigator or other personnel involved in a study, up to and including dismissal, pursuant to School of Medicine policies and procedures.

Failure to secure necessary NDMU IRB approval before commencing human subjects research must be reported to the appropriate Dean for disciplinary action.

Investigators should also be aware that, in general, NDMU indemnifies them from liability for adverse events that may occur in NDMU studies approved by the NDMU IRB. Failure to follow approved procedures may compromise this indemnification and make the investigator personally liable in such cases.

11.3. NDMU Students and Employees as Subjects

When NDMU students and/or employees are being recruited as potential subjects, researchers must ensure that there are additional safeguards for these subjects. The voluntary nature of their participation must be paramount and without undue influence on their decision. Researchers must emphasize to subjects that neither their academic status or grades, or their employment, will be affected by their participation decision. Record of the participation cannot be linked to an academic record. The IRB also ensures when necessary a certificate of confidentiality is sought in sensitive research topics such as Mental Health, drug/alcohol abuse, sexual behavior, or others that fall into this category. The Investigator is also responsible for seeking the approval from Human Resources, before approval of any project focused on recruitment of employees.

To minimize coercion, investigators should avoid, whenever possible, the use of their students and employees in procedures which are neither therapeutic nor diagnostic. In these latter situations, investigators should solicit subjects through means such as bulletin board notices, flyers, advertisements in newspapers, and announcements in classes other than their own. When entering a classroom to recruit students and conduct research, e.g. administer a survey, investigators must do so at the end of the class period to allow non-participating students the option of leaving the classroom, thereby alleviating pressure to participate.

11.4. Case Reports Requiring IRB Review

In general, an anecdotal report on a series of patients seen in one's own practice and a comparison of these patients to existing reports in the literature is not research and would not require IRB approval. Going beyond one's own practice to seek out and report cases seen by other clinicians creates the appearance of a systematic investigation with the intent to contribute to generalizable knowledge and therefore would be considered research and would require IRB approval. Case reports will need IRB approval from the institution from where the case is derived.

Definitions

Single Case Report

The external reporting (e.g., publication or poster/verbal presentation) of an interesting clinical situation or medical condition of a single patient. Case reports normally contain detailed information about an individual patient and may include demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The patient information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience.

Case Series

The external reporting (e.g., publication or poster/verbal presentation) of an interesting clinical situation or medical condition in a series of patients (i.e., more than one patient). Case series usually contain detailed information about each patient and may include demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience.

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