

LCB File No. R159-05

**PROPOSED REGULATION OF THE
NEVADA INSTITUTIONAL REVIEW BOARD**

(Note that sections 3.1.3 and 3.2 are located in LCB File No. R154-05)

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1. INTRODUCTION

The Nevada Institutional Review Board (NIRB) is committed to the ethical principles for the protection of human subjects in research set forth in the Belmont Report of the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research. The NIRB recognizes and accepts responsibility, which it shares with its investigators and other researchers for determining that research involving human subjects fulfills these ethical principles.

These policies and procedures are intended to serve as a guide for investigators and their staff who conduct human subject research. While these policies and procedures provide a general overview of the human research protection process and the main regulatory requirements designed to protect human subjects of research, the field of human subject research is continually evolving. Therefore, investigators should ensure that they and their staff understand the information contained herein and follow any mandatory requirements, obtain additional information on any regulatory requirements or expectations relevant to their specific research, and contact the NIRB with any questions they may have. As NIRB policy evolves, and rules change, the information will updated. Please make sure you have the latest information by checking the NIRB Website: TBA.

1.1 NIRB Mission Statement

The mission of the Nevada Institutional Review Board is to:

- 1. ensure that comprehensive and integrative medical diagnostics, treatments, and substances are studied in a fair and consistent manner;*

2. *encourage ethical medical research and literature reviews of therapeutic options;*
3. *support documentation for validity and safety of diagnostics, treatment protocols, and therapeutics by appropriate means of evaluation;*
4. *review, and recommend where appropriate, safe and promising medical diagnostics, treatments, and substances;*
5. *promulgate reasonable and rational practices of the art and science of medicine leading to the integration of efficacious diagnostics, therapeutics, and substances into all healing disciplines;*
6. *establish model guidelines in the efficacy, benefits, and safety of comprehensive medicine;*
7. *promote the health and well-being of Nevada citizens by ensuring that all safe and effective medical diagnostics, therapies, and substances are available for use;*
8. *protect Nevada citizens from high risk and ineffective medical practices, treatments, and substances;*
9. *provide information and access on healthcare choices to Nevada citizens; and*
10. *develop a means for integrating collegiality among healthcare disciplines.*

1.2 NIRB Oversees “Human Subject Research”

“Human subject” means a living individual about whom a professional or healthcare investigator conducting research obtains data through intervention or interaction with the individual or collects identifiable private information. “Human subject” includes an individual who is or becomes a participant in research, either as a recipient of a test article or as a control. A “subject” may be a healthy human or a patient.

“Research” is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalized knowledge. Research includes, surveys and interviews, behavioral investigations, retrospective reviews of medical information, experiments with bodily fluids (e.g., urine, saliva, blood, etc.) and tissues, demonstration and service programs, clinical trials, and any use of a Food and Drug Administration (FDA) regulated product except for use of a marketed product in the practice of medicine.

In their review of human subject research, the NIRB has jurisdiction over all aspects of research involving human subjects, including:

- *methods of identifying potential subjects;*
- *methods proposed for contacting potential subjects;*
- *materials to recruit subjects and proposed remuneration;*
- *pilot studies;*
- *proposals to use or provide stored bodily fluids, tissues, or confidential data;*
- *surveys and interview questions;*
- *the informed consent process and form;*
- *the protocol and summary of the research;*
- *proposed changes to the research;*
- *unanticipated problems involving risk to the subjects or others;*
- *continuing reviews;*

- *uses of investigation drugs and devices in emergencies; and*
- *humanitarian use devices.*

These activities cannot be carried out without prior NIRB review and written approval.

1.3 The Foundation for Human Subject Protection: The Belmont Report.

The basic ethical principles on which the federal regulations for the protection of human subjects are founded are set forth in The Belmont Report. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, which was established in 1974 under the National Research Act, submitted this Report in 1978. The Commission was charged with identifying the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects. The Report sets forth three principles that are basic to the protection of human subjects: Respect for persons, Beneficence, and Justice.

Respect for Persons: Respect for persons involves the recognition of the personal autonomy and dignity of individuals, and the need for special protection of individuals with diminished autonomy. Under this principle, individuals must be given sufficient information to decide whether to participate in a study, they must be able to comprehend the information, and their consent must be voluntarily given, free from coercion and undue influence. Investigators are expected to be particularly sensitive to these factors when vulnerable subjects are involved, to ensure that extra measures are taken to protect the immature and incapacitated, and may even require that they be excluded from participating in certain research. Respect for persons also means honoring the subjects' privacy and confidentiality.

Beneficence: This principle entails an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm. This principle requires assessing the nature and scope of the risks and benefit, and systematically assessing the risks and benefits. All possible harms must be considered, not only physical and psychological injury. All possible benefits, including societal benefits that might be gained from research must also be considered. Benefits to the subjects, or generalizable knowledge to be gained from the research should always outweigh the risks. In assessing the risks and benefits, the appropriateness of involving vulnerable populations is considered.

Justice: The principle of justice requires that the benefits and burdens of research be distributed fairly. Subjects must be fairly selected, and may not be selected either because they are favored by a researcher or held in disdain. Social justice requires an order of preference in the selection of classes of subjects, for example, adults before children. The principle cautions that researchers should not systematically select subjects because of their easy availability, their compromised position, or their social, racial, sexual, or economic position, or because of cultural biases institutionalized in society. Investigators should base inclusion criteria on those factors that most appropriately address the research problem.

1.4 NIRB Review of Human Subject Research

The NIRB must review all human subject research before it may begin, and may approve only research that meets the established regulatory and ethical criteria. In conducting their reviews and providing feedback to investigators on required changes, etc., the NIRB serves to educate its investigators on important human subject research issues.

2. OVERSIGHT OF HUMAN SUBJECT RESEARCH AT NIRB

2.1 Jurisdiction of the NIRB

The NIRB is responsible for reviewing all research falling within the following categories:

- Research sponsored by NIRB;*
- Research conducted by or under the direction of any principle investigator registered with the NIRB;*
- Research conducted by or under the direction of any investigator registered with the NIRB;*
- Research which uses NIRB non-public information to identify or contact potential human subjects for research; and*
- NIRB also oversees all uses of investigational drugs and devices.*

NOTE: These categories cover all research in which NIRB and its staff and investigators may be involved.

NIRB must review research even if it will be conducted at another location out of state. In such situations, the principle investigator and his primary institution remain legally responsible for the conduct of research at the other location. Where another Institutional Review Board (IRB) also has jurisdiction over the research, the investigator should inform the NIRB. The general policy of the NIRB is to require submission of the project to the NIRB for review first, with submission to the other IRB to follow. Final NIRB approval of the project (e.g., consent document, etc.) as amended by the other IRB may be required.

2.2 Reporting Relationships

The Executive Director of the NIRB is responsible for the oversight of human subject research activities. NIRB committees are responsible for overseeing the effective operation, policies, and compliance of the research projects and the conduct of human subject research under NIRB. However, the NIRB committees are independent. No person or other committee—whether internal or external—can overturn an NIRB decision to disapprove, terminate, or suspend a research protocol.

2.2.1 Reporting of Transactions

The NIRB shall keep a record of all transactions and provide the Board of Homeopathic Medical Examiners (BHME), the State Board of Medical Examiners, and the State Board of

Osteopathic Medicine with quarterly reports of all transactions. The BHME may require the NIRB to provide additional reports or recommendations upon request. Such reports may be communicated via website, email, fax, or mail.

2.2.2 Reporting to the Nevada State Board of Homeopathic Medical Examiners

The BHME shall supervise the activities of the NIRB including, without limitation, approving or denying the regulations adopted by the NIRB.

2.2.3 Reporting to the Nevada State Legislature

The NIRB shall submit an annual report to the Nevada State Legislature and make recommendations to the Legislature concerning the enactment of legislation relating to alternative and complementary integrative medicine, including, without limitation, homeopathic medicine.

2.3 Scope of Authority of NIRB

NIRB has the following authority and responsibility over research:

- 1. Review all research projects that will involve human subjects prior to contact of subjects or involvement of human subjects;*
- 2. Approve, disapprove, or require changes in all research (incl. the protocol, consent document, etc.);*
- 3. Notify state government agencies and sponsors of approvals and disapprovals, or forward such notifications to investigators for submission as applicable;*
- 4. Ensure prompt reporting by investigators to the NIRB as well as any sponsoring agency of unanticipated problems involving risk to subjects or others;*
- 5. Ensure prompt reporting to the NIRB by investigators of noncompliance with the IRB or state policies or regulations, and report serious or continuing noncompliance to appropriate state agencies;*
- 6. Suspend or terminate a previously approved project and notify applicable agencies;*
- 7. Conduct continuing reviews of ongoing research as well as any other monitoring such research may require; and*
- 8. Review and monitor the treatment use of investigational drugs, biologicals, and devices outside of the context of research.*

2.4 NIRB Approval or Disapproval or Revision Decision

The NIRB notifies investigators by written document of approval, revisions, and disapprovals (or terminations), with enough detail to explain the decision to the investigator.

Should the NIRB disapprove or terminate a research project, the principal investigator may request to present more information either in person or in writing to the NIRB, explaining why he or she believes the project should be approved or continued. However, a final NIRB decision to require modifications in, disapprove, suspend or terminate a project is

incontrovertible. No other committee or official can override these NIRB decisions. Further, no committee or person can approve an investigator to conduct any research that the NIRB has not approved.

2.5 Notification to Other Agencies of Approvals, Suspensions or Terminations, and Serious or Continuing Non-Compliance

The NIRB may be required to certify certain approvals and to notify agency heads regarding certain actions and activities. In the case of a suspension or termination, the Executive Director will consult with the NIRB Chair for Research and the NIRB. The Executive Director will notify the sponsors or funding agencies of the NIRB decision.

Should the Executive Director receive a report of noncompliance with NIRB policies or procedures or state guidelines or regulations, the Executive Director will inform the NIRB Chair for Research and the NIRB. If it appears that a project has been initiated without required NIRB approval, or that other serious violations may have occurred, the NIRB will require the investigator to suspend all activity at once (consistent with the safety of the subjects). The NIRB then implements procedures for investigating, remedying, and reporting noncompliance.

2.6 Serving as the NIRB for an Unaffiliated Entity

Generally, the NIRB reviews only research involving healthcare professionals registered with the NIRB, sponsorship, or information. However, on occasion, such as where another entity that does not have an IRB is the recipient of a grant under which a NIRB member will be conducting the research (under a subcontract/award), the NIRB may agree that it can serve as the IRB for the grantee. Where the NIRB agrees to this arrangement, the federal granting agency will require the other entity to file an assurance with it (called a Single Project Assurance)—on other entity letterhead—which is then signed by the NIRB Executive Director, NIRB Chair for Research, and NIRB Chair to permit the NIRB to act as the review committee. Different requirements may apply for different arrangements. The NIRB attorney will ensure that any necessary legal documents for these arrangements will also be drafted, reviewed and approved.

2.7 Cooperative Research

Cooperative research projects are those that involve more than one institution. In the conduct of such projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with their respective state or federal regulations. Cooperative research being conducted by a NIRB member at another institution will include NIRB as the approval authority for such research. In such cases, the NIRB will review documents presented by the other institution and may seek consultation with its legal representative.

2.8 Research Conducted by NIRB Members

A NIRB member may conduct research as either an Investigator or Co-Investigator. All Investigators and Co-Investigators must be registered with the NIRB in order to participate in a research project. No research may begin until all approvals have been obtained for the individual submitting a request to participate in a research project.

3. NIRB MEMBERSHIP

The NIRB is comprised of seven regular voting members. They may utilize, as they deem necessary, non-voting members and consultant reviewers.

3.1 Regular Voting Members

3.1.1 Composition

State regulations require the NIRB to have one appointee from the Governor's Office, one appointee from the Senate Majority Leader, one appointee from the Speaker of the House, and four appointees from the Nevada State Board of Homeopathic Medical Examiners (BHME).

The NIRB appointees should be sufficiently qualified through the experience and expertise of its members, and the diversity of its 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. Further, the NIRB will be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice.

Professionals: Professional members of the NIRB generally are to represent the various medical disciplines in Nevada and are to be appointed by the BHME after consultation with the other medical boards.

Non-Professionals: Non-Professionals are laypersons in the general public and residents of Nevada and who are not licensed in any medical discipline.

3.1.2 Terms

NIRB members appointed by the Governor, Senate Majority Leader, and Speaker of the House shall serve four-year terms. NIRB members appointed by the BHME shall serve three-year terms. All NIRB members serve at the pleasure of the appointing authority. An appointing authority must fill a vacancy in the same manner as the original appointment.

3.1.3 (SEE R154-05)

3.2 (SEE R154-05)

3.3 Non-Voting Members

Non-voting members may assist the NIRB in conducting their duties. A non-voting member cannot be counted in the quorum and cannot vote, but can participate in discussions and deliberations. The NIRB Chair may appoint a non-voting member who will serve for only as long as requested.

3.4 Consultants

The NIRB may invite consultants to participate in discussions and deliberations on particular projects where they believe that additional expertise would assist in reviewing a particular protocol. The NIRB Chair has the authority to invite such persons to participate. However, a consultant cannot be counted in a quorum, and cannot vote.

3.5 NIRB Committee Chairs

The NIRB will have a Chair for each committee. Each of these will be chosen from the membership of the NIRB, who are knowledgeable in human subject research, including the regulations, NIRB policies, and ethics relevant to such research. The Committee Chair generally will serve for three-years. The Committee Chair may in his/her discretion extend the term.

3.5.1 Duties of NIRB Chair

The NIRB Chair is responsible for expedited reviews, initial reviews of adverse event reports, and reviews of requests for exemption. The NIRB Chair is responsible for ensuring that the NIRB members are adequately informed about the requirements of the regulations for protocol review so that they conduct appropriate reviews.

The Chair for each committee will designate at least one appointee to serve in his/her absence. Whenever the Committee Chair is not available, one of the designated appointees will assume the responsibilities of the Committee Chair during the period of his or her absence.

3.6 Duties of NIRB Members

Serving as an NIRB member is considered to be an important role of citizenship as well as an honor. It is recognized and appreciated that members serve in addition to their regular occupation and other service. Therefore, it is understood that on occasion a member may need to miss a scheduled NIRB meeting. However, it is very important for continuity, scheduling, and well-rounded reviews that members attend NIRB meetings.

Membership is chosen based on the unique expertise that each member brings to the NIRB. If a member cannot make a meeting, he/she should notify the Executive Director in advance (at least one week before meeting) so that other arrangements (phone) can be secured.

3.7 Liability of NIRB Members

NIRB Members are granted immunity from prosecution. No action may be brought against any member of the NIRB, its employees, consultants, contractors, or researchers for any actions or omissions performed while exercising due care, in the execution of a statute or regulation, as provided in NRS 41.032 to 41.038, inclusive, 485.318, subsection 3, and any statute which expressly provides for governmental immunity

All Nevada statutes of limitations are applicable to NIRB Members including, but not limited to, NRS 41.035, which limits damages sounding in tort. In the event of a complaint, the Nevada Attorney General's Office will defend the NIRB.

4. NIRB MEETINGS

Each NIRB committee is scheduled to meet once a month throughout the year and will be convened as needed. Meeting agendas will be noticed in compliance with Nevada Revised Statutes.

4.1 Committee Meetings/Deadlines

NIRB meetings are generally held at the beginning of each month in which research protocols need full board review. Those protocols exempt from full board review will be reviewed through the expedited process. Categories for submission are as follows:

- Full Committee Review: Proposals with adequate copies must be received two (2) weeks prior to the scheduled monthly meeting of the full committee.*
- Expedited Category: Proposals will be processed and reviewed on a weekly basis throughout the year.*

4.2 NIRB Meeting Agenda

The NIRB Executive Director prepares an agenda for each NIRB meeting, listing all projects that will be reviewed at the upcoming meeting (new and continuing), any adverse event reports to be reviewed by the committee, the projects that have been approved by expedited review, and any other items for discussion.

4.3 NIRB Meeting Procedures

Reviews of all full committee applications (all projects other than expedited) will be conducted only at convened meetings at which four (4) NIRB members (a quorum) are present.

To approve a project, the majority of the members present at the meeting must have voted for approval. Any NIRB member who is involved in any way in a research project being reviewed, or who has any other potential for conflict of interest, may neither participate in the discussions or deliberations (other than to provide information as requested), nor vote on it. The NIRB policy is to have such member leave the room during deliberations. The meetings will be chaired by the Chair, or in his/her absence, a designee.

4.4 Actions that the NIRB May Take at Meetings

NIRB members will discuss each project and vote to approve or disapprove the project or proposed modification to an already approved project, or to defer a decision until revisions are implemented, additional information is provided, or further expert review is obtained (including invitation of consultants). Under certain circumstances, if minor revisions in the submitted documents are required or a missing document of minor importance is to be obtained, the NIRB may delegate the Executive Director to subsequently issue an approval of the project on behalf of the NIRB, upon completion of these tasks.

4.5 NIRB Meeting Minutes

The Executive Director will prepare the NIRB minutes of each meeting. The minutes will include the following information: 1) attendance; 2) actions taken by the NIRB; 3) the number of members voting for, against, and abstaining in the decisions; 4) the basis for requiring changes in a project, or disapproving, suspending or terminating a project; and 5) summary of the discussion of issues of concern and their resolution.

4.6 NIRB Notification of Meeting Decisions

After each NIRB meeting, the Executive Director will notify the principal investigator in writing of the outcome of the review. The investigator will be informed, in writing, of whether the project was approved, whether it requires revisions before approval may be granted, whether additional information is needed from the investigator before approval can be voted upon, or whether it was disapproved (in sufficient detail for the investigator to understand). The investigator will also be informed at the time of approval, in writing, when an application for extension is due.

4.7 Time Sensitive Protocols

Normally, human research protocols must be received at least two weeks prior to the committee meeting at which they will be reviewed. This allows assigned reviewers enough time to conduct a thorough review prior to the scheduled meeting of the full committee.

On certain occasions, however, some protocols require a rapid response due to extenuating circumstance that fall beyond the control of the principal investigator. Protocols in this category may warrant a waiver of the required two-week submission period to allow a review by the NIRB at the earliest regularly scheduled meeting. In such cases, the protocol package must be submitted with a memorandum explaining the circumstances giving rise to the request in enough detail that the request may be considered. The NIRB Chair will make a determination whether the protocol qualifies for special handling and if it does, will advance the protocol to the very next NIRB meeting for early review. The investigator will be notified by Executive Director of the decision to grant or deny the request.

NOTE: Research protocols involving protected populations (fetuses, pregnant women, children/minors, cognitively impaired persons, prisoners, etc.) will be reviewed through normal time frame process only.

5. LEVELS OF NIRB REVIEW: EXEMPT, EXPEDITED, FULL COMMITTEE REVIEW

Not all research requires review and approval by the NIRB. Some research is “exempt” under federal regulations, but may still be reviewed according to NIRB policy. This category of research is reviewed via the “expedited review” process. However, investigators are required to submit all research to the Executive Director to formally determine the category of research.

5.1 Exempt Research

Some research is exempt from having to meet the requirements set forth in the regulations. These exemptions do not apply to research involving prisoners, children, fetuses, pregnant women, or human in vitro fertilization. Further, the exemption for certain research involving surveys or interviews does not apply to research involving children. No research involving FDA regulated products is exempt.

5.1.1 Existing Records Recorded Anonymously

The most common exemption from full board review for research with NIRB is research involving the collection or study of existing data, documents, records, data sources 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.

This provision permits the NIRB to grant an exemption only when the data that the investigator proposes to use for the study already exist at the time the investigator submits the proposal. Similarly, if the data recorded can be linked back to the subject (i.e. by codes), the research does not fall into this category (though it may still qualify for expedited review).

5.1.2 Surveys, Interviews, Public Observations, and Educational Tests

This exemption is available for research falling in these categories involving adults unless the information is both recorded in such a way that the human subjects can be identified and the disclosure of the subjects’ responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, or reputation. Thus, surveys involving sensitive topics (i.e., drug or alcohol use, sexual habits, etc.) where there is any code or other link between the information and the subject, is not exempt. However, research under this category that would not otherwise be exempt is exempt if it involves elected or appointed public officials or candidates for public office. The exemption does not apply to research involving children, except for research involving observations of public behavior when the investigator does not participate in the activities being observed.

5.1.3 Other Exemptions

Other categories of exemptions include: 1) research conducted in established or commonly accepted community settings involving normal community practices; 2) research and demonstration projects which are designed to study, evaluate, or otherwise examine: public benefit or services programs; procedures for obtaining benefits or services under those programs; possible changes in or alternatives to those programs or procedures; or possible changes in methods or levels of payment for benefits or services under those programs; and 3) taste and food quality evaluation and consumer studies if: a) wholesome foods without additives are consumed; or b) a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical or environmental contaminant at or below the level found to be safe by the FDA, or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

5.2 Expedited Review

5.2.1 Categories of Research Eligible for Expedited Review

If the proposed research is minimal risk and it is of a type of research that falls into one of the categories of research listed below, the Chair (or an experienced designated reviewer) may review and approve the research. “Minimal risk” means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests. Investigators should note that “risks” include more than just physical risks. Thus, risks due to possible breaches of confidentiality, social/economic or psychological repercussions, etc. must be considered in determining the degree of risk as well. For this reason, although research on specimens may require only minimal intervention (or no intervention where specimens may be archived), some such research may not fall into this category of review.

Expeditable Categories:

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met:

(a) Research on drugs for which an investigational new drug application is not required (NOTE: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review); or

(b) Research on medical devices for which: (i) an investigational device exemption application is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

(a) from healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week.

(b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples:

(a) hair and nail clippings in a non-disfiguring manner;

(b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;

(c) permanent teeth if routine patient care indicates a need for extraction;

(d) excreta and external secretions (incl. sweat);

(e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;

(f) placenta removed at delivery;

(g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;

(h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;

(i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;

(j) sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. NOTE: Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications. Examples:

(a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;

(b) weighing or testing sensory acuity;

(c) magnetic resonance imaging;

(d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity,

(e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate weight, and health of the individual.

5. Research involving materials (e.g., data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (i.e., as medical treatment or diagnosis).

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

8. Continuing review of research previously approved by the convened NIRB as follows:

(a) where: (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

(b) where no subjects have been enrolled and no additional risks have been identified; or

(c) where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the NIRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Additional expeditable review:

In addition, the NIRB may approve minor changes to already approved projects through expedited review (e.g., changes of an administrative nature, minor revisions in the text of an informed consent document or advertisement, corrections in the text of documents, and other minor changes), provided that the changes do not increase the risks involved. Extension review may be conducted by expedited review only where the study falls into one of the above categories and is minimal risk, or where a study has been closed to accrual, and intervention has been completed, but the investigator is still collecting follow-up data.

An investigator may apply for expedited review, or the Chair may review a full submission by expedited review if it meets the regulatory criteria. If the Chair determines that the project submitted for expedited review requires full board review, the investigator will be notified in writing, and the investigator will be required to submit the information requested.

A NIRB member who reviews research under this expedited process may not disapprove the research protocol or minor changes through this process. Instead, if he/she disagrees with the submission, the materials will be submitted to a full NIRB committee for review and decision.

5.3 Full Committee Review and Application Process

All other research related issues will be reviewed by the full NIRB. To obtain such review, investigators must submit adequate number of copies of the completed protocol package to the Executive Director.

If the protocol package an investigator submits to the Executive Director is not complete, the Executive Director will notify the investigator that the project cannot be reviewed and will identify the missing items. The protocol package will not proceed through the process until the package is complete.

6. CRITERIA FOR NIRB REVIEW AND APPROVAL OF RESEARCH

6.1 General NIRB Review

When reviewing a protocol, the NIRB follows the criteria below:

6.1.1 Risks and Benefits

One of the NIRB's major responsibilities in reviewing research is to ensure that risks to subjects are minimized, and that the risks are reasonable in relation to the anticipated benefits, if any, to subjects and to the importance of the knowledge that may reasonably be expected to result.

Risk: The probability of harm, including: physical (e.g., in biomedical studies, the risks of adverse events or the risk of randomization and not receiving the treatment that turns out to be more efficacious); psychological (e.g., depression, confusion, fear, stress, loss of self-esteem); and social or economic (e.g., breaches of confidentiality and privacy in research involving drug or alcohol use, sexual behavior, mental illness, illegal activities, or in genetic research, which could lead to embarrassment in a social group, prosecution, or loss of employment, insurability concerns, etc.). Both the probability and magnitude of possible harm may vary from minimal to significant. Risks include immediate risks of study participation as well as risks of long-term effects.

Benefit: A benefit is a valued or desired outcome—an advantage. Anticipated benefits may express the probability that subjects and society may benefit from the research procedures. Research may benefit the individual, for example, by alleviating a condition or providing a better understanding of his or her disease. Research that has no therapeutic intent may still benefit society as a whole. If research will not benefit individuals, it is required to provide a reasonable likelihood of resulting in benefits to society, e.g., the advancement of important knowledge.

In reviewing the risks to ensure that they are minimized, the NIRB may consider: whether previous studies have been done; whether the investigators serve a dual role as instructor/investigator or physician/investigator role to the subject and, if so, whether safeguards are necessary; whether the research is designed to yield useful data; whether there are any monitoring mechanisms if necessary; and whether follow-up counseling or other care will be provided (i.e., genetic research) as applicable. Thus, the NIRB may consider the study design in reviewing investigators' studies, since putting subjects at any risk or even

inconveniencing them with a study that is methodologically flawed such that little or no reliable information will be obtained would be unethical.

6.1.2 Selection of Subjects

In making this determination, the purpose of the study, as well as the setting of the study, are relevant. Proposed uses of vulnerable populations such as children, prisoners, pregnant women, mentally disabled are more closely scrutinized. Investigators must take care to ensure that women of child-bearing age are not inappropriately restricted from entering Phase 1 and 2 trials and that sufficient methods to monitor for pregnancy are proposed and followed.

6.1.3 Issues of Privacy and Confidentiality

The NIRB addresses issues of subject privacy and confidentiality. These issues are of particular concern in requests to review databases and medical records without patient consent, and research that will elicit potentially sensitive or damaging information (i.e., interview or genetic research) about the subject or a group to which the subject belongs. Factors that may be considered include: the importance of the research; the sensitivity of the information sought to be obtained and to which the investigator will have access; whether links to identifiers will be maintained; the procedures the investigator has devised for protecting the information; and, if the review is for the purpose of identifying potential subjects, whether there are other feasible methods for recruiting subjects. Investigators should address these issues of confidentiality and privacy under the “Risk” section of their protocol package.

Investigators may consider applying for a “Certificate of Confidentiality” for certain types of biomedical, behavioral, clinical, or other research where the disclosure of information learned about a subject could be particularly damaging. The Certificate protects against compulsory disclosure (i.e., a subpoena or court order) of research data that identifies a specific individual (not information in the aggregate), although review by state agencies is still permitted. Certificates are issued only when the research is of a sensitive nature where the protection is judged necessary to achieve the research objectives. The categories of research explicitly covered include:

- 1. Research relating to sexual attitudes, preferences, or practices;*
- 2. Research relating to the use of alcohol, drugs, or other addictive products;*
- 3. Research pertaining to illegal conduct;*
- 4. Research involving the collection of information that if released could reasonably be damaging to the individual’s financial standing, employability, or reputation;*
- 5. Research involving the collection of information that would normally be recorded in a patient’s medical record which, if disclosed, could reasonably lead to social stigmatization or discrimination; and*
- 6. Research involving the collection of information pertaining to an individual’s psychological well-being or mental health.*

In addition, Certificates may be issued for other categories of research considered sensitive because of specific cultural or other factors, upon justification.

Various governmental agencies within the Department of Health and Human Services (HHS) provide these certificates: the National Institute of Health (NIH), the National Institute on Alcohol Abuse and Alcoholism, the National Institute on Drug Abuse, the National Institute of Mental Health, and the Center for Disease Control.

6.1.4 The Informed Consent Process

The NIRB carefully reviews the proposed informed consent method and form to ensure that human subjects will be adequately informed regarding the proposed research.

6.1.5 Additional Monitoring or Safeguards

A NIRB may decide that it requires review frequency more than annual or that it needs verification from other sources that no material changes have been made since the previous review, and/or that the project needs additional monitoring or procedures to ensure the safety of the subjects. Both of these determinations generally will be based on the degree of risk in the study, taking into account any vulnerability of the subject population.

6.2 Additional Requirements for Vulnerable Populations

Certain groups of human subjects are considered to be particularly vulnerable to coercion or undue influence in a research setting. Vulnerable populations include: children (also indirectly an infant, if a nursing mother is a subject of research), mentally disabled (cognitively impaired) persons, prisoners, pregnant women, and economically or educationally disadvantaged persons. The regulations identify additional requirements for review and approval of research involving fetuses, pregnant women, and human in vitro fertilization, prisoners, and children. In reviewing research projects involving all categories of vulnerable subjects, the NIRB ascertains the use of the vulnerable population being adequately justified and that additional safeguards are implemented to minimize risks unique to each group, as appropriate. A summary of the additional requirements for review and approval of research involving children, prisoners, and pregnant women and fetuses is presented below:

6.2.1 Review of Research Involving Children

“Children” are defined as persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. Therefore, “children” include any persons under the age of 18 (unless the child has been emancipated by court order, marriage, or is on active military duty).

Research involving children can be classified into one of four categories depending upon the risks and benefits of the proposed research, which can be approved as follows:

1. *Research involving no greater than minimal risk. “Minimal risk” means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests. This research is approvable in accordance with the general NIRB review criteria provided that adequate provisions are made for soliciting the assent of the child and parental permission. NOTE: Requires assent from child and permission from one parent/guardian.*
2. *Research involving greater than minimal risk, but presenting the prospect of direct benefit to individual subjects. This research is approvable in accordance with the general NIRB review criteria if: a) the risk is justified by the anticipated benefit to the subjects; b) the relationship of risk to benefit is at least as favorable as any alternative approach; and c) adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians. NOTE: Requires assent from child and permission from one parent/guardian.*
3. *Research involving greater than minimal risk and no prospect of direct benefit to individual subjects but likely to yield important generalized knowledge about the subject’s disorder or condition. This research is approvable in accordance with the general NIRB criteria if: a) the risks represent a minor increase over minimal risk; b) the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations; c) the intervention or procedure is likely to yield generalized knowledge about the subjects’ disorder or condition, which is of vital importance for the understanding or amelioration of the subjects’ disorder or condition; and d) adequate provisions are made for soliciting assent of the children and permission of their parents or guardians. NOTE: Requires child assent and permission from both parents, unless one is not reasonably available, deceased, unknown, legally incompetent, or does not have legal responsibility for care of the child.*
4. *Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. This research is generally not approvable by the NIRB without the appointment of and review by a separate panel of experts. NOTE: Requires assent from child and permission from one parent/guardian.*

Wards of State. Where children are wards of the state or another agency or institution, additional restrictions apply, and they may only be included in research that is related to their status as wards, or which is conducted in schools or other institutions in which a majority of children are not wards. If the NIRB approves research under this provision, it must appoint an advocate for each child that is a ward.

No Exemption for Research involving Surveys or Interviews. Unlike research involving adults, the exemption for research involving survey procedures, interviews, educational tests, or public observations (except where the investigator does not participate in the activities being observed) does not apply to research involving children.

Child Abuse Reporting. The State of Nevada requires the reporting of suspected child abuse and neglect. NRS 432B.010-390. Investigators are not exempt from this law. NRS 432B.220(3). If the protocol involves interviewing children about topics that might lead to a suspicion or to knowledge on the part of the investigator of child abuse or neglect, the child (and parent or guardian) must be informed of the reporting requirement as part of the informed consent process.

Considerations for research involving children. What follows are some questions that may be appropriate, depending upon the study, for investigators and NIRB to consider in conducting or reviewing research-involving children:

- Has the research been addressed first in adults if possible (while children usually should not be the initial group to be involved in research studies, in some instances, the nature and seriousness of the illness may warrant their participation earlier based on careful risk and benefit analysis)? Will older children rather than younger be used?*
- Have any adult research results shown that the research is likely to benefit children or that it will at least not be harmful?*
- Are normal volunteers and the number of subjects justified?*
- Does the research hold out a prospect of direct benefit to individual children and can that benefit be obtained in a less intrusive way?*
- Are the proposed techniques the least invasive to achieve the desired result?*
- Will efforts be made to ensure that parental permission is non-coercive and expectations are realistic? That child assent is appropriate?*
- Are special needs of adolescents such as counseling or confidentiality addressed?*
- Are there any issues of confidentiality and reporting in sensitive research about child abuse, sexuality, drug use, etc. that need to be addressed?*
- Does the research address whether parents should/will be present?*

6.2.2 Requirements for Review of Research Involving Prisoners

Additional safeguards for prisoners should be provided since Prisoners may be under constraints because of their incarceration that could affect their ability to make a truly voluntary and non-coerced decision whether or not to participate as subjects of research.

A “prisoner” includes any person who is sentenced to a penal institution under a criminal or civil statute as well as individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution. NOTE: Research involving prisoners does not qualify for an exemption.

Research involving prisoners is approvable if it falls into one of the following categories:

- Studies’ regarding the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;*

- *Studies of prisons as institutions, or of prisoners as incarcerated persons, if those studies present no more than minimal risk or inconvenience to the subjects;*
- *Research on conditions affecting prisoners as a class; and*
- *Research on practices that are intended, and reasonably likely, to enhance the well-being of the subjects; however, if some of the prisoners will be assigned to control groups which will not benefit from the research, then the study must first be approved by the Nevada Department of HHS.*

In addition to the general requirements for review, in reviewing prisoner research, the NIRB is required to:

- *Ensure that the membership of the NIRB reviewing the protocol includes a prisoner or a prisoner representative with appropriate background and experience to serve in that capacity, and that the majority of the NIRB not be associated with the penal institution involved;*
- *Review that any advantages that prisoners will realize as a result of participating in the research, when compared to the general living conditions within the prison, are not so great as to impair prisoner's ability to weigh the risks and benefits of participation and freely choose whether to participate;*
- *Review that the risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;*
- *Review procedures for selecting subjects to determine whether they are fair, and free from arbitrary manipulation by prison authorities or prisoners;*
- *Review that control subjects will be selected randomly from among the group of eligible volunteers, unless the principal investigator justifies a different procedure;*
- *Review the information presented during the recruitment and consent procedures to ensure that it is in a language, and level of complexity, that is understandable to the subject population;*
- *Ensure that the parole board will not take participation in the study into account, and that each prisoner will be informed that participation will have no effect on parole; and*
- *Ensure that adequate provision will be made for follow-up care as necessary.*

6.2.3 Requirements for Review of Research Involving Fetuses, Pregnant Women, In vitro Fertilization; and Dead Fetuses, Fetal Material, and Placenta

Additional protections are required for research involving fetuses, pregnant women, and in vitro fertilization and dead fetuses, fetal material and placenta, all of which types of research do not qualify for an exemption .

In addition to the general requirements for review, the NIRB is required to: determine that adequate consideration has been given to the manner in which potential subjects will be selected; and that adequate provision has been made by the applicant for monitoring the actual informed consent process, including, where appropriate, involvement of the NIRB or subject advocates in such oversight.

With regard to fetuses in utero (for research aimed at the mother or the fetus), the regulations prohibit any research unless:

- *Appropriate animal studies and studies with non-pregnant women are completed;*
- *The risk to the fetus is minimal unless the activity is to meet the health needs of the mother or the health needs of the fetus (in all cases, it is the least possible risk for achieving the objectives of the study);*
- *Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate the pregnancy or in determining the viability of the fetus at the time of termination;*
- *No procedural changes which may cause greater than minimal risk to the fetus or the pregnant woman will be introduced into the procedure for termination of the pregnancy solely in the interest of the activity;*
- *No inducements, monetary or otherwise, may be offered to terminate the pregnancy; and*
- *Informed consent of both the mother and father has been obtained unless the research is for the health needs of the mother or the father is not reasonably available, the pregnancy resulted from rape, or the father's whereabouts or identity is unknown.*

With regard to research involving fetuses ex utero:

- *No research is permitted until it has been determined whether the fetus is viable unless: 1) there will be no added risk to the fetus resulting from the activity, and the purpose is the development of important biomedical knowledge which cannot be otherwise obtained; or 2) the purpose is to enhance the possibility of survival;*
- *No research may be conducted on a nonviable fetus (one that cannot possibly survive even with available medical therapy) unless vital functions will not be artificially maintained, experimental activities would not terminate the heartbeat or respiration of the fetus, and the purpose of the activity is to develop important biomedical knowledge which cannot otherwise be obtained; and*
- *Research involving dead fetuses, fetal material, and the placenta has been permitted since a Presidential memorandum lifting the moratorium was issued in February 1993. Such research must be conducted in accordance with state and local laws. Where fetal tissue transplantation research is conducted, written informed consent of the woman is required (to include disclosure of the physician's interest, if any, in the research), which consent may only be obtained after the decision to abort, no alteration in the timing or methods of the procedure, informed consent of the donor and a statement by the researcher to include that the tissue may have been obtained from a spontaneous or induced abortion, and that the researcher had no part in the timing, method, or procedures used to terminate the pregnancy.*

In addition, the purchase or sale of fetal tissue is prohibited, as is the directed solicitation or donation or solicitation of such tissue obtained from an induced abortion.

6.3 Additional Requirements for Drug Studies

6.3.1 Investigational New Drug Application

Drugs that have not been approved for marketing by FDA under an approved new drug application (“NDA”) may only be studied pursuant to an investigational new drug application (“IND”) in effect for a particular use (unless an exemption applies). This requirement applies regardless of the phase of study. A “drug” includes products listed in the USP, which are intended for use in the diagnosis, mitigation, or cure of disease, or that is intended to affect the structure of function of the body of a person. Naturally-occurring substances or dietary supplements are generally regarded as safe.

Typically, a drug company will be the holder of the IND and will contract with NIRB to conduct research using the investigational drug. In these cases, the investigator does not submit the IND application to FDA. Occasionally, an investigator may seek to initiate studies him/herself, using an investigational drug, or a marketed product that requires an IND. In such cases, the investigator is responsible for preparing the FDA Form-1571 (the IND application) according to the requirements set forth in 21 CFR 312.23, but should list NIRB as the “sponsor” of the study and forward the form and attached documentation to NIRB approval. The principal investigator will become responsible for fulfilling the additional requirements of a sponsor as set forth in FDA regulations, and must familiarize him/herself with these requirements. Investigators may not begin these studies until 30 days have passed since the submission of the IND application. Within this period, FDA will have provided the IND number and communicated with the investigator regarding any necessary changes/additions.

Investigators should inform the NIRB in their application that their study is investigator initiated, and attach the IND application and the FDA’s IND response letter.

6.3.2 Studies Involving Marketed Drugs

Questions sometimes arise regarding whether research involving an approved drug (for instance, marketed drugs for different uses) requires the submission of an IND. FDA does regulate studies involving marketed drugs, and an IND is required for such a study unless all of the following are met:

- 1. The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;*
- 2. If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;*
- 3. The investigation does not involve a routine of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;*
- 4. The investigation is conducted in compliance with the requirements for institutional review set forth in NIRB approval and with the requirements set forth in Informed Consent; and*
- 5. The investigation is conducted in compliance with the requirements of restrictions on promotion and charging for investigational drugs.*

If an investigator is uncertain whether FDA would require an IND (e.g., it is not clear whether FDA may consider the proposed use to significantly alter the risks), he/she should contact FDA. Investigators should address these criteria in their NIRB submission and, if they have submitted an IND application, attach it and the FDA IND response letter.

6.3.3 Radiopharmaceuticals

Certain research designed only to study the basic metabolism of a radioactive drug or to gather basic information about human physiology, or biochemistry, but not intended for immediate therapeutic, diagnostic or similar purposes, or to determine the safety and effectiveness of the drug in humans for such purposes, is exempt from the IND requirement provided that the radiation dose falls within the limits prescribed by FDA, the study design meets certain criteria, and the protocol is approved by a Radioactive Drug Research Committee. Such studies still require NIRB approval.

6.4 Additional Requirements for Device Studies

6.4.1 Investigational Device Exemption

Medical devices may be subject to FDA regulation. A “device” includes any instrument, machine, implement, or other product that does not achieve its primary intended purpose by chemical action or by being metabolized and which is intended for use in the treatment, cure, diagnosis, or mitigation of disease or other conditions in humans. With limited exceptions, devices that have not been approved by FDA under the pre-market approval process (“PMA”) or cleared for marketing under the 510(k) process (or an exemption) cannot be used on humans except pursuant to an approved investigational device exemption (“IDE”). The IDE permits a new device to be studied for its safety and/or effectiveness. In addition, a device that is to be studied for a different indication from its approval may also be subject to this requirement.

An IDE may be obtained in one of two ways. If the study is a “significant risk” (“SR”) device study, FDA must approve the IDE. If the study is a “non-significant risk” (“NSR”) device study, the NIRB may approve the study, as set forth below, and the investigation will be deemed to be subject to an IDE.

A SR device is defined as one that is:

- 1. Intended as an implant and that presents a potential for serious risk to health, safety, or welfare of a subject;*
- 2. purported or represented to be for use in supporting or sustaining human life and that presents a potential for serious risk to health, safety, or welfare of a subject; or*
- 3. for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and that presents a potential for serious risk to health, safety, or welfare of a subject; or 4) otherwise presents a potential for serious risk of harm to a subject.*

To obtain approval of a device study, the investigator should inform the NIRB whether there is an FDA approved IDE for the study, and provide the NIRB with the IDE investigational plan and number. If FDA has not approved an IDE, the investigator must submit the information set forth below. In such cases, the NIRB makes the following two separate determinations (unless it concludes that the study is exempt):

1. Non-significant Risk Determination. First, the NIRB determines whether the device study is NSR. The sponsor should have made this determination (with which the NIRB can agree or disagree), and this information should be provided to the NIRB, along with a description of the device, reports of prior investigations with the device, information on any other NIRB reviews, the proposed investigational plan, a description of subject selection criteria and monitoring procedures, and any other information the NIRB needs to make its determination.

The risk determination is based on the proposed use of the device in the investigation, not solely on the device alone. Thus, if a subject must undergo a procedure as part of the study, the potential harm from the procedure as well as from the device is considered. However, the amount of potential reduced risk associated with the investigational device versus a commercially available product is considered only in the next step, when assessing whether the study can be approved.

2. Study Approval or Disapproval. If the NIRB concludes that the device is NSR, the NIRB next considers whether the study should be approved using the same criteria as employed for any study.

Investigators are required to make reports of each use of an investigational device on a subject, among other device-specific study requirements (as well as follow the informed consent and NIRB requirements), even for NSR device studies.

7. ADVERTISING AND COMPENSATION IN HUMAN SUBJECT RESEARCH

7.1 Policy on Advertisement. The NIRB's policy on advertisements of human research studies does not prohibit the inclusion of monetary amounts for compensation. Studies and advertisements in which the amount offered for participation is felt to be coercive, however, will not be approved by the NIRB. Likewise, if the compensation amount listed is felt to be the focal point of the ad or is felt to be "eye-catching" or would change someone's mind about participation, then it most likely will not be approved.

7.2 Policy on Compensation. If compensation is being offered, it is preferred to state in an advertisement that "Participants will be compensated for their time and inconvenience." An advertisement most likely will be approved if worded, "Participants will be compensated up to \$___ for their time and inconvenience," so long as the amount is not felt to be coercive and the statement is not in bold or larger letters so as to attract someone's attention. Consent forms for such studies should have a "Payment for Participation" section that should state something similar to, "In return for the time and inconvenience of participating in this study, you will be paid \$___ for your participation. If you do not complete the study, you will

receive partial compensation for partial participation.” Participants should be informed if, when, and how they will receive compensation.

7.3 NIRB Funding. *The NIRB is accountable to the BHME for all the financial activities of the NIRB as follows:*

- 1. All monies received by the Nevada Institutional Review Board must be deposited in financial institutions in the State of Nevada that are federally insured or insured by a private insurer approved pursuant to NRS 678.755;*
- 2. The money must be kept separate from any money to be used by or for the BHME; and*
- 3. The deposited money must only be used to carry out the activities of the NIRB and to pay the expenses incurred by the NIRB in the discharge of its duties.*

To assist the NIRB in carrying out its duties, the NIRB may be funded by:

- 1. A nonprofit organization, created by the Board of Homeopathic Medical Examiners, which is exempt from taxation pursuant to 26 U.S.C. § 501(c)(3); and*
- 2. Grants, gifts, appropriations or donations.*

The NIRB may not be funded by any money from:

- 1. The sponsor of any research study; or*
- 2. The manufacturer of any device, drug or other substance regulated by the BHME.*

8. INFORMED CONSENT REQUIREMENTS

8.1 *The Process of Informed Consent and its Exceptions.*

Informed consent for research involves presenting information orally and obtaining a written consent on a form that has been approved by the NIRB prior to entering a subject into a study. The NIRB may waive the requirement for both obtaining informed consent and for documenting consent under certain circumstances. However, unless an investigator has obtained approval for other than the standard, written informed consent from the NIRB, he or she may not alter the method by obtaining consent in any other way, including over the telephone.

Investigators should keep in mind that informed consent is also an ongoing process. Thus, where an investigator obtains new information that may impact the subject’s continued willingness to participate in the research (e.g., new information about the study, adverse events, alternative new treatments, etc.), this information should be provided to the subjects, after review and approval by the NIRB.

8.2 *Content Requirements for Consent Forms*

Consent forms must be understandable by potential subjects. Translating technical language into lay language at about an eighth grade level facilitates understanding. Programs are available to assist in translating technical consent form information into lay language.

The regulatory requirements are discussed below, but are set forth in a simple to follow “Consent Form Template.” Following the template will ensure that all required elements for informed consent are addressed.

1. Purpose of Study. This section requires a clear and accurate statement that the study is research, and an explanation regarding the purposes of the research. To allow subjects to make an informed decision whether to participate, this section should clearly explain if a study is a pilot study or a phase I drug study, informing the subject that he or she will be the first to participate in the treatment, intervention, or process. This section also explains the approximate number of subjects for drug and device studies.

2. Procedures. This section fully describes procedures that will be used, preferably in order of their occurrence, identifying all experimental procedures, and the approximate duration for each procedure or activity. For instance, a survey study may explain that the subject will be asked to answer x number of questions about a topic, which should take about x minutes to complete. Each type of study’s procedures are described—e.g., a genetic testing study would describe whether samples will be linked, who will have access to information and codes, whether samples may be used for a secondary research use and/or commercial development, and, if so, whether subjects will be re-contacted, among other things.

3. Potential Risks or Discomforts Potential Risks or Discomforts. In this section, the investigator must clearly explain any risks or discomforts that are reasonably foreseeable. In biomedical research, the investigator should explain, in lay language, the statistical probability of risk occurrence, risk prevention measures, reversibility, and treatment, as known. In behavioral research, investigators should consider such risks as stress, embarrassment, breach of confidentiality, etc. The investigator should note that the treatment or procedure may involve risks that are currently unforeseeable. If there is any possibility that a study may involve risks to the embryo or fetus if the subject becomes pregnant, this should also be stated, and any required prevention measures should be discussed.

4. Anticipated Benefits Anticipated Benefits. A subject or society, or both, may benefit from research. If there are any direct benefits to the subject reasonably expected from the research, the consent form must state them. The potential benefits should not be overstated or guaranteed. If there are no benefits to the participant that are expected, this section must state so.

This section should also explain the potential benefits to society, for example, the advancement of knowledge, improved safety, or the potential health benefits to others. All research should have some potential benefit for society; if it is not intended to provide any useful information, it should not be conducted. An example of a statement regarding expected benefits where no benefit to the subject is expected is as follows:

“You should not expect to benefit directly from this research. However, your participation in this research may lead to information that could help individuals with similar concerns as yourself if it identifies a new and better way to assist such people.”

NOTE: Payment for participation is not a benefit of the research and should not be listed as a benefit, but can be listed in the “Procedures” section.

5. Alternatives to Participation Alternatives to Participation. In biomedical research the investigator must state any available alternative procedures or course of treatment/training/education that might be advantageous to the subject. Alternatives might be no treatment at all, or watchful waiting. When appropriate, the relative risks and benefits of the therapeutic intervention compared to the research should be stated. Where a medical protocol is not therapeutic, the form should explain that because the research is not therapeutic, the only alternative is not to participate in the research.

6. Confidentiality of Records. This section must explain the extent to which information obtained in connection with the research and that could identify the subject will remain confidential and will not be disclosed without the subject’s permission. Consent forms should generally refrain from broadly stating that records will be kept confidential, because a number of agencies or people may have access to the records. For example, in a drug study, FDA and the sponsor will have access to the information. In addition, the NIRB, Executive Director, or even other physicians and nurses, where emergency care must be given to a subject, may have access to the information. Also, the investigator or others may use the records to publish articles. While the subject will not be identified, the information in the records will be used, so the information is not kept strictly confidential. Further, research records may be subpoenaed in a court of law. Thus, these and other limits on confidentiality, including the State of Nevada requirement for reporting of suspected child abuse or neglect, and adult abuse or neglect, must be clearly explained in the consent form, as applicable. This section must explain the extent to which information obtained in connection with the research that could identify the subject will remain confidential and will not be disclosed without the subject’s permission.

NOTE: Where a research study involves sensitive topics, researchers should consider applying for a Certificate of Confidentiality. However, such certificates should not be used to attempt to avoid reporting of suspected abuse or neglect.

7. Emergency Care and Compensation for Injury. For studies that are greater than minimal risk, subjects must be told whether any compensation and/or medical treatment is available if injury should occur as a result of the research. The extent and nature of the compensation should be explained.

The following language is required for those studies conducted that are at greater than minimal risk:

“If you are injured as a result of this study, you will be provided with emergency treatment at usual charge. No commitment is made to provide free medical care or money for injuries to participants in this study.”

8. Contact Information. Investigators are required to provide names and telephone numbers of persons to contact if the subject has questions regarding the research. Investigator

concerns or questions regarding subjects' legal rights, and injuries, should be directed to the NIRB attorney.

9. *Participation and Withdrawal.* This section must indicate that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. When appropriate, this section should state the medical or health consequences of a subject's decision to withdraw. In addition, where applicable, the consent form should also state any anticipated circumstances under which the subjects' participation may be terminated without regard to the subject's wishes (e.g., adverse reactions or non-adherence to protocol instructions). Further, if a subject will need to continue in some form of treatment due to entry into the study that should be explained to the subject. Sample statements, where applicable, would be follows:

"Your participation in this research is strictly voluntary. You have the right to choose not to participate or to withdraw your participation at any point in this study without prejudice."

"Although you are free to decide to stop participating in the research at any time, because you are entering into a study of X, you will need follow-up treatment consisting of X."

"The investigator may decide to withdraw you from this research activity without your consent if he/she feels that your continued participation places you at too much risk [describe]."

10. *New Findings New Findings.* If new information—such as a change in the risk/benefit ratio, new alternatives to participating to the research, or new and significant adverse events—develops during the course of the study, the subject will be informed so that he or she may consider whether to continue to participate in the study. An example statement would be follows:

"You will be informed of any significant new findings that become available during the course of the study, such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation that might change your mind about participating."

Should new information develop the investigator should document information in writing, along with a new consent form, and submit it to NIRB review.

11. *Closing Paragraph.* NIRB consent forms require the following closing paragraph:

"You will be given a copy of this consent form to keep. By signing this consent form, you are not waiving any of your legal rights, claims, or remedies. If you have any questions about such rights, claims or remedies, you may contact the Nevada Institutional Review Board."

"I have read (or someone has read to me) the information provided above. I have been given an opportunity to ask questions and all of my questions have been answered to my satisfaction. By signing this consent form, I willingly agree to participate in this study. I have been given a copy of this consent form."

8.3 Modification (including Waivers) of Informed Consent

8.3.1 No Deviation from Written Informed Consent in Research without NIRB Approval

The general rule is that to involve a subject in research, the investigator must obtain documentation of informed consent. In some cases, however, the NIRB is permitted to waive the requirement that a consent form be signed. In those instances, the consent is obtained orally. In other situations, the NIRB may waive particular elements of informed consent or waive the requirement for informed consent entirely. Unless these modifications are approved by the NIRB in writing, they may not be used.

8.3.2 Short Form Informed Consent

The NIRB recognizes a “short form” of the documentation of informed consent. The short form process does not alter any of the elements of informed consent that are required to be given to a subject. Rather, it merely allows the elements to be provided to the subject orally, along with a written summary. The “consent form” states only that consent information has been provided (rather than detailing in writing all of the information). Specifically, the short form process consists of: 1) a written summary of what will be presented to the subject; 2) a written “short form” which states that the elements of the informed consent have been presented; and 3) an oral explanation of the summary information in front of a witness. Both the summary and the short form are approved by the NIRB and signed by the witness and the person obtaining consent. The subject (or legally authorized representative) signs only the short form consent (along with the witness and person obtaining consent). A copy of the written summary of the information and of the short form documenting the consent are given to the subject or the subject’s legally authorized representative.

8.3.3 Waiver of Documentation of Informed Consent:

In two (2) situations, the NIRB may agree that a consent form need not be signed, although informed consent must still be obtained orally: 1) where the only record linking the subject and the research would be the consent form and the principal risk of harm from the research is a potential breach of confidentiality (e.g., a sensitive survey or interview research). NOTE: In this case, the subject is asked whether he/she wants the documentation linking the subject with the research and his/her wishes govern; and 2) where the research presents no more than minimal risk and involves no procedures for which written consent is normally required outside of the research context.*

**Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests. Investigators should be aware that genetic research would not generally be considered to be “minimal risk” whereas research in social, psychological, and economic risks may be so considered.*

Under this consent modification, even though a consent form is not signed and retained, informed consent still must be obtained orally. The NIRB may also require the investigator to provide a written explanation of the study, which the NIRB approves, to the subject.

8.3.4 Waiver or Alteration of Elements of Informed Consent for Minimal Risk Studies

The NIRB may waive the requirement for informed consent entirely (writing and oral presentation), or waive some of the required elements of informed consent, if it finds the following criteria are met:

- 1. The research involves no more than minimal risk to subjects; the waiver will not adversely affect the rights or welfare of the subjects; the research could not practicably be carried out without the waiver or alteration; and whenever appropriate, subjects will be provided with additional pertinent information after participation; or*
- 2. The research or demonstration project is conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: a) programs under the Social Security Act, or other public benefit or service programs; b) procedures for obtaining benefits or services under those programs; c) possible changes in or alternative to those programs or procedures; or d) possible changes in methods or levels of payment for benefits or services under those programs; and e) the research could not practicably be carried out without the waiver or alteration.*

NOTE: Investigators occasionally suggest that research on biological samples, or using medical record information, automatically qualifies for a waiver of informed consent, citing the lack of physically risky procedures. Thus, the use of biological samples for research involving in vitro diagnostic products, for example, are not eligible for consideration of a waiver of informed consent. Such research does not qualify for an automatic waiver for a number of reasons. First, where any samples or data to be used will be collected prospectively (i.e., after the proposal to the NIRB, even if it will be collected for non-research reasons), it is not likely that the third requirement of paragraph 1, above—which requires that the research not be able to be practicably carried out without the waiver—will be met. The principle of respect for persons requires consent to be obtained where at all feasible. Second, even in retrospective research (where the samples/data already exist), the research may not be “minimal risk” for social, psychological, or other reasons. Risks related to disclosure of information (i.e., from genetic research) must be considered. Some such research may have significant effects on the subjects’ psychological well-being, insurability, etc. In addition, even in retrospective research, the waiver may not be necessary to permit the research to be practicably carried out. That it may be inconvenient for investigators to obtain consent, alone, does not meet this requirement.

9. NIRB MONITORING AND INVESTIGATOR REQUIREMENTS REGARDING RESEARCH IN PROGRESS

9.1 Amendments in Protocol or Informed Consent and Application Procedure

The NIRB reviews requests for amendments to previously approved projects during their meetings. Investigators are not permitted to implement any amendments without approval by the NIRB except to eliminate apparent immediate hazard to the subjects. To obtain approval for proposed changes, investigators should submit a cover letter explaining the rationale for the revision, a revised protocol package (where appropriate), and any other information that will assist the NIRB in understanding the revision. Investigators should be aware that a change in risks and benefits may require a change in the consent form and re-consenting of subjects.

Minor changes that do not affect the degree of risk, and that do not raise any other concerns, may be approved by the NIRB through the expedited review procedure. The date of approval of an amendment does not change the date by which the regularly scheduled continuing review of the project is to be completed.

9.2 Required Reporting of Adverse Events and Problems

Investigators are required to report to Executive Director in writing any unanticipated adverse event within five (5) days of the occurrence. Even if an adverse effect was anticipated by the protocol (and disclosed to a subject), if the effect has changed in nature, severity, or frequency in the study, this must be reported to the NIRB. Required reporting also includes, but is not limited to, any procedural errors during the research, a breach in confidentiality or privacy, emotional disturbances, noncompliance with the regulations or NIRB policies, or any other problems occurring during the research. Investigators should err on the side of caution when determining whether an event is reportable to the NIRB. Life-threatening adverse events must be reported to the Executive Director within 24 hours.

Some adverse event reports received by the NIRB may be reviewed through the expedited review process, while others will be forwarded to the full committee for review and determination depending upon the concern raised by the event. The NIRB's review of adverse event reports generally focuses on the degree to which risks to human subjects may have changed, if there is any need to revise the consent document, if changes in the consent document are adequate, or if there is a need to increase monitoring of the project or terminate a project.

Investigators are also required to promptly report adverse events and problems within five (5) days, in writing, to any state agency sponsoring the research. However, investigators should not report minor adverse effects that are anticipated by the study protocol. The NIRB is concerned about more serious issues that arise in the course of a study, such as those that injure subjects or others or that were otherwise unanticipated and involve risks to the subjects. If an investigator is unclear about what should be reported, he or she should contact the Executive Director. Investigators must report any adverse events reported to a funding agency to the NIRB as well.

9.3 Additional Measures to Monitor Active Research Projects

In its discretion, and depending upon the perceived risk of the research, an NIRB may require more active monitoring of a research project. The NIRB can make this determination during their initial review of the research project.

9.3.1 Required Re-Approval of Study no less than Annually, but may be More Frequent

To remain active, all protocols must be reviewed no less than annually. The NIRB may require more frequent reviews if it considers that more oversight is necessary due to the nature of the study, vulnerability of the population, or degree of risk.

The investigator will be informed in the original approval notice when the next review must be obtained and may be reminded prior to expiration of the approval period (at least one month ahead of time). However, it is the explicit responsibility of the investigator to ensure that his/her project is approved for extension before expiration.

9.3.2 Investigator Submission of Research Protocol Extension

The principal investigator should submit a completed Protocol Extension Form at least 30 days in advance of the expiration date. If approval for continuation has not been issued by the NIRB prior to the expiration date, the investigator must terminate the research, and the project will need to be reviewed and approved as a new study.

The purpose of extension review is to determine the appropriateness of permitting the project to continue, not solely to review any new developments. To make this determination, the NIRB may require information on, among other things, adverse events or unanticipated problems involving risks to subjects or others or withdrawals, and a summary of any changes that may affect the study. Investigators should summarize the status of the study, and report any advancements or changes generally in the area under study that may impact the appropriateness of continuing the study.

Generally projects seeking extension may be reviewed through the expedited review process.

10. RESEARCH RECORDS

10.1 Investigator Records

Record (e.g., consent forms, study-related correspondence, treatment records, etc) retention requirements vary depending upon the nature of a research study, but the general rules are as follows:

- 1. Records must be kept for at least three (3) years;*
- 2. For device studies, records must be kept for two (2) years after the latter of: 1) the date on which the investigation is terminated or completed; or 2) the date that the records are no longer required for purposes of supporting a premarket application or a notice of completion of a product development protocol;*

3. *For drug studies, records must be kept for at least two (2) years following the date of approval of a marketing application for the drug studied, or for two (2) years after the investigation is terminated and FDA is notified of termination;*
4. *Maintain records in a secured place with limited access for the research team, to maintain the confidentiality that has been promised to the subjects, as well as to the sponsors.*
5. *Before transferring custody of the records or destroying study records, contact the sponsor of the study if applicable; and*
6. *Where a subject's participation may affect his or her medical care, a copy of the consent form should also be placed in the subject's medical chart.*

10.2 NIRB Records

The Executive Director maintains a file for each study, containing the following information: 1) application forms; 2) consent documents; 3) research protocol(s) (all versions of the protocol are retained); 4) any other approval documents from other committees or agencies; 5) texts of advertisements for subject recruitment; 6) notifications of NIRB decisions; 7) records of protocol extension activities; 8) reports on amendments and adverse events; 9) statements on significant new findings; and 10) correspondence between NIRB and investigators of the project.

The files on a research project will be retained for at least three (3) years after completion of the research.

10.3 NIRB Meeting Records

Agendas and minutes of the NIRB meetings are stored either on the computer or by hard copy and are kept for three (3) years.

10.4 NIRB Member Records

Curricula vitae of active members of the NIRB will be maintained in the files of NIRB Office, and will be updated in content as necessary. Each member's membership term status will be monitored and updated, as necessary.

11. MISCELLANEOUS POLICIES

11.1 Evidence of Assurance Training

All research protocol packages must include a copy of the Assurance Training Certificate. The Executive Director cannot accept protocols from research investigators without certificate copies. Certificates can be obtained as the result of on-line training at the following websites:

<http://ohrp-ed.od.nih.gov> or <http://cme.nci.nih.gov>

12. AVAILABLE REGULATIONS, POLICIES, AND EDUCATIONAL MATERIALS

The NIRB will make available to the Nevada research community documents relevant to human subject research through postings on a website, sending electronically via email or, if an investigator lacks Internet access, by mailing hard copies.

12.1 Federal Regulatory & Advisory Documents

- 1. Nevada Revised Statutes (NRS) 630A—Homeopathic Medicine.*
- 2. “Human Participant Protections Education for Research Teams,” prepared by the National Cancer Institute (Nov. 2002).*
- 3. “The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research” prepared by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1979).*
- 4. “The Nuremberg Code” derived from the Trial of Criminals of World War II by the International Military Tribunal (1949).*
- 5. “World Medical Association Declaration of Helsinki” (adopted in 1964; most recently amended in 1989).*
- 6. “NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects” (March 6, 1998).*
- 7. “White House Commission on Complementary and Alternative Medicine Policy: Final Report” (March 2002).*
- 8. FDA Guidance for Institutional Review Boards and Clinical Investigators (1998).*
- 9. “Protection of Human Research Subjects” Title 45 CFR, Part 46, issued by HHS.*
- 10. “Protection of Human Subjects,” Title 21 CFR, Part 50, issued by FDA.*
- 11. “Institutional Review Boards,” Title 21 CFR, Part 56, issued by FDA.*
- 12. “Investigational Drugs,” Title 21 CFR, Part 312, and Part 314, issued by FDA.*
- 13. “Investigational Devices,” Title 21 CFR, Part 812, issued by FDA.*
- 14. “Federal Policy for the Protection of Human Subjects,” which represents a consolidation of related regulatory policies of all federal agencies, issued by HHS.*

NOTE: Researcher making request will be responsible for the reasonable costs of copying and shipping.