OFFICE OF THE VICE PRESIDENT FOR RESEARCH AND ECONOMIC DEVELOPMENT

RULES AND PROCEDURES FOR CONDUCTING HUMAN SUBJECT RESEARCH

RESPONSIBLE ADMINISTRATOR:	**OFFICE OF THE VICE PRESIDENT FOR RESEARCH AND ECONOMIC DEVELOPMENT**
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Mary S. Croughan, Vice President for Research and Economic Development — *Date*

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1. AUTHORITY

The Research Involving Human Subjects Policy establishes the authority of the University of Nevada, Las Vegas ("UNLV" or "University") to review all research that involves or may involve human subjects.

Where federally funded research is concerned, or otherwise deemed appropriate, the following federal regulations apply: the Department of Health and Human Services ("HHS") Regulations for the Protection of Human Subjects 45 CFR part 46; HHS Regulations for Standards for Privacy of Individually Identifiable Health Information ("HIPAA") 45 CFR parts 160 and 164; United States Food and Drug Administration ("FDA") Regulations for the Protection of Human Subjects 21 CFR part 50 and for Institutional Review Boards 21 CFR part 56. Research involving investigational drugs or biologics falls under FDA regulations to include 21 CFR Part 312, Investigational New Drug Application, and Part 314, Applications for FDA Approval to Market New Drugs. Research involving investigational devices falls under FDA regulations to include 21 CFR Part 803, Medical Device Reporting, Part 812, Investigational Device Exemptions, and Part 814, Pre-market Approval for Medical Devices.

The HHS and FDA publicize additional guidance documents that are applicable to these Rules and Procedures for Conducting Human Subject Research ("Rules and Procedures"). Additionally, State of Nevada regulations (Nevada Revised Statutes) may be applicable when considering the protection of human subjects. These include NRS 388.135 (mandatory reporting of bullying and cyber-bullying for teachers and school staff); NRS 200.5093 (mandatory reporting of abuse of older persons); NRS 432B.220(1) (mandatory reporting of child abuse and neglect); and NRS 159.0805 (court approval required before any guardian may consent to the participation in research of a ward of the court). Research with human subjects must comply

with all applicable federal and state laws and regulations, and equivalent protections are provided to all human subjects. In the case of discrepancy between federal and state law or regulations, federal regulations take precedence. The Office of Research Integrity – Human Subjects has access to legal counsel to assist in the application of state, provincial, or local laws that govern research involving human participants.

2. PURPOSE & INTRODUCTION

2.1 Purpose

The purpose of these Rules and Procedures is: 1) to provide guidance to researchers who work with human subjects in research, 2) to describe the mechanism for review of human subjects research, and 3) to comply with federal requirements for the protection of human subjects in research.

The Office of Research Integrity-Human Subjects ("ORI-HS") and UNLV's Institutional Review Boards ("IRBs") maintain and update these Rules and Procedures. These Rules and Procedures are an integral part of the human research protection program (HRPP) at UNLV. UNLV's HRPP is a shared responsibility between institutional administrators, departments, and committees whose roles and responsibilities include human subject research, as well as Principal Investigators, research team members, and student researchers who conduct research.

2.2 Introduction

UNLV is committed to the ethical principles for the protection of human subjects in research as set forth in *The Belmont Report* of the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research. The University recognizes and accepts responsibility, which it shares with its researchers, for determining that research involving human subjects fulfills these ethical principles. UNLV maintains adequate resources to fulfill these responsibilities. In order to ensure that UNLV continues to maintain adequate resources, the ORI-HS Director meets with the Associate Vice President for Research/Institutional Official once a year to evaluate resources needed for the HRPP, including but not limited to: space, personnel, HRPP education program, legal counsel, conflict of interest, quality improvement plan, community outreach, IRBs, IRB membership, IRB review agreements.

The basic ethical principles on which the federal regulations for the protection of human subjects are founded are set forth in *The Belmont Report*. This Report was published in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, which was established in 1974 under the National Research Act. 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. IRBs 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 the systematic assessment of the nature and scope of the risks and benefits to potential human subjects. All possible harms must be considered, not only physical but also 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 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.

While these Rules and Procedures provide a general overview and current information about 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, researchers should ensure that they and their staff understand the information contained herein, follow any mandatory requirements, and review applicable documents and guidance frequently to obtain additional information on any regulatory requirements or expectations relevant to their specific research. Investigators should contact the ORI-HS with any questions about these Rules and Procedures. As federal and UNLV policies evolve and rules change, these Rules and Procedures will be updated. Please make sure you have the latest information by checking the ORI-HS website. More detailed guidance can be found within the Standard Operating Procedures (SOPs) that are available on the ORI-HS website. These SOPs clearly identify and describe responsibilities of investigators, the IRB, and ORI-HS, and provide a step-by-step outline of procedures to be used. Revisions to the Rules and Procedures and to the SOPs are also disseminated through the Division of Research and Economic Development's in-

house, online publication (“Research News”), and through other university-wide venues such as monthly meetings of the Research Council and the Associate Deans for Research.

2.3 Applicability

These Rules and Procedures apply to all research conducted by UNLV researchers and students, and all research conducted on UNLV premises. In addition, federal government agencies, such as HHS, require institutions and persons who apply for federal funding to sign an assurance that they will comply with federal human subject research regulations and requirements. UNLV has a Federal Wide Assurance (FWA 00002305), which sets forth a number of conditions with which the IRBs and UNLV researchers are required to comply.

2.4 Scope and Definition of Research with Human Subjects

"Research" is "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge."

> **“Systematic investigations”** include, but are not limited to, surveys and interviews, behavioral investigations, retrospective reviews of medical information, experiments with blood and tissue, demonstration and service programs, and clinical trials. In addition, the FDA includes under the definition of reviewable research, any use of a FDA regulated product.
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> **“Generalizable knowledge”** is scholarly work that is intended to be shared, published, or presented to colleagues. It is intended to have a theoretical or practical impact on others within a specific discipline. Contributions to generalized knowledge include activities that are disseminated with the intent to influence behavior, practice, theory, and future research designs.

"Human subject" means a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or collects identifiable private information. "**Human subject"** under FDA regulations 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.

“Engagement in research” occurs when the employees or agents of an institution obtain for research purposes: 1) data about the subjects of the research through intervention or interaction with them; 2) identifiable private information about the subjects of the research; or 3) the informed consent of human subjects for the research.

Projects that fit both the federal definitions for research and for human subject are subject to the Rules and Procedures in this document. Projects that may fit either definition may be subject to these Rules and Procedures, and researchers must contact the ORI-HS for assistance prior to conducting any project activities.

3. ROLES AND RESPONSIBILITIES

3.1 Institutional Review Boards

UNLV has two IRBs, the Biomedical IRB and the Social Behavioral IRB. Their constitution, function, and operation are governed by HHS Regulations for the Protection of Human Subjects 45 CFR part 46.

The IRBs are responsible for reviewing all research within the following categories:

- Research sponsored by UNLV;
- Research conducted by or under the direction of any employee or agent of UNLV in connection with his or her responsibilities as an employee, even if conducted elsewhere;
- Research conducted by or under the direction of any employee or agent of UNLV using any property or facility of UNLV;
- Research that uses UNLV non-public information to identify or contact potential human subjects for research.

IRBs have the following authority and responsibility over research at UNLV:

1. Review all research projects that will involve human subjects prior to researcher contact with subjects;
2. Approve, disapprove, or require changes in all human subjects research (including the protocol document, consent document, and other documents);
3. Ensure prompt reporting by researchers to the Federal Office of Human Research Protections (OHRP) as well as any sponsoring agency of unanticipated problems involving risk to subjects or others as may be required by the Terms of the UNLV FWA, or as otherwise deemed necessary;
4. Review instances of researcher noncompliance with these Rules and Procedures, and/or IRB requirements, and/or applicable regulations, and/or policies;
5. Suspend or terminate previously approved research that has exhibited serious harm to subjects, and/or is not being conducted in accordance with IRB requirements, and/or is suspected/confirmed to be in noncompliance with applicable rules, procedures, and/or policies;
6. Issue corrective actions, including but not limited to: modification to an approved study procedure(s) and/or the information provided during the consent process; monitoring of the research and/or consent process; active participant re-consent, modification to the continuing review schedule; additional training for the researchers; or prohibiting or limiting the use of study data;
7. Conduct continuing reviews of ongoing research as well as any other monitoring such research may require;

8. Notify researchers, and/or appropriate institutional officials, and/or agencies of relevant IRB decisions and/or requirements.

UNLV IRBs also oversee all uses of investigational drugs and devices. These categories cover all research in which UNLV researchers may be involved.

Under the FWA, the IRB may review research or enter into a collaborative agreement to ensure proper review if it will be conducted at another institution. In such situations, the investigator and home institution remain legally responsible for the conduct of research at the other institution. Where another IRB also has jurisdiction over the research, the UNLV affiliated researcher must inform ORI-HS.

The IRBs are independent committees, and only the IRBs may approve research. Attempts to inappropriately influence the IRB should be reported immediately to the Institutional Official (IO), who has been granted the responsibility and authority to respond to such attempts. The IO will investigate the allegation, and if it is determined that undue influence occurred, the IO will develop a corrective action plan that may include possible actions including, but not limited to, the possible suspension of research privileges, and /or a recommendation to the Vice President of Research and Economic Development to initiate disciplinary action under the procedures set forth in Chapter 6 of the NSHE Code. Research covered by this policy that has been approved by the IRB may be subject to further appropriate review and approval or disapproval by officials of the institution, such as the Vice President for Research and Economic Development (VPRED), the Executive Vice President and Provost (EVPP), and the President. However, those officials may not approve the research if it has not been approved by the IRB.

3.2 Principal Investigators and Other Researchers

Principal Investigators (PIs), as defined in the Division of Research and Economic Development Policy on PI Eligibility, are the only individuals eligible to submit to the IRBs and to supervise human subject research conducted or supported by UNLV. PIs are the individuals primarily responsible for protecting the rights and welfare of individuals enrolled in their research projects.

PIs are responsible for submitting high quality, complete research protocols that are ready for review by the IRB. PIs are also responsible for attending the IRB meeting if requested, complying with all portions of the research protocol, and providing updates and notification of changes to the IRB. Finally, PIs are responsible for completing human subject research training and ensuring all team members complete appropriate training. Research protocols are not approved until education requirements are completed; evidence of completion must be provided when requested and training certificates maintained.

All research team members are responsible for following instructions from the PI and following the procedures outlined in the research protocol(s) approved by the IRB. Each research team member must complete human subjects research training that meets UNLV and federal standards prior to any interaction with human subjects. All research team members must understand the principles outlined in *The Belmont Report* and utilize these principles in their interactions with human subjects.

3.3 Office of Research Integrity – Human Subjects

The ORI-HS is responsible for supporting the effective operation, policies, and compliance of the IRBs and the conduct of human subject research at UNLV. The ORI-HS has the authority to determine the need for IRB review of research that may involve human subjects. The ORI-HS is responsible for communication between the IRB, Institutional Official, Principal Investigators, and federal agencies. Research administrators in ORI-HS are also available to provide protocol assistance to PIs, research team members, and student researchers.

3.4 Institutional Official (IO)

The Associate Vice President for Research is the UNLV signatory for its FWA, and is ultimately responsible for the oversight of human subject research activities that fall under these Rules and Procedures. The IO is responsible for keeping the VPRED apprised of relevant human subject research activities.

4. CRITERIA FOR IRB REVIEW AND APPROVAL OF RESEARCH

4.1 General Review Requirements

Federal regulations specify the criteria by which IRBs must review a protocol. Additionally, federal regulations (45 CFR 46.103(f)) require that grant applications for federally supported human subjects research be reviewed and approved by an IRB. As part of this review, IRBs are required to ensure that the activities described in the grant are consistent with the proposed or IRB-approved protocol. The UNLV IRBs consider, at a minimum, the following points during the protocol review process.

4.1.1 Risks and Benefits

The IRBs must 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 from the proposed study. Investigators can minimize risks to subjects through "using procedures consistent with sound research design which do not unnecessarily expose subjects to risk and by using procedures already being performed on the subjects for diagnostic or treatment purposes" (45 CFR 46.111.a.1).

In reviewing the risks to ensure that they are minimized, IRBs may consider whether previous studies have been completed, 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 there are any monitoring mechanisms if necessary, and whether follow-up counseling or other care will be provided, as applicable.

4.1.2 Scientific Review

The IRBs may consider the study design in reviewing investigators' studies. Allowing any risk to subjects with a study that is methodologically flawed would be unethical since little or no reliable information would be obtained. IRBs must not consider possible long-range effects of applying knowledge gained from the research as mitigation for research risk.

4.1.3 Selection of Subjects

The IRBs must ensure that rights and welfare of subjects are protected and that selection of subjects is equitable. The IRB will consider the purpose and setting of the study as relevant factors for subject selection. Proposed uses of vulnerable populations such as children, college students, prisoners, pregnant women, and mentally disabled (cognitively impaired) must be more closely scrutinized. Selection must be equitable so all members of the population have the possibility of inclusion in the study.

4.1.4 Privacy and Confidentiality

Privacy and confidentiality must be evaluated and respected in all human subject research. Privacy and confidentiality are of particular concern in requests to review databases and medical records without proper consent, and for research that will elicit potentially sensitive or damaging information about the subject or a group to which the subject belongs.

Factors that the IRB may consider include the potential importance of the research, the sensitivity of the information to be obtained and to which the investigator will have access, whether links to identifiers will be maintained, the procedures the researcher 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.

5.1.5 Informed Consent

Informed consent includes all of the processes and documentation that allow human subjects to be made aware and give permission for participation in a research project. The IRB must review the proposed informed consent method and documentation to ensure that human subjects will be adequately informed regarding the proposed research.

A legally effective informed consent must be obtained from the subject or the subject's legally authorized representative prior to initiation of study procedures. The consent process must occur in a manner that minimizes the possibility of coercion or undue influence. The consent language must be understandable to the subject or representative and must not include exculpatory language. Informed consent must be

documented for all projects unless they qualify for exemption or for a waiver of documentation of informed consent.

4.1.6 Additional monitoring or safeguards

Where appropriate, the IRB will review research plans and ensure that subject safety is maximized through adequate provisions for monitoring collected data. The IRB may also establish additional safeguards for a protocol including:

- A more frequent, but at least annual continuing review;
- Verification that no material changes have been made since the previous review;
- Authority to observe, or have a third party observe, the consent process and the research (45 CFR 46.109.e).

4.2 Additional Requirements for Vulnerable Populations

Certain groups of human subjects are considered 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), cognitively impaired persons, prisoners, pregnant women, and economically or educationally disadvantaged persons. In addition, terminally ill persons may be vulnerable as well since they may be willing to "try anything." 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 IRB ascertains the use of the vulnerable population being adequately justified and that additional safeguards are implemented to minimize risks unique to each group.

College students may also be considered a vulnerable population due to issues of confidentiality and coercion.

4.3 Additional Requirements for Drug and Device Studies

The FDA has specific requirements for research involving investigational new drugs, marketed drugs, radiopharmaceuticals and investigational devices.

4.4 Requirements for Research in Progress and Ongoing Review

Ongoing communication between the IRB and PIs is essential to protect subjects and conduct sound research. This communication must be documented appropriately to ensure compliance with applicable rules, policies, and regulations.

4.4.1 Continuing Review

Routine continuing review of protocols is essential. Non-exempt studies require at a minimum annual continuing review and re-approval.

4.4.2 Post-Approval Modifications

Researchers are not permitted to implement any post-approval modifications without review and approval by the IRB except to eliminate apparent immediate hazard to a subject(s). In such an instance, the researcher(s) must make every effort to notify the IRB within two days of the occurrence and arrange for a review of the occurrence.

4.4.3 Reporting of Adverse Events and Problems

Investigators are required to report to ORI-HS in writing any serious, unanticipated adverse event or problem within two days of the occurrence. If an adverse effect was anticipated by the protocol (and disclosed to a subject), but has otherwise changed in nature, severity, or frequency, this must be reported to the ORI-HS within ten days. 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 IRB requirements, or any other problems occurring during the research. Researchers should contact the ORI-HS for consultation if unsure whether an event is reportable. Life-threatening adverse events or problems must be reported to the ORI-HS within 24 hours.

5. NONCOMPLIANCE

All acts and/or allegations of noncompliance with applicable rules, procedures, policies, and/or regulations are initially reviewed by ORI-HS and/or the IRB. This process is described in more detail in ORI-HS SOP 11.02 – Researcher Noncompliance: Investigation, Reporting, and Corrective Action. Following an investigative process, there may be an official notice of findings and/or an official determination of noncompliance. Corrective action(s) may be proposed and/or required at any time during a noncompliance resolution process.

6. RECORDS

The ORI-HS is the primary record keeper of all IRB documents related to human subject research protocols at UNLV. At a minimum, as required by 46 CFR 46.115, the ORI-HS must maintain the following for at least three years after completion of a research project:

- copies of all research proposals reviewed, scientific evaluations (if any) that accompany the proposals, approved sample consent documents, continuing review progress reports submitted by investigators, and reports of injuries or adverse events to subjects;
- minutes of IRB meetings;
- records of continuing review activities;

- copies of correspondence between the IRB and investigators;
- a list of IRB members;
- written IRB procedures;
- statements of significant new findings provided to subjects.

Principal Investigators must maintain their own human subject research records and must have a copy of all IRB approved documentation and official communications. Such documentation includes evidence that all research team members have completed and maintained human subject protection training.

7. CONTACT INFORMATION

UNLV Office of Research Integrity – Human Subjects
Phone: 702-895-2794
email: IRB@unlv.edu

8. GLOSSARY

Benefit – 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 or society as a whole. If research will not benefit individuals, it is required to provide a reasonable likelihood of resulting in benefits to society. UNLV's human research application requests information about the direct benefits accruing to the research participants and to society. Compensation or incentives given to participants are not considered a benefit.

Clinical Investigation - includes test articles on human subjects that either meet the requirements for FDA research application or FDA marketing permit. The terms *research, clinical research, clinical study, clinical trial, study, and clinical investigation* are synonymous.

Collaborative Research – also called cooperative research. Human subjects research projects conducted by more than one institution. Each institution is responsible for safeguarding the rights and welfare of human subjects. Arrangements for joint review, relying upon one qualified IRB, or similar arrangements are acceptable.

Exempt Review - the code of federal regulations (45 CFR 46.101(b)) identifies several categories of minimal risk research as exempt from the Federal Policy for the Protection of Research Subjects.

Expedited Review - the code of federal regulations (45 CFR 46.110 and 21 CF 56.110) identifies several categories of minimal risk research which may be reviewed through an expedited review process.

Federal Wide Assurance (FWA) - a written agreement that establishes standards for human subjects' research as approved by the Office for Human Research Protections and is executed by the institutional official.

Full Board Review –all human subject research which does not meet the exempt or expedited review categories must be reviewed by the full IRB. Review of proposed research occurs at a convened meeting at which a majority of the membership of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting. Generally, studies that undergo full board review are studies involving greater than minimal risk, risky or novel procedures, or vulnerable populations.

Identifiable - federal regulations define identifiable to mean that the identity of the individual subject is or may readily be ascertained by the investigator or may be associated with the information.

Institutional Review Board (IRB) – a specially constituted, federally mandated review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research.

Interaction - includes communication or interpersonal contact between an Investigator or his/her research team and the research participant.

Intervention - includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subjects' environment that are performed for research purposes.

Minimal Risk – the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination. *Note: the definition of minimal risk for research involving prisoners differs somewhat from that given for non-institutionalized adults.*

Modification - any change to an IRB-approved study protocol regardless of the level of review it receives initially.

Office for Human Research Protections (OHRP) - the office within the Department of Health and Human Services that is responsible for implementing HHS regulations (45 CFR 46) governing research involving human subjects.

Office of Research Integrity-Human Subjects (ORI-HS) – the office at UNLV that supports the review of research involving human subjects.

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

Risk - the probability and magnitude of harm, including: physical, psychological, social or economic. 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. Federal regulations define only “minimal risk.”