Department of Human Resources (DHR)

- Procedures for Research Involving Human Subjects

- Protocols and Guidelines

Adopted: August 5, 1999
State of Nevada

Table of Contents

DEPARTMENT OF HUMAN RESOURCES (DHR)
PROCEDURES FOR RESEARCH
INVOLVING HUMAN SUBJECTS
PROTOCOL APPLICATION AND GUIDELINES

Overview:

On July 12, 1974, the National Research Act was signed into law creating the National Commission for the Protection of Human Subjects of Biomedical Research. This commission's deliberations resulted in the Belmont Report. The Belmont Report sets forth the basic ethical principles and guidelines underlying the acceptable conduct of research involving human subjects. These are identified in this report as respect for person, beneficence, and justice. "Respect for person" involves a recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy. "Beneficence" entails an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risk of harm. "Justice" requires that the benefits and burdens of research be distributed fairly. The Belmont Report set forth the criteria used by the Department of Health and Human Services to propose and establish rules for institutions regarding research. These rules were codified as 45 CFR 46, and in 1991 a common rule was established and all federal agencies have adopted this rule.

Under the terms of DHR's assurance of compliance with the federal government, all research involving human subjects must be reviewed for compliance prior to application for funding or the initiation of the project. The projects of both staff, university faculty and students are subject to compliance review if human subjects are involved. The DHR Deputy Director's Office serves as the clearinghouse for all information and actions necessary for institutional compliance with federal rules regarding the use of human subjects.

Purpose:

The purpose of this procedural guide is to assist DHR staff and/or collaborating agencies in the preparation of a protocol involving the use of human subjects and to provide instructions and suggestions for proper and expeditious review.

Operational Definitions:

Projects to which this guide applies are those which involve the use of human subjects.

> "A human subject" is defined as a living individual about or from whom a DHR staff or collaborator obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information.
>
> "Research" means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. The "DHR Institutional Review Board (IRB)" for research involving human subjects reviews all proposed research projects involving human subjects.

Adopted: August 5, 1999
Department of Human Resources
State of Nevada

Procedures for Obtaining Approval for Projects Involving Human Subjects:

DHR staff planning to initiate research involving human subjects may discuss the concept of the proposed research with the DHR Deputy Director to obtain advice and guidance concerning preparation of the protocol. Questions concerning the review process or the elements of the protocol can be discussed at that time.

Notification of approval will be sent to the principal investigator. For collaborating agencies or agencies or students it will be sent to the responsible DHR Agency who will forward the approval notice to the student. **It is the responsibility of the researcher and/or sponsor depending on who has primacy, to retain records relating to the research for at least 5 years after the completion of the project.** Attached are the guidelines and forms needed for the preparation of the protocol. The Deputy Director's Office of DHR will be pleased to provide assistance in interpretation of the guidelines and preparation of protocols.

Protocols must be approved by the Division Administrator and be received in the Deputy Director's Office of DHR by no less that 30 days prior to the desired approval date. Protocols involving healthy adults whose anonymity is protected and the research involves uneventful methods and procedures may be reviewed more quickly.

Public Health Exemption from IRB Review:

The Center for Disease Control and Prevention (CDC) does not submit public health activities to IRB review even though these deal with human subjects and produce data, some of which may be generalizable. Thus it is our policy to exclude the following from IRB review when conducted exclusively as public health practices: disease investigation, program evaluation, program needs assessment, immunization coverage levels, construction and maintenance of disease health registries, public health clinical screenings, environmental health activities, vital statistic and record keeping, behavioral risk factor surveillance, disease surveillance and laboratory testing, public awareness and education campaigns, maintenance and protection of clients' confidentiality as this relates to public health activities and patients' rights, etc.

DHR Policies and Procedures on the Use of Human Subjects in Research

1. BACKGROUND:

On July 12, 1974 the National Research Act was signed into law creating the National Commission for the "Protection of Human Subjects to Biomedical and Behavioral Research." This commission's deliberations resulted in the Belmont Report. This report sets forth the basic ethical principles and guidelines underlying the acceptable conduct of research involving human subjects:

- "respect for person" - recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy.
- "beneficence" - an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risk or harm.
- "justice" - requires that the benefits and burdens of research be distributed fairly.

The Belmont Report set forth the criteria used by the Department of Health and Human Services (DHHS) to propose and establish rules for institutions regarding research. These rules were codified as 45 CFR 46 and in 1991 a Common rule was established and all Federal agencies have adopted this rule.

The following policy is based on the federal rules described above.

2. OPERATIONAL DEFINITIONS:

Projects to which this policy applies are those which involve the use of human subjects (45 CFR 46 46.102 Definitions).

A **"Human Subject"** is defined as a living individual about or from whom a project obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information.

"Research" means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purpose of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

"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 examinations or tests.

Adverse event means any untoward happening or unanticipated benefit in a patient or client after the patient or client signs the consent form, even if the patient or client hasn't taken a study medication or been involved in any other intervention.

Serious-adverse event means a death, hospitalization, disability, life-threatening occurrence, cancer, congenital anomaly or significant event that occurs during the study period or is reasonably related to events that took place during the study period even though the serious adverse event happened after the termination of the study.

Adopted: August 5, 1999
Department of Human Resources
State of Nevada

The "Institutional Review Board (IRB)" is the party responsible for the development and monitoring of departmental policy and procedures involving use of human subjects in research and development. The IRB's purpose is to facilitate optimum protection of human subjects while also facilitating the academic freedom of researchers. The IRB will not be concerned with the quality, direction, or scope of activities being proposed except when such consideration is required as part of the actual protection of human subjects.

"Prisoner" means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

"Informed Consent" Is the process by which subjects are informed about the research and agree to participate. No DHR agency may provide informed consent for an individual within its custody. A surrogate or legal guardian must be appointed to provide informed consent for incompetent subjects, including minors. See Appendix A for informed consent and basic elements of informed consent.

3. PURPOSE:

The purpose of these policies and procedures is to: (1) establish standards for any research conducted within DHR programs and involving the use of human subjects; and (2) establish a review process to ensure that all such research meets the established standards.

4. STATEMENT OF PRINCIPLES:

The Department of Human Resources accepts as basic principles of research the following:

Protection from Risk

No human being is to be exposed to unreasonable risk to health or well-being. All research activities will be conducted to avoid, or keep to the absolute minimum, risk to the health or well-being of the participants.

Benefits Greater than Risks

The risks to the individual must be outweighed by the potential benefit to him or her or by the importance of the knowledge to be gained.

Rights of Subjects

The rights and welfare of all subjects involved shall be adequately protected. For patients or clients with impaired decision making capacity, parameters of acceptable research practices should be incorporated that protect the public from harm via an independent assessment of a subject's capacity to decide whether to participate in a study.

DHR Policies and Procedures on the Use of Human Subjects in Research

Informed Consent

Adequate, appropriate and effective informed consent will be obtained in accordance with 45 CFR 46. Every opportunity to educate consumers and family members about informed consent procedures to help them understand the nature risks and benefits of specific research should be utilized.

Responsibility of Investigator(s)

The investigator conducting the research has primary responsibility for the subjects' health and well-being. The investigator(s) must attend any start up meetings by the agency or sponsor, document protocol compliance, have rating scale training and certification, adhere to the good clinical practices, detail serious adverse event reporting, coordinate patient or client recruitment, and in the care if investigational drugs, account for the study drugs. Investigator(s) must also prove his/her clinical qualifications to do proposed studies. Investigator employment status must be clarified to avoid any conflict of interect. The DHR Institutional Review Board must review research involving human subjects unless specifically exempted. Exemptions will be determined by the IRB Chair or his or her designee.

Qualifications of Student Investigators

Staff who collaborate in research conducted by students must determine whether the students are able to safeguard the health and well-being of the subjects.

Clients as Subjects

If participation as a subject is part of the clinical treatment of a client, it must not be a coercive or mandatory requirement, and appropriate informed consent must be obtained. Research may involve clients under 18 years of age if adequate informed consent is obtained.

Freedom to Withdraw

If a subject indicates that he or she does not wish to participate further in a study, participation must be ended promptly, safely, and without penalty.

Privacy and Confidentiality

The subject's personal privacy must be respected.

A. Investigators must protect confidential information obtained from subjects and advise them of any limits on that ability. Research data are seldom protected from subpoena. A Certificate of Confidentiality may be requested from DHHS for special projects. Questionnaires, inventories, interview schedules, and other data-gathering procedures must be carefully designed to insure that only information relevant to the project will be obtained. When body tissues, fluids, or other similar materials are used in the research, only a code or hospital number should be used, not the patient's name.

B. Investigators must inform subjects about their plans to disseminate research information.

Adopted: August 5, 1999
Department of Human Resources
State of Nevada

C. The principal investigator must make provisions for the safe retention of complete records of human subjects for at least three years following the completion of the project or activity. This period may be extended for certain studies at the discretion of the board.

Unanticipated Risks

If the investigator discovers unanticipated risks to a subject, the investigator must immediately inform the DHR's Institutional Review Board and the subject.

A. Adverse events must be reported within five working days; serious adverse events must be reported within 24 hours.

B. A written report of a serious adverse event to the medical director of the facility will be forwarded within 24 hours which includes but is not limited to: date reported, follow up date, case ID, local ID, source, research facility, project code, investigator, title, address, patient information, and study intervention, investigation of drugs should include the experimental route, start and end dates, permanent stop date, blinded study, narratives, event summary description, corrective treatment, relevant history, concurrent conditions, adverse events, overview, drug name, diagnosis or symptoms, concomitant drugs, principal event, event indicators, continuing, abate on dechallenge or reduction of dose, reappear on rechallenge, investigator opinion of possible relatedness, cause and date of death, autopsy performed, lab data, and any additional narratives that clarify the events.

C. The Board must determine whether to suspend or terminate the research and must inform the sponsoring agency of both the unanticipated risks to the subjects and its determination of the investigation.

Compensation

Compensation for subjects shall not be of such magnitude that a subject might not appropriately weigh the risks of participation in the research.

Prior Animal Research

Whenever possible and relevant, animal research must precede research on human subjects.

Vulnerable Populations

Research involving persons with mental illness or developmental disabilities, persons with physical disabilities, children, pregnant women, prisoners, parolees, addicts, and others in conditions of dependency requires additional precautions to ensure the protection of the rights of subjects. Subjects will be assessed for impaired decision making capacity. If there is impaired decision making capacity, then an independent assessment of subject's capacity to decide whether to participate in a study will ensue, without stigmatizing individuals with mental disorders but providing meaningful protections to research participants, so as not to impede progress in our understanding of mental disorders.

Sensitivity Toward Ethnic Background

Ethnic differences should always be on the investigator's mind when working in a culture different than his or her own. The investigator must consider the ethical principles of that culture in addition to the principles listed above.

5. DHR POLICY:

Under the terms of this policy, ALL proposed research development and related activities involving human subjects done under the auspices of DHR must be reviewed for compliance prior to application for funding OR the initiation of the project. This policy is in accordance with the requirements set forth in Title 45 Code of Federal Regulations Part 46 (45 CFR 46) from the Office for Protection from Research Risks (OPRR), National Institutes of Health (NIH), Department of Health and Human Services (DHHS) and Title 21 Code of Federal Regulations part 56 (21 CFR 56) from the Food and Drug Administration (FDA). Copies of these CFRs are available from the DHR Deputy Director's office.

This provision applies to all studies in all locations whether funded or unfunded and whether conducted by staff, students, or collaborating agencies such as the universities. Collaborative projects involving universities, faculty and students (i.e., student and faculty classroom studies/projects, theses, dissertations, grant research, and contracts) are subject to compliance review by the Institutional Review Board (IRB) if human subjects are involved. No such study may begin before it has been so approved and may not continue past its approved term.

The Department of Human Resources, Deputy Director's Office serves as the clearinghouse for all information, application package, and actions necessary for institutional compliance with federal rules regarding the use of human subjects.

6. DHR INSTITUTIONAL REVIEW BOARD - MEMBERSHIP AND FUNCTIONS:

A. The DHR will establish an Institutional Review Board (IRB) in accordance with the requirements set forth in Title 45 CFR Part 46.

B. The purpose of the IRB is to assure that research conducted with human subjects complies with the policies of DHR and those set forth in 45 CFR Part 46.

C. The DHR Institutional Review Board shall consist of at least 5 members with varying backgrounds to promote complete and adequate review of research activities within DHR.

1. Each agency within DHR who conducts research with human subjects shall have a representative on the Board.

2. The IRB shall have at least one member who is not employed by DHR and who is not an immediate family member of any DHR staff.

3. The membership shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in non-scientific areas.

4. The membership shall be sufficiently qualified through experience and education and reflect diversity in race, gender, cultural backgrounds and community attitudes to:

   (a) promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects;

   (b) determine the professional validity of scientific research activities;

   (c) ascertain the acceptability of proposed research in terms of institutional communities and regulations, applicable law, and standards of professional conduct and practice.

5. The membership shall include at least one individual knowledgeable about working with vulnerable populations as subjects, such as: children, prisoners, pregnant women or persons with mental illness or developmental disabilities, and/or persons with physical disabilities.

6. The membership shall not consist entirely of one gender or of members of one profession.

7. The IRB may, at its discretion, invite individuals with specialized competence to assist in the review of research projects. These individuals may not vote with the IRB.

8. Any IRB member who has a conflicting interest in any research project shall not participate in the IRB's initial or continuing review of that project, except to provide information requested by the IRB.

9. Members are appointed for a one-year term by the Director of DHR.

D. IRB Functions and Operations

1. The IRB will meet periodically and at least annually to review human subjects guidelines and proposed research projects.

2. A majority of the membership constitutes a quorum for review and approval purposes.

3. DHR will provide adequate meeting space and sufficient staff to support the IRB's review and record keeping duties.

4. Except when an expedited review is used, the IRB will review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in non-scientific areas. In order for the research project to be approved, a majority of these members must vote for approval.

5. The IRB will follow the procedures detailed in this policy in reviewing research projects.

E. IRB Documentation

The IRB shall prepare and maintain adequate documentation of IRB activities. The records required by this policy shall by retained for at least 3 years, and records relating to research which is conducted shall be retained for at least 3 years after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the Federal Department supporting the project at reasonable times and in a reasonable manner. These records include the following:

1. Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects;

2. Minutes of IRB meetings which shall be of sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution;

3. Records of continuing review activities;

4. Copies of all correspondence between the IRB and the investigators;

5. A list of IRB members by name; earned degrees; representative capacity; credentials such as board certifications, licenses; and employment status;

6. Written procedures for the IRB;

7. Statements of significant new findings provided to subjects.

F. Communication with Federal Departments and Agencies

1. The IRB shall prepare and submit a written assurance that the Department of Human Resources is in compliance with the requirements set forth in Title 45 CFR Part 46. The written assurance may be submitted to the Department or Agency funding a specific DHR research project approved by the IRB, or a general assurance may be filed with the U.S. Office for Protection from Research Risks, National Institutes of Health, DHHS (OPRR) for approval on a Federal-wide basis. When the existence of an DHHS-approved assurance is accepted in lieu of requiring submission of an assurance, Federal reports required by this policy shall be sent to the specific Federal Department or Agency as well as OPRR.

2. Any assurance filed must include the following:

   (a) A copy of these procedures;

   (b) A list of IRB members to include:

Name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution, (e.g. full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant);

(c) Changes in IRB membership shall be reported to the Federal Department or Agency head, unless in accord with CFR 46.103(a) the existence of a DHHS-approved assurance is accepted. In this case, change in IRB membership shall be reported to the Office for Protection from Research Risks (OPRR), National Institutes of Health, DHHS.

7. IRB REVIEW PROCEDURES:

A. DHR staff planning to initiate research involving human subjects may discuss the concept of the proposed project with the IRB Chair or the Director of DHR or his or her designee to obtain advice and guidance concerning preparation of the protocol and any questions regarding the review process or elements of the protocol.

B. A protocol MUST BE submitted for review for all research involving human subjects. Research project protocol forms are submitted to the IRB through the Director of DHR or his or her designee, reviewed, and placed in the following review categories:

1. "Exempt" from Full IRB Board Review

The "Exempt" review category of protocols are considered by the IRB to be exempt from full IRB review or expedited review. Protocols involving healthy adults whose anonymity is protected and the research involves uneventful methods and procedures can be reviewed and approved by the IRB Chair.

Studies which involve the following procedures are considered to entail minimal risk and are exempt from full IRB review:

(a) Observations without intervention in public places or in settings where the supervising institution has granted permission for the observation;

(b) Participant observations of public behavior when: 1) observations are recorded so that subjects cannot be reasonably identified, AND, 2) the purpose of the observation would not be objectionable to the subject if he/she were aware of the observation;

(c) Surveys that do not deal in depth with sensitive topics such as sexual behavior, drug or alcohol use, illegal conduct or family planning, and which protect the confidentiality of the individual;

(d) Research solely involving the use of standard educational diagnostic, aptitude, or achievement tests, if the information taken from these sources is recorded so that subjects cannot reasonably be identified (tests involving children under 18 must be reviewed by the full IRB);

(e) Research pertaining to normal adult cognitive, perceptual, or social processes, if research is not to evaluate the competence of the individual subjects, AND, if the research does not deal with sensitive topics;

(f) Voice recordings for purposes such as linguistic analysis or investigation of speech defects, if the investigator protects the identity of the individual speakers;

(g) Program evaluation activities that do not interfere with normal activities of the persons in the program;

(h) Research solely involving the study of documents, records, or data sets, if the information taken does not identify subjects.

2. "Expedited" Review by the IRB

Research activities involving human subjects in which there is minimal or no risk and in which the only involvement of human subjects would be in one of the categories listed in 45 CFR 46 under "Research Activities which may be reviewed through expedited review procedures" (46.110), are reviewed by the IRB Chair or by one or more experienced members of the IRB. If disapproved by any member, the protocol must be reviewed by the full Board.

Studies which involve the following procedures are considered to entail minimal risk and may be reviewed under expedited procedures:

(a) Research solely involving the study of pathological or diagnostic specimens in which the subjects cannot reasonably be identified;

(b) Collecting of blood samples by venipuncture, in amounts not exceeding 450 mm in a six-week period and no more often than two times per week, from normal subjects 18 years of age or older;

(c) Recording data from adults through the use of physical sensors that are non-invasive and do not input significant amounts of energy into the subject. Such procedures include weighing, electrocardiogram, electro-encephalogram, thermography, detection of naturally occurring radioactivity, diagnostic echography, and electroretinography;

(d) Collection of both supra- and subgingival plaque, provided the procedure is not more invasive than routine prophylactic scaling of the teeth, and uses accepted prophylactic techniques;

(e) Collection, in a non-disfiguring manner, of hair, nail clippings and deciduous teeth;

(f) Collection of excreta and external secretions, including sweat, saliva, placenta expelled at delivery, umbilical cord blood after the cord is clamped at delivery, and amniotic fluid at the time of artificial rupture of the membrane prior to or during labor;

(g) Moderate exercise by healthy volunteers.

3. "Full" IRB Review

Research activities involving human subjects in which there is more than minimal risk and/or that do not fall under the "exempt" or "expedited" categories must be reviewed by the full IRB. Research involving protected groups such as children, fetuses, pregnant women (including in vitro fertilization), prisoners, or persons with mental illness and/or developmental disabilities, requires full Board review.

C. Timelines for IRB Review and Approval

1. Application for IRB review must first be approved by the Division Administrator, and research protocols must be received in the DHR Deputy Director's office no less than 30 days before approval is needed.

2. The researcher will be notified in writing of the results of the IRB within one (1) week of its review. If there is some urgency involved, the results of the review may be obtained by phone from DHR.

D. Notice of Review

1. If the protocol is approved, the IRB shall issue a Certificate of Compliance and Acceptance of the project. This certification shall include the date of the next required review.

All projects shall be subject to continuing review at intervals appropriate to the degree of risk, but not less than once per year, and the IRB shall have authority to observe, or have a third party observe, the consent process and the research.

The frequency of required reviews shall be specified by the IRB in the certificate of compliance and acceptance.

2. If the IRB decides to disapprove a research project, the IRB shall include in its written notification a statement of the reasons for the decision The investigator must respond in writing before the protocol can be considered again. The investigator may request an opportunity to respond in person. The Board may seek consulting opinions from experts in relevant fields.

E. An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action, and shall be reported in writing promptly to the investigator, appropriate DHR officials, and the Federal Department or Agency head if applicable.

8. CRITERIA FOR APPROVAL OF RESEARCH PROTOCOLS:

Research approved by this policy must meet eight requirements.

1. Risks to subjects are minimized: 1) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and 2) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and to the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive if not participating in the research). The IRB will not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

3. Selection of subjects for participation is equitable. In making this assessment the IRB will take into account the purposes of the research and the setting in which the research will be conducted and will be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, persons with mental illness and/or developmental disabilities, or economically or educationally disadvantaged persons.

4. Informed consent is sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by this policy and 45 CFR Part 46.

5. Informed consent is appropriately documented, in accordance with, and to the extent required by this policy and 45 CFR Part 46.

6. The research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

7. There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

8. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, persons with mental illness and/or developmental disabilities, or economically or educationally disadvantaged persons, additional safeguards are included in the study to protect the rights and welfare of these subjects.

Patients with severe mental illness may not participate in placebo studies, since a serious adverse event risk outweighs the benefits.

9. APPEAL PROCEDURES:

Investigators who disagree with changes requested by the Board may appeal.

A. Any complaints or concerns may be discussed with the Board Chairperson.

B. The IRB may invite investigators to attend a meeting to explain their research.

C. Investigators may wish to submit supporting information, such as consulting opinions, journal articles, or precedents of approval at other institutions.

D. If investigators are dissatisfied with the final decision of the Board, they may consult with the Director of DHR, who will, if warranted, refer the matter back to the Institutional Review Board.

E. The decision by the Board whether to approve or deny an appeal is discretionary and the decision of the Board is final.

10. GUIDELINES FOR SUBMISSION OF RESEARCH PROTOCOL TO DHR:

A. Title and Sponsor

The protocol should bear the same title as any accompanying contract or grant proposal.

1. Sometimes the protocol represents a sub-section of a larger application. When the protocol title is different from the title of the grant or contract, the protocol title shall be listed first, with the proposal title in parentheses.

2. If multiple applications reflect essentially the same study, they will be treated as modifications to one human subjects protocol. These may be submitted in the form of a memorandum requesting that certification be made to additional agencies.

B. Description of Study Use this format as numbered.

1. SUBJECTS: Indication of efforts that will be made to assure equitable (both male and female) selection, if applicable. When vulnerable populations are involved, description of why they are necessary. If subjects are to be paid, description of payment method.

2. PURPOSE, METHODS, PROCEDURES: Description in detail of the purpose, methods, and procedures of the study.

3. RISKS: Description of any potential risks to the subjects—physical, psychological, social, or legal—and assessment of the likelihood and seriousness of those risks. If the methods of research create potential risks, description of other methods, if any, that were considered and why they will not be used. Description of procedures—including confidentiality standards for minimizing potential risks.

4. BENEFITS: Description of the anticipated benefits of the research to the individual subjects, to the particular group or class from which the subject population is drawn, and/or to society in general.

5. RISK-BENEFIT RATIO: Assessment of the relative weights of the study's risks and benefits.

6. COSTS TO SUBJECTS: If the investigation involves the possibility of added expense to the subject or to a third party, such as an insurer or employer (e.g. longer hospitalization, extra laboratory tests, travel, time missed from work), indication of how this is justified. Be sure this is mentioned in the consent form.

7. INFORMED CONSENT: Description of the method of obtaining informed consent, the person(s) who will be responsible for obtaining it, and where the informed consent forms will be stored. ATTACH CONSENT FORMS.

8. CHILD ASSENT: When children are subjects for research ASSENT from child and CONSENT from parent or legal guardian must be obtained.

C. Other Required Information

1. Copies of all materials and circumstances that will be used to obtain consent must be attached to the protocol form. Include the text of a verbal presentation or a newspaper advertisement, as well as formal consent documents and information sheets.

   Informed consent requirements and a model consent form are set forth in Attachment A. All elements of the informed consent (45CFR 46.116) must be present for ALL research in the form of a separate informed consent document to be signed and a copy given to subject, a separate document to be read only by the subject and then given to subject, or in the form of a cover letter/page requesting completion of a survey, etc., with no signature involved with copy given to subject. All subjects must be given a copy of the consent form which should include the phone numbers for the agency of the researcher and the DHR Deputy Director's Office for questions regarding rights of research subjects.

2. Location(s)

   The following location issues should be addressed:

   (a) The adequacy and/or appropriateness of the facilities or location for the study;

   (b) If the subjects will be located at a public school or other institution, permission of that institution must be obtained. In some instances, other institutions will require their own review for protection of human subjects. Letter of approval from the institution, agency, or business must accompany the protocol;

(c) If the study takes place among persons whose primary language is not English, or in a foreign country, the consent process must be in his or her first language and in English.

3. Attachments to Protocol

(a) Survey instruments. Any questionnaire, interview schedule, pencil-and-paper test, or list of questions should be attached to the protocol. Standardized tests, such as the MMPI or the Stanford-Binet, should also be attached.

(b) One copy of "Investigational Drug Information Record" plus one copy of the drug company protocol must be sent to the Board.

(c) The federal regulations regarding investigational devices are not included in these Procedures because they are very long and the need for them does not occur very often. If the study involves an investigational device, please obtain information from DHR.

(d) All studies involving ionizing radiation used in vitro for research require prior review and approval by the Division of Health before being considered by the IRB.

(e) All elements of informed consent must be present even if the "signature" or signed consent form is not used or required. (See Appendix A)

(f) A copy of approval to conduct research at a public or private institution, agency, or business must be attached. (See 2(b))

(g) A copy of the sponsorship or other funding agreement to conduct the project, or any relevant contract or other agreement to conduct this investigation.

D. Format Modifications

Simple modifications do not require the submission of a new protocol form. Researchers send a memo to the IRB Chair stating the modification. If there are substantial changes in the study, however, it may be necessary to fill out a revised protocol form. It may be appropriate to include a memo explaining the reasons for the changes indicated on the protocol form. If the proposed change affects the information to be given to the subjects, a revised consent form must be submitted.

E. Continuation/Renewal Submissions

Approval for use of human subjects in research is for a period of one year from the date of approval. Researchers will receive a Request for Status Memo form prior to the expiration date of the approval and the researcher is responsible for requesting a continuation of the approval including a brief progress report of the previous year's activities. The protocol Certification of Compliance and Approval will automatically terminate if there is no response.

Appendix A

INFORMED CONSENT REQUIREMENTS

Most investigators obtain consent through personal discussion. This process is recommended since it allows questions to be answered on the spot. Consent documents, added to oral consent, may appear to be an unnecessary and quasi-legal burden. However, in addition to the legal requirements, there are two practical uses for a consent form: 1) It can aid the investigator by providing a checklist of discussion items; and 2) It can aid the subject as a memory tool to be used at a later time.

A consent form should tell reasonable persons from proposed populations the information they need to know in language they are likely to understand in order to make informed decisions. The consent form must be genuinely comprehensible to lay-persons, and it should make very clear the voluntary and elective nature of participation in procedures. In studies on patients, the consent form should honestly express the realistic expectations of such participation, carefully avoiding inducement by raising false hopes.

The explanatory portion of the consent form should be written in the second person with a final consent statement in the first person. A fair explanation of the nature, purpose and duration of the experiment must be given in terms comprehensible to the intended subjects. As a rule, most technical terms require some lay explanation. It should be written in language understandable at an 8th grade level. Researchers should consider the age of the child when writing the child assent form. Researchers should try to limit the consent/assent document to one page. If the consent form requires two or more pages, the title, name of investigator, and a number of pages should be identified on each page, and a space should be provided for the subject to initial the pages preceding the signature page. The date of typing and page number should appear on each page.

BASIC ELEMENTS OF INFORMED CONSENT

Federal regulation (45 CFR 46.116) specifies the basic elements of information necessary for informed consent, and relative to our policies and procedures should include:

A. A statement identifying yourself and your affiliation with the Department of Human Resources in your opening sentence;

B. A request for the subject to participate in the study as part of a research project;

C. A statement that the study involves research. The statement should include:

1 An explanation of the purposes of the research, clearly stated to assist the subject in balancing the risks and benefits for himself or herself;

2 The expected duration of the subject's participation;

3 A description of the procedures to be followed; and

4 The identification of any procedures which are experimental.

All of the procedures to be used in the investigation should be clearly stated in lay terms. If the procedure is in addition to normal patient care, a brief reference to the normal care is needed but the emphasis should be on the investigational procedures. Blind and randomized studies should include all procedures with notation that the subject will be assigned to one of the regimens. Quantities such as amount of blood to be withdrawn should be expressed in terms familiar to the subject.

D. A description of any reasonably foreseeable risks or discomforts to the subject and a description of any benefits to the subject or others which may reasonably be expected from the research. The attendant risks and discomforts of each experimental procedure should be included. It is appropriate to estimate the degree of risk—to characterize a drug's side effects, for example, as rare or common. It is especially important to be candid about high risk procedures. Remember that "risk" is to be evaluated from the lay-person's viewpoint. Consider any event happening more often than one case in ten thousand as a "risk" that needs explanation. Four categories of risk are recognized: psychological, social, legal, and physical. Confidentiality of data or identity falls within these categories and should be spoken to if appropriate. Investigators can guarantee confidentiality only to the extent provided by law. Sometimes a research procedure includes accepted methods or procedures which also involve risk. (When the risk is present only because the subject has volunteered for the study, it should be included in the consent.)

The consent form must include an honest estimate of the benefits that may be expected as outcomes of the research. The distinction between personal benefits and benefits to society must be apparent in this statement so that the potential subject may make an informed decision. If there is no direct benefit to the subject, this should be stated.

E. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject (if applicable). Alternative procedures should be included with the statement that the risks and benefits of those procedures have been explained to the subject. The discussion of the alternatives must be fair and should attempt to balance the alternatives against the experimental therapy or procedure proposed. In the case of normal volunteers or of surveys and questionnaires, the alternative procedure would be non-participation and need not be stated.

F. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.

G. For research involving more than minimal risk, an explanation as to whether there is any compensation for participation (money, extra course credit, etc.), and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained (if applicable). Acknowledgment of payment to subjects when subjects withdraw prior to the completion of the study should be addressed in the consent document. If money is offered to pay for expenses, inconvenience, time and trouble, it should not provide "undue influence" and thus the amount must be balanced with the risk.

H. An explanation of whom to contact for answers to pertinent questions about the research (researcher's DHR address and phone number) and research subjects' rights and whom to contact in the event of a research-related injury to the subject.

I. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. It is necessary to assure the subject of his or her freedom to decline to participate or to withdraw from the study at any

time without prejudice to usual medical care, class standing if a student, behavior record if a prisoner, or job status if an employee, etc.

J. A concluding paragraph should contain a statement of consent written in first person and should include:

1. I have read the consent form and consent to participate;

2. I understand that I am free to ask questions or consult other people about the study or the consent form;

3. I understand that I am free to withdraw from the study at any time for any reason and without prejudice of any sort as a consequence of withdrawing;

4. I understand that the Investigator may terminate my participation at his or her discretion;

5. I will be given a copy of the signed consent document;

Exculpatory phrases releasing DHR or the investigator from responsibility may not be used. If the study includes both normal volunteers and clients, it is preferable to make up separate consent forms written from the point of view of clients and volunteers.

K. Signature and date lines for the participant and investigator plus one for a witness if necessary. On child assent form, there should be lines for the child assent, the parent or guardian consent, and the investigator's signatures. If separate parental or guardian consent is received, there must be a signature line for a witness in the case of child assent, or if an individual is unable to sign.

SPECIAL CIRCUMSTANCES RELATED TO INFORMED CONSENT

Informed consent may be especially difficult when dealing with certain classes of subjects. Such subjects would include, but not be limited to, minors, persons with mental illness and/or developmental disabilities, pregnant women, and any subjects drawn from an institution or "captive population" (e.g. prisoners, parolees, students, seminarians, military, mentally or physically ill, etc.). In these circumstances it becomes even more critical that precautions be taken so that subtle coercion to participate is eliminated.

Parental or Guardian Consent

When the proposed investigation involves a subject who is legally incompetent to give consent, the consent form must clearly indicate that procedures are being consented to on behalf of the subject by the legally designated responsible guardian. Minors are considered legally unable to give informed consent and parental or guardian consent is required. Usually, one parent may sign the consent but in some cases it is desirable, and even essential, to obtain the agreement of both parents.

When a research procedure involves minors who are old enough to understand the nature of the procedure, a special problem of tact and empathy arises. The parents or legal guardian must sign the consent form in order to give it any legal force, yet the comprehending minor's assent should be secured. At times it is possible to write an assent form that a minor of 10 or 12 years can understand and sign. A minor of 16 or 17 years should be able to understand an assent form written in clear lay language (8th grade level). The signature of a comprehending minor on an assent form, as well as that of the parents or

guardian, is necessary. Ordinarily, consent forms for minor subjects should assure the parents or guardian that exhibition of fear or resistance by the child will be sufficient reason to terminate the procedures not deemed necessary for the child's health. The child assent form should be brief and contain language written at the appropriate age level. The child's assent form should include:

A. Identification of researcher and affiliation with DHR;

B. Statement of the purpose of the research;

C. Description of the procedures to be applied to the minor;

D. Description of potential risks and discomforts associated with the research;

E. Description of any direct benefits to the minor;

F. Statement that the minor does not have to participate if he or she does not want to;

G. Statement that the minor is free to withdraw at any time;

H. Statement that the minor should discuss whether or not to participate with his or her parents or guardian prior to signing the assent form;

I. Statement that the parents or guardian of the minor will be asked to consent on behalf of the minor;

J. An offer to answer all questions; and

K. A simplified concluding assent statement.

Research Involving Mentally Incompetent Subjects of All Kinds

When the subject has been declared incompetent, consent of the legally appointed guardian is required. Whenever possible, the consent of the subject should also be obtained, thereby ensuring that the subject has been informed within the limits of his or her understanding.

Persons who are mentally ill, have developmental disabilities that may impede judgement or comprehension, are undergoing deterioration of mental function as a result of intoxication, advanced age, disease, or other causes, may not be competent even though no legal process establishing incompetence has occurred. Additionally, subjects who, by virtue of their illness, may have periods of impaired judgment, may not be competent to give informed consent. The burden of establishing that a subject is competent resides with the investigator and methods of establishing such assurance of competence should be specified in the protocol. A non-involved professional will sometimes be recommended to judge the adequacy of the consent by that subject at that time. Investigators are strongly urged to contact the IRB Secretary or Chair for current DHHS regulations prior to submitting a protocol involving mentally incompetent persons.

Pregnant Women and Fetuses

DHR requires that the Board give careful consideration to the manner in which potential subjects will be selected when pregnant women or fetuses are used as research subjects. Additionally, the actual process of obtaining informed consent is subject to monitoring. The Board may request that a non-involved observer be present for overseeing the consent procedure. Executed consent forms must be available to the Board and DHR for review and audit purposes. The subject must be given a copy of the consent form. Due to the stringent requirements for obtaining informed consent, it is recommended that pregnant women and fetuses be excluded from all research projects except when they are the only subject population suitable for the research.

Prisoners and Others Involved in Criminal Proceedings

When prisoners are to be used as research subjects, DHHS has proposed special restrictions on the manner in which informed consent is obtained. Additionally, DHHS proposes that persons detained pending arraignment, trial, or sentencing will be excluded from acting as research subjects unless it meets the special requirements defined in Federal Regulations CFR 46.301-306 inclusive, subpart C.

The Investigator as Subject

An investigator may act as a subject for his or her own experiment. However, he or she must submit a protocol and obtain Board approval for such action. For protocols in which the investigator is one of a number of subjects, a cover letter stating the investigator's intention to be a subject will suffice as the informed consent, although the investigator can, of course, sign the usual study consent form instead.

Research Involving Only Pathological Specimens

Any research which makes use only of pathological specimens removed for diagnostic or therapeutic purposes, and for which no extra specimen was taken, and where confidentiality will be preserved, constitutes a situation in which there is no "subject at risk" and qualifies for exempt status. If the investigator contemplates such research he/she should describe it in the protocol, stating that no procedures, specimens, etc., are to be undertaken for the sole purpose of research, and that confidentiality will be preserved. In this case no consent form need be used.

A special circumstance arises in the case of the use of fetal tissue. The delicacy of the situation and the possibility of strong feelings on the part of the parents has caused the Board to require investigators who plan to use such tissues to obtain verbal consent from both parents (or if only the mother is available, from her alone) for the research use of the dead fetus. This should be done via the physician caring for the woman. This restriction does not apply to tissues from less-than-three-month-old abortuses. Such tissues are regarded as pathological specimens, as is a term placenta.

Consultation with Independent Physician

As a precaution against the general social risk of abusing certain vulnerable subject groups in the pursuit of medical progress, the Board will, at times, require that a "physician-friend" participate at key moments in the decision-making process.

When subjects of an experiment are patients under the direct care of a physician other than the investigator (e.g., hospitalized patients) and participation in the research by the patient might in some way affect his or her care, then it is important that the attending physician's consent be obtained before the patient's participation is sought. The physician's consent should be noted in the protocol and a place for his or her signature should be provided on the consent form. Where appropriate, a physician not involved in an experiment should be available to advise patients about any contraindications to the study, to request that the patient be removed from the study if it appears to be detrimental to the patient's well-being and to act as an " ombudsman" on behalf of the patient. Participation of an uninvolved physician is particularly crucial where the researcher is also the patient's regular physician. Protocols should describe these circumstances in detail where applicable.

In research involving psychiatric patients of all kinds, a non-involved physician is particularly needed to judge the adequacy of the consent given by that patient at that time. Special sensitivity is also needed in the case of parental or guardian consent for therapeutic research involving persons with marginal developmental disabilities, for here the parents or guardians themselves may have ambivalent feelings toward their children, and an "ombudsman" physician may be needed to weigh their motives for granting consent before such is accepted.

The Timing of Consent

For some studies, primarily those undertaken by anesthesiologists, consent must be secured in a short time prior to a therapeutic procedure. This often causes difficulties since many other things are often happening at the same time, such as operative consent. It is of concern to the Board that the act of consenting to be a subject in an experiment be sufficiently separated from these other events so that the subject can make a truly informed and considered decision. Where

protocols involve these sort of circumstances, the investigator is requested to pay particular attention to this issue so that the Board can be assured that informed consent will, in fact, occur.

There are circumstances where a patient might be enrolled in a study on the basis of a quickly given consent although the procedures will continue for an extended period of time (e.g., studies involving trauma or stroke patients). In such cases, it is usually desirable to provide for a confirmation of consent at a time when considered reflection and consultation would be possible.

Consent should, of course, be obtained when the subject is free of the judgment-impairing effects of psychoactive agents (including analgesics and sedatives).

Compensation

If subjects are to be paid, the amount of the compensation must be specified in the consent form and provisions must be detailed for partial remuneration in the event a subject withdraws from the study if his or her participation is terminated by the investigator. Compensation should be appropriate to the degree of investment by the subject, but caution is needed in populations where financial need may serve as an undue inducement to participate. No one except the subject may receive compensation for participation in a research project (e.g., the parent or guardian may not be compensated for participation by a minor child) except to reimburse expenses related to the study.

Compensation other than monetary in nature is discouraged by the Board and must be carefully and fully explained in the protocol.

When the True Purpose of Procedure or the Investigation Cannot Be Revealed

There are instances, most often in the behavioral sciences, in which the investigator's purposes or procedures in conducting the study cannot be revealed prior to the subject's consent to participate. If the study is to be at all useful in all investigations, the principle must be maintained that in giving their consent the subjects must be fully aware of all risks involved in the study for which they are volunteering. Hidden or incompletely revealed purposes or procedures must never be injurious or potentially injurious to the interests of the subjects, as they would be perceived by the subjects if they were fully aware of the purposes or procedures. If a study must incorporate a feature which involves omission of information about the study, or the inclusion of incomplete, false or potentially misleading statements, this feature must not in itself expose the subject to risk of any kind, since it will not be divulged prior to consent.

Investigators should take great care in the design of the study to provide the subject with as much accurate information as possible. It is always more acceptable to specify a set of alternative procedures which includes the actual procedure, or a list of possible purposes which includes the two purposes. For example, an investigator studying reactions to startling stimuli should inform the subjects they will be startled (and by what possible means) but that the startling may occur at unexpected times or by one of a number of means.

Studies which are deceptive in nature must contain little or no risk and include a "debriefing" feature in which a true statement of the procedure or purpose is provided to the subjects, at which time they are given the opportunity to withdraw consent. If this element is omitted, then the study must be such that it would be reasonably perceived as innocuous by the subjects had they been aware of it.

Studies in which the true purposes or procedures cannot be revealed must follow these guidelines:

A. This fact must be fully revealed to the review Board;

B. Compelling justification for omission of full information in obtaining consent must be furnished to the Board, including relevant discussion of possible alternative methods and a thorough analysis of the risk/benefit ratio;

C. All risks involved in participation, of whatever category, must be fully comprehended by the subjects prior to consent;

D. Incompletely revealed purposes or procedures must not be such that they reasonably would be perceived by the subjects as injurious to their interests or exposing them to risks if they had been revealed prior to volunteering;

E. The element of the hidden purpose or procedure must not itself constitute a risk, since it will not be revealed. Sensitivity is also needed in the case of parental of guardian consent for therapeutic research involving persons with marginal developmental disabilities, for here the parents or guardians themselves may have ambivalent feelings toward their children, and an "ombudsman" physician may be needed to weigh their motives for granting consent before such consent is accepted.

Communication Problems

Informed consent should be secured in the native language of the subject if English is not readily understood. If research is to be done in a cultural setting where signed statements are mistrusted, or where the concept of experimentation itself is unfamiliar, the investigator's protocol should clearly indicate how the project will be explained, how the consent of the subjects will be obtained, and who will witness the act of the consent.

Variant Modes of Obtaining Consent

Circumstances arise especially in observational studies in the social sciences, where the obtaining of written consent may be inordinately cumbersome, defeat the purpose of the experiment, or be otherwise undesirable. The policies provide for this eventuality by allowing approval of a modified procedure for consent if the investigator can establish that the risk to any subject is nil or minimal, that use of the primary procedures for obtaining informed consent would surely invalidate objectives of considerable immediate importance, and that any reasonable alternative means for attaining these objectives would be less advantageous to the subject. Where the risk is almost nil, the Board has allowed oral consent if the obtaining of a more standard form of consent can be shown to vitiate the research or present an insurmountable hardship.

In the case of survey, questionnaire, and standard interview studies, the subject must be informed as to the purpose of the research, as to the confidentiality (or its absence) of his or her answers, as to the potential benefits of the research, as to the freedom to discontinue participation at any point, and that the researcher will answer any questions. Coercion is to be scrupulously avoided.

Written consent is not always needed if:

A. The subject comes from a class of people well able to protect themselves and the research makes use of their expert knowledge or position. This includes public officials, university administrators, etc. If a researcher was investigating efficiency in city government by interviewing public officials, he or she would probably not be required to obtain written informed consent from each official interviewed. Public officials are quite accustomed to being interviewed and questioned. The Board sees no need to invoke complicated, perhaps negative procedures, when the subjects are well able to protect themselves, provided the purpose of the research is made clear;

B. The research is performed using existing data held by a third party. Researchers occasionally use existing data such as union membership records or the results of a questionnaire conducted by others. In such cases, it is often very difficult and sometimes impossible to obtain written consent from the individuals who were the subjects of the original data. Where there is no substantial risk to the subjects, either from invasion of privacy or other cause, the Board may waive the requirement for written informed consent;

C. The research is performed by mailed questionnaires, interviewing people in public places or otherwise requesting participation in a survey where the subject is free to not participate simply by not responding or walking away. The opening statement of such a questionnaire or interview should clearly indicate that participation is voluntary and the subject need not respond to any or all of the questions unless he or she wishes to do so. In these cases, participation will be deemed sufficient informed consent. However, the investigator has the responsibility to explain the purpose of the research prior to requesting participation by the subject. All elements of informed consent should be conveyed to the participants.

Risk/Benefit Statements

Any procedure that is normally harmless might on very rare occasions, cause serious complications, just as any drug, however benign, may have unforeseen side effects. Since all possibilities cannot be predicated, a rigid interpretation of informed consent could insist on some blanket statement that any experiment might cause death. This is clearly unreasonable. However, the likelihood of any specific complications should be quantified, if possible. It is appropriate to write "this procedure is frequently done for diagnostic/therapeutic purposes. The complications described are quite unusual, occurring in less than 1 in 100 cases." It is also appropriate to spell out for the subject what precautions will be taken to avoid undesirable complications. It is important, too, that minor discomforts or hazards as well as major complications be spelled out if they are anticipated.

In studies that randomize patients into treatment groups there is a subtle risk which should be stated on the consent form. The risk is that the patient may be randomized into what will be demonstrated to be the least effective treatment group. This is implicit in the randomization design, but should be made explicit to potential subjects.

Benefit too, should be discussed candidly. The primary goal of most studies even those involving patients, is not direct benefit to the subject, but rather is to answer some general questions. Whenever this is the case, it should be stated. Therapeutic benefit to the subject, if any, should be stated as a secondary goal or benefit. Forms must be extremely circumspect in holding out the

prospect of direct benefit to a patient unless this is indeed true or likely. Engendering inflated hopes becomes an unethical inducement.

No Exculpatory Clause

Forms must not contain any exculpatory clause, such as "I hereby release Dr. X (or DHR) from liability..." This is expressly forbidden, and such waiver of rights has no force in law.

Unforeseen Adverse Effects

The researcher must clearly state what will be done in case of adverse effects resulting for the subject as a result of participating in research. The subject also needs to know that DHR may not provide compensation or free medical care for an unanticipated injury sustained as a result of participating in the research. Adverse event means any untoward happening or unanticipated benefit in a patient or client after the patient or client signs the consent form, even if the patient or client hasn't taken a study medication or other intervention. Serious adverse event means a death, hospitalization, disability. life-threatening occurrence, cancer, congenital anomaly or significant event that occurs during the study period or is reasonably related to events that took place during the study period even though the serious adverse event happened after the termination of the study.

Storage of Signed Consent Forms

Signed consent forms should clearly indicate the particular study to which they belong, either in the title or the body of the form. All forms should be properly executed and dated. Retention period is a minimum of three years or longer as prescribed by the agency requirements. Consent forms must be treated as confidential material which may not be disclosed without the consent of the subject or as required by law. In all research involving patients, copies should be included in the patient's medical records.

When the subject is participating in a research project which may have an effect on any non-project-related material treatment, the subject may need to carry a copy of the consent information on his or her person concerning the study at all times. Examples of this would be a drug study where adverse reactions might occur in ambulatory patients or an emergency treatment where the subject has been rendered unconscious. The investigator should provide the subject with a copy of the consent form and make sure that he understands the importance of having it in his/her possession at all times.

APPENDIX B

MODEL CONSENT FORM

(Use Language That Your Subject Will Easily Be Able To Understand)

DEPARTMENT OF HUMAN RESOURCES:
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

TITLE OF STUDY: _____

INTRODUCTION OF RESEARCHER AND AFFILIATION WITH DHR

I am (_____) and am a (position/title) in the (Agency) of the Department of Human Resources.

PURPOSE

You are being asked to participate in a research study. We hope to learn (in lay language, state as clearly and precisely as possible what the study is designed to discover or establish). This research is supported by (a grant from) (name of entity).

PROCEDURES

If you decide to volunteer, we will [in plain language describe the procedures to be followed, including their purposes, duration, frequency, and recovery time, if applicable. Any drug or device should be described. If a placebo is to be administered to a portion of the subjects, this information must be included, though individual subjects need not be informed as to whether they will actually receive a placebo. Quantities, such as blood to be withdrawn, should be stated in terms familiar to the subject. If audio/video taping or motion pictures are a procedure of the study, insert a statement permitting subject to review/edit. Define permitted usages and detail disposition of such material at the end of the study to review/edit. (i.e., delete inappropriate portions). State where any recordings will be retained for a period of three years.]

ALTERNATIVES

[Describe alternatives procedures or treatments that might be advantageous to the subject. Any standard treatment that is being withheld must be disclosed, with its relative risks and benefits. Particularly when treatment is hazardous or very unpleasant, or the quality of a prolonged life is seriously to be questioned, the option of no treatment must be candidly presented. If no alternative drug or treatment is available, this should also be stated. Only use if applicable to your research.]

RISKS

I understand that I should notify the investigator if I am pregnant or become pregnant.
[A fair, reasonably detailed and understandable (lay language) description of any physical, psychological and/or social risks as a result of the research. Patients should be warned that their condition might become worse despite participation.]

BENEFITS

A fair, reasonably detailed and understandable description of any potential benefits or values which might reasonably result from the research. If the individual subject will receive no direct benefit, this should be explicitly stated.

CONFIDENTIALITY

State the way in which the subject's confidentiality will be maintained. State the persons or agencies to whom information from the study will be furnished, the nature of the information to be furnished, and the purpose of the disclosure.

RIGHT TO REFUSE OR WITHDRAW

You may refuse to participate and still receive the care you would receive if you were not in the study. You may change your mind about being in the study and quit after the study has started. If the study design or use of the data is to be changed, I will be so informed and my consent re-obtained.

QUESTIONS

If you have any questions, please ask us. If you have additional questions later, _____ (give name of the principal investigator or assistant will be happy to answer them at (give an address and phone number. In many instances, especially those involving investigational drugs, a 24-hour number should be included. For questions concerning the rights of research subjects, you may contact the Department of Human Resources at (775) 684-4000.

****

I understand that I am to notify the investigator in the event that I become pregnant.

I understand that I am free to ask questions or consult other people about the study or the consent form.

I understand that I am free to withdraw from the study at any time for any reason and without prejudice of any sort as a consequence of withdrawing.

I understand that the investigator may terminate my participation at his or her discretion.

I have read the consent form and consent to participate.

_____ _____
Signature of Participant or Legal Representative *Date*

_____ _____
Signature of Principal Investigator *Date*

_____ _____
Signature of Witness (If Applicable) *Date*

Adopted: August 5, 1999
Department of Human Resources
State of Nevada

Appendix C

BASIC ELEMENTS OF INFORMED CONSENT

The following information must be communicated in writing to all research subjects or respondents before they agree to participate in a research project that qualifies for exempt certification. Additional elements of informed consent may be required when children are involved in the research, and when investigational activities require complex adherence to protocols, special risks, and other matters unique to the research. In these instances, investigators may be required to provide additional information in their "Informed Consent" forms either prior to or after IRB review.

The following are the minimum required elements of informed consent. Additional information may be included at the discretion of the investigator:

1. a statement identifying yourself and your affiliation with the Department of Human Resources;

2. a request to participate in the study as part of a research project;

3. an explanation of the purposes of the research, the expected length of time of the subject's involvement, a description of the procedures to be followed, and identification of any procedures which are experimental in nature, including

   a) a description of the potential risks and discomforts associated with the research
   b) a description of any benefits to the subject or others which may reasonably be expected from the research;

4. a description of compensation for participation (money, extra course credit, etc.) if any;

5. a statement describing the subject's anonymity or the extent to which confidentiality of records identifying the subject will be maintained;

6. the names, addresses, and phone numbers of the people to contact for answers to questions about the research, including DHR, for information regarding the rights of research subjects;

7. an assurance that participation is voluntary and that the subject may withdraw from participation at any time, and when appropriate that a subject may be removed from a study by a doctor of investigator based on non-compliance with study protocols, because of adverse reactions, or because of other reasons thought to be appropriate.

8. A Child Assent Form that must be brief and contain language written at the appropriate age level. The following elements must be present on the Child Assent Form if the subject is 7 to 18 years of age, both a Child Assent Form and a Parental of Guardian Consent Form is required.

   a) a statement of the purpose of the research;
   b) a description of the procedures to be applied to the minor;
   c) a description of the potential risks and discomforts associated with the research;
   d) a description of any direct benefits to the minor;
   e) a statement that the minor does not have to participate if he/she does not want to;
   f) a statement that the minor is free to withdraw at any time;

g) a statement that the minor should discuss whether or not to participate with his/her parents or guardian prior to signing the assent form;

h) a statement that the parents or guardian of the minor will be asked to consent on behalf of the minor;

i) an offer to answer all questions;

j) a simplified concluding assent statement.

Adopted: August 5, 1999
Department of Human Resources
State of Nevada

Appendix D

PROTOCOL GUIDELINES AND FORMAT

Please review Section 10 and Appendix A of the DHR Policies and Procedures on Use of Human Subjects in Research.

DESCRIPTION OF STUDY: Using the numbering format below, provide the following information:

1. **ABSTRACT:** This abstract should contain a clear and succinct description of the long-term objectives and specific aims of this project with specific reference to its health relatedness. It should also include an accurate description of the experimental design and methods of achieving these goals. This abstract is meant to serve as a complete description of the proposed study.

2. **SUBJECTS:** Indicate efforts that will be made to assure equitable (both male and female) selection. When vulnerable populations are involved, describe why they are necessary. If subjects are to be paid, describe.

3. **PURPOSE, METHODS, PROCEDURES:** describe in detail the purpose, research methods, and procedures of the study.

4. **RISKS:** Describe any potential risks to the subjects - physical, psychological, social, or legal, and assess the likelihood and seriousness of these risks. If the methods or research create potential risks, describe other methods, if any were considered, and why they will not be used. Describe procedures, including confidentiality standards, for minimizing potential risks.

5. **BENEFITS:** Describe the anticipated benefits of the research to the individual subjects, to the particular groups or class from which the subject population is drawn, and/or society in general. In the event of monetary gain, include all payment arrangements, including reimbursement of expenses, free medication, stripends, etc.

6. **RISK-BENEFIT RATIO:** Assess the relative weights of the study's risks and benefits.

7. **COSTS TO SUBJECTS:** If the investigation involves the possibility of added expense to the subject or to a third party, such as an insurer or employer (e.g. longer hospitalization, extra laboratory tests, travel, time missed from work) indicate how this is justified. Be sure this is mentioned in the consent form.

8. **INFORMED CONSENT:** Describe the method of obtaining informed consent, the person(s) who will be responsible for obtaining it, and where the informed consent forms will be stored. Be sure to include all elements of an informed consent (see attached).

9. **OTHER REQUIRED INFORMATION:**

a. Copies of all materials and circumstances that will be used to obtain consent;
b. Location Issues - see DHR Policy and Procedures Section 10C;
c. Other attachments - see DHR Policy and Procedures Section 10C.
d. Copies of sponsorship agreements and/or investigational/research contracts or other signed documents, grant awards or scholarships that define the requirements and stipulations of the relationship between these parties and the investigator(s), and their expectations relative to the use of human subjects who are patients or clients of any DHR Division or program.