

## 8 Special Classes of Research Subjects

There are a number of research populations described in the federal regulations as "vulnerable" or that require additional consideration or protection. "Vulnerable" or special classes of subjects specifically described in the regulations include children, prisoners, pregnant women, fetuses, and mentally disabled persons, handicapped persons, or economically or educationally disadvantaged persons [\[45 CFR 46.111\]](#). Additionally, the regulations include specific provisions for research involving fetuses, pregnant women, and neonates [\[45 CFR 46 Subpart B\]](#); prisoners [\[45 CFR 46 Subpart C\]](#); and children [\[45 CFR 46 Subpart D\]](#). Exemption from IRB review **does not** apply to some research involving vulnerable populations or special classes of subjects. The following section is a brief discussion regarding some "vulnerable" subject populations.

### Fetuses and Human *In Vitro* Fertilization

Research involving the human fetus poses challenges for investigators and IRB's reviewing such projects as the fetus has an inextricable relationship to the mother. A fetus cannot provide informed consent to participate as a research subject. The National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research studied the subject of fetal research. The Commission, in its findings, did not define the "personhood" of the fetus; however, it did recognize the genetic heritage and vulnerability of the fetus and affirmed that it should be treated respectfully and with dignity, regardless of its life prospects. The Commission also affirmed the legitimacy and importance of fetal research for improving the health of fetuses both in the present and future. The DHHS refined regulations pertaining to pregnant women and fetuses in 2001 [\[45 CFR 46 Subpart B\]](#).

The federal regulations provide the following definitions:

1. "Pregnancy": encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery."
2. Fetus: "the product of conception from implantation until delivery." Delivery means "complete separation of the fetus from the woman by expulsion or extraction or any other means."
3. Dead Fetus: "a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord."
4. Delivery: "complete separation of the fetus from the woman by expulsion or extraction or any other means."
5. Viable: "as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the Federal Register guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in

accordance with the requirements of the general federal regulations or the subpart on children as research subjects.”

### **Research Directed Toward the Fetus *In Utero***

Three circumstances may affect *in utero* research. In the first, the study is directed toward pregnant women, in which the fetus is indirectly involved in the research, while in the second, the study is directed toward the fetus. Finally, there are situations where both the pregnant woman and the fetus are the subjects of the research activity. *The IRB may only approve in utero research when one of the following two criteria are met in addition to all other applicable institutional, federal, State and local requirements:*

1. The purpose of the research is to meet the health needs of the fetus and is conducted in a way that will minimize risk (for example a new technique for fetal transfusion for Rh incompatibility); or
2. The research poses **no more than minimal risk** to the fetus and the purpose of the activity is the development of important biomedical knowledge that is unobtainable by other means.

In order to address the numerous concerns which are raised by research activities involving the use of fetuses, the federal regulations have outlined the following:

### **Research Involving the Fetus *Ex Utero***

The federal regulations indicate that an *ex utero* (delivered) fetus is viable if, in the judgment of physicians, it is likely to survive to the point of sustaining life independently, given the benefit of available medical therapy. If the expelled or delivered fetus is viable, the regulations for research involving children will apply.

A nonviable fetus is defined by the federal regulations as “an expelled or delivered fetus which, although it is living, cannot possibly survive to the point of sustaining life independently, even with the support of available medical therapy. Although it may be presumed that an expelled or delivered fetus is nonviable at a gestational age less than 20 weeks and weight less than 500 grams, a specific determination as to viability must be made by a physician in each instance.”

**Research involving a nonviable fetus that would either artificially maintain vital functions or hasten their failure is forbidden by the federal regulations.** Ethical considerations require respect for the dignity of a dying human subject and an avoidance of unseemly intrusions into the process of dying for research purposes.

### **Consent for Research Involving Fetuses *In Utero* and *In Vitro* Fertilization**

Because of the father’s continuing responsibility for his offspring, the consent of *both* parents generally is required for research involving a fetus. The consent of the father is *not* required, however, in the following circumstances:

1. The research is designed to meet the health needs of the pregnant woman; or
2. The father is not competent; or

3. The father's identity or whereabouts cannot reasonably be ascertained; or
4. The father is not reasonably available; or
5. The pregnancy resulted from rape.

Research involving the produces of human *in vitro* fertilization requires the consent of the donors of both the sperm and the ova to be used in the specific research that is planned.

### **RESEARCH INVOLVING HUMAN *IN VITRO* FERTILIZATION**

The federal regulations require that all investigators proposing research involving human *in vitro* fertilization with or without embryo transfer must submit a full protocol to the Sunrise Health Institutional Review Board (SHIRB) for review. In order to obtain federal funding for the research, the project must receive review by a national Ethics Advisory Board [\[45 CFR 46.204\(d\)\]](#). The SHIRB may consult with the American College of Obstetricians and Gynecologists (ACOG) and/or the American Fertility Society (AFS) when reviewing protocols involving human *in vitro* fertilization.

The greatest problem regarding *in vitro* fertilization for the SHIRB involves the use of "spare" embryos. Consent forms for all *in vitro* fertilization procedures should address what will happen to embryos that are not used in the particular embryo transfer procedure for which they were created (*e.g.*, will they be used for research purposes, will they be implanted into another woman, or will they be destroyed).

### **Research with Dead Fetuses, Fetal Material, and the Placenta**

The use of dead fetuses, fetal material, and the placenta is gaining considerable attention due to the lifting of a moratorium on federally-funded research involving the therapeutic transplantation into humans of fetal tissue obtained from induced abortions. The moratorium, issued by the Assistant Secretary for Health in 1988, was lifted by a Presidential memorandum published in the Federal Register 58:7457 (February 5, 1993). Interim guidelines for the support and conduct of therapeutic human fetal tissue transplantation research were published in the NIH Guide for Grants and Contracts 22 (No. 11, March 19, 1993).

Investigators are required to conduct research involving human fetuses, fetal material, and the placenta according to the following regulatory requirements:

#### ***Separating Abortion from Research***

1. The decision to terminate a pregnancy and procedures of abortion must be kept independent from the retrieval and use of fetal tissue.
2. The timing and method of abortion should not be influenced by the potential uses of fetal tissue for transplantation or medical research.

#### ***Prohibiting Payments and Other Inducements***

Payments and other forms of remuneration associated with the procurement of fetal tissue are prohibited, except payment for reasonable expenses occasioned by the actual retrieval, storage, preparation, and transportation of the tissue.

### ***Informed Consent***

- Potential recipients of fetal tissues, as well as research and health care participants, should be informed about the source of the tissues in question. This information should be provided to prospective subjects in the informed consent form.
- The decision and consent to terminate pregnancy must precede discussion of the possible use of the fetal tissue in research and any request for such consent that might be required for that use.
- Fetal tissue from induced abortions should not be used in medical research without the prior consent of the pregnant woman. Her consent to donate fetal remains is sufficient for the use of fetal tissue.
- Consent should be obtained in compliance with state law and with the Uniform Anatomical Gift Act.

### ***Prohibiting Directed Donations***

- The pregnant woman should be prohibited from designating the transplant recipient of the fetal tissue.
- Anonymity between donor and recipient should be maintained, so that the donor does not know who will receive the tissue, and the identity of the donor is concealed from the recipient and transplant team.
- Experimental transplants performed with fetal tissue from induced abortions provided by a family member, friend, or acquaintance should be prohibited.

### ***Compliance with State and Local Laws***

- Currently, there are no State of Nevada statutes governing fetal research or fetal tissue transplants. Investigators will be bound by State law should the state address this issue in the future.

### ***Ethical Review of Research***

- The federal regulations require SHIRB review all protocols proposing the use of fetal tissue for transplantation or in research obtained prospectively or after submission of an SHIRB application.

### ***Determining When Progress to Clinical Studies is Justified***

- Investigators should provide the SHIRB with as much information as possible regarding animal experimentation and previous clinical experience for any

proposed transplantation research including the use of fetal tissue. It is difficult to determine when enough information exists to ensure safety regarding this type of activity. A well established historical foundation will facilitate the process of SHIRB review.

### ***Research in Anticipation of Abortion***

After lengthy review, the National Commission determined that there is a difference between the moral status of a fetus destined for abortion and that of a fetus which is expected to be carried to term. Therefore, only those research procedures that are acceptable for a fetus going to term may be performed in anticipation of abortion, to preserve the mother's right to change her mind about ending the pregnancy. Please see the section entitled "*Research Directed Toward the Fetus In Utero*" indicated above.

## **WOMEN**

Historically, in order to avert harm to a developing fetus in an unsuspected pregnancy, physicians and the lay community have expressed concerns regarding women of child-bearing potential participating in research. As a result, federal agencies developed special guidelines ostensibly for the protection of the developing fetus that excluded women of childbearing potential from participating in some research. In 1977, for example, the FDA published a guideline that excluded most women of child-bearing potential from early phases of drug trials. An exception was made for studies involving women with serious and life-threatening diseases.

Over the past two decades, questions raised by grass roots, professional, consumer, and governmental groups regarding the adequacy and fairness in the distribution of the benefits and risks of research resulted in changes to the regulations for the involvement of women in research. At the same time improved pregnancy tests and methods of contraception became widely available. In 1988, the FDA issued guidelines that called for safety and efficacy profiles for women, elderly, and diverse racial groups as part of new drug applications (NDAs). Then in 1993, following broad public discussion about women participating in clinical trials, the FDA issued a new guideline that eliminated restrictions on women of child-bearing potential from participating in all phases of drug trials. The guideline detailed procedures for minimizing the risks of pregnancy in women participating, such as contraceptive counseling, pregnancy tests, timing of short term studies in relation to the menstrual cycle, and the process of informed consent. Though the FDA emphasized the importance of risk/benefit determinations for subjects entering various phases of clinical trials, they underscored that initial determinations regarding whether risks to a fetus were adequately addressed were best left to patients, physicians, local human subject protection committees, and study sponsors. The new guideline also called for gender analysis with special attention to factors affecting the role of the menstrual cycle and exogenous hormone therapy in relation to the drug, as well as the influence of the drug on oral contraceptives.

The DHHS has also carefully examined the issue of women participating in research. Since the primary aim of clinical trials is to provide scientific evidence leading to a change in health policy or a standard of care, it is imperative to determine if the intervention or therapy being studied affects men and women differently. As stated in its new guideline, *NIH Outreach Notebook of the Inclusion of Women and Minorities in Biomedical and Behavioral Research* (1994), the NIH has concluded that the inclusion of women in research is sufficiently important that the only

justifiable reason to exclude non-pregnant women of child-bearing potential from research is compelling evidence that the proposed project would be inappropriate with respect to the health of the subject or the purpose of the research.

The policy statement referenced above pertains primarily to the inclusion of women as subjects in clinical trials, *i.e.*, medical research testing new treatments. However, the inclusion of women in behavioral research is also important and should be accomplished unless there is a compelling rationale which establishes that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research.

Significant portions of the text below are presented verbatim as published in the Code of Federal Regulations and the Federal Register.

### **Pregnant Women as Human Research Subjects**

Drug research using pregnant women as subjects is governed by the federal regulations **[45 CFR 46, Subpart B]**.

In accordance with [\[45 CFR 46.207 \(a\)\]](#), "No pregnant woman may be involved as a subject in a human clinical research project unless: (1) the purpose of the activity is to meet the health needs of the mother and the fetus will be placed at risk only to the minimum extent necessary to meet such needs, or (2) the risk to the fetus is minimal."

Research involving pregnant women is permitted only if the mother and father are legally competent and both have given their consent after having been fully informed regarding the possible impact on the fetus, except that the father's consent need not be secured if (1) the purpose of the activity is to meet the health needs of the mother; (2) his identity or whereabouts cannot reasonably be ascertained; (3) he is not reasonably available; or (4) the pregnancy resulted from rape [\[45 CFR 46.207\(b\)\]](#).

### **Women of Childbearing Potential as Human Research Subjects**

Non-pregnant women should not be excluded from any phase of research unless the science of the project or the health of the subject will be compromised. Regarding clinical drug research, Phase I, II and III trials should have the proportion of women in the study which at least reflects the proportion of women in the population which will receive the drug when it is marketed, and should enroll numbers adequate to detect clinically significant sex differences in drug metabolism and response.

#### ***Risk to Fertility***

It is expected that both male and female subjects will be informed about potential risks to their fertility including the development of any abnormalities or abnormalities in function of reproductive organs as a consequence of the proposed study intervention.

"Where abnormalities of reproductive organs or their function (spermatogenesis or ovulation) have been observed in experimental animals as a consequence of the proposed study intervention, the decision to include patients of reproductive age in a clinical study should be based on a careful risk/benefit evaluation, taking into account the nature of the abnormalities, the dosage needed to induce them, the consistency of

findings in different species, the severity of the illness being treated, the potential importance of the drug, the availability of alternative treatment and the duration of therapy.

“Where [subjects] of reproductive potential are included in studies of drugs showing reproductive toxicity in animals, the clinical studies should include appropriate monitoring and/or laboratory studies to allow detection of these effects. Long-term follow-up will usually be needed to evaluate the effects of such drugs in humans.” (**Federal Register, Vol. 58, No. 139, p39411, H, Thursday, July 22, 1993**)

### ***Risk to Fetus and/or Infant***

1. **General Guidelines:** “Appropriate precautions should be taken in research studies to guard against inadvertent exposure of fetuses to potentially toxic agents and to inform subjects and patients of potential risk and the need for precautions. In all cases, the informed consent document and investigator’s brochure [drug information] should include all available information regarding the potential risk of fetal toxicity. If animal reproductive toxicity studies are complete, the results should be presented, with some explanation of their significance in humans. If these studies have not been completed, other pertinent information should be provided, such as general assessment of fetal toxicity in drugs with related structures or pharmacological effects. If no relevant information is available, the informed consent should explicitly note the potential for fetal risk.

“In general, it is expected that reproductive toxicity studies will be completed before there is large-scale exposure of women of child-bearing potential, *i.e.*, usually by the end of Phase II and before any expanded access program is implemented.” (**Federal Register, Vol. 58, No. 139, p 39411, G, Thursday, July 22, 1991.**)

2. **Minimizing the Possibility of Fetal Exposure:** “Pregnancy testing may be used to detect unsuspected pregnancy prior to initiation of study treatment. Timing of the start of the study to coincide with or immediately follow the onset of menses is also an adequate indication that the subject is not pregnant. The investigator should ascertain that the subjects will responsibly employ a reliable method of contraception or abstinence for the duration of the drug or treatment exposure, which may exceed the length of the study. If requested, the investigator should be able to refer the subject to a knowledgeable counselor or physician for contraceptive advice.”
3. **Inclusion of Women in Early Clinical Trials (Phase I and Early Phase II)**

“In some cases, there may be a basis for requiring [inclusion] of women in early studies. When the disease under study is serious and affects women, and especially when a promising drug for the disease is being developed and made available rapidly under FDA’s accelerated approval

or real access procedures, a case can be made for requiring that women [be allowed to] participate in clinical studies at an early stage. When such a drug becomes available under expanded access mechanism (for example, treatment IND or parallel track) or is marketed rapidly under subpart E procedures because an effect of survival or irreversible morbidity has been shown in the earliest controlled trials, it is medically important that a representative sample of the entire population likely to receive the drug has been studied, including representatives of both genders. Under these circumstances, clinical protocols should not place unwarranted restrictions of participation of women.” (**Federal Register, Vol. 58, No. 139, p39409, G, Thursday, July 22, 1993**)

4. **Risk to Infant of Nursing Mother:** The potential for harm from exposure to a drug with unknown risks exists for nursing infants as well as fetuses. Therefore, this policy applies to breast feeding female subjects who are potential subjects in a drug trial in the same manner in which it applies to gestating women.

#### ***Active Recruitment of Women***

In order to assure that adequate numbers of women are included, researchers are encouraged to actively recruit women into clinical trials. For specific outreach methodologies, researchers should refer to the *NIH Outreach Notebook of the Inclusion of Women and Minorities in Biomedical and Behavioral Research (1994)*.

#### ***Sample Informed Consent Statement to be Included for a Potentially Toxic Drug Study***

The following language is recommended when women of child-bearing potential (non-pregnant) will be enrolled into a potentially toxic drug study:

“If you are a woman who is able to become pregnant, it is expected that you will use a medically accepted method of birth control [outline recommended forms of birth control] to prevent exposing a fetus to a potentially dangerous agent with unknown risk. If you are pregnant or currently breast feeding, you may not participate in this drug study. *If you are pregnant, if you become pregnant, or if you are breast-feeding during this study, you or your child may be exposed to an unknown risk. There are also known risks to you or your unborn baby, including [state specific risks].*

“To confirm to the extent medically possible that you are not pregnant, you are required to agree [to have a pregnancy test done before beginning this research study] [to begin the study after the onset of your next menstrual period] [choose one]. You must agree to avoid sexual intercourse or use a birth control method judged to be effective by the investigator and which will not interfere with the proposed investigation. Pregnancy could still result despite the responsible use of a reliable method of birth control while participating in this research study. You agree to notify the investigator as soon as possible of any failure of your birth control method, or if you become pregnant, either of which may result in your

being withdrawn from the study.” **Prior to enrollment, investigators are required to discuss with subjects what will happen if pregnancy occurs.**

## MINORITIES

In addition to requiring the equitable selection of women as research subjects, federal regulations require the equitable selection of minorities as research subjects [\[45 CFR 46.111\(a\)\(3\)\]](#). The inclusion of minorities in research is important both to ensure that they receive an equal share of the benefits of the research and to ensure that they do not bear a disproportionate burden.

Most diseases affect all population groups. In order to contribute to the pool of generalizable knowledge, investigators are required to include the widest possible range of population groups in their research. However, sometimes minorities are subject to a different risk. For example, some research pertains to conditions such as sickle cell anemia or Tay Sachs disease that specifically affect only a few minority groups. Other research focuses on characteristics of diseases or effectiveness of therapies in particular populations (e.g., HIV transmission, treatment for hypertension), and may also concern conditions or disorders that disproportionately affect a certain racial or ethnic group. Exclusion or inappropriate representation of these groups, by design or inadvertence, would be unjust. Further, to the extent that participation in research offers direct benefits to the subjects (in HIV research, for example, the receipt of a promising new drug), under-representation of minorities denies them, in a systematic fashion, the opportunity for direct benefit. A glaring example of this type of research abuse of minority populations' bearing the burden of research can be found in the Tuskegee Syphilis study, in which a group of African-American men suffering from syphilis were left untreated, despite the availability of penicillin, in order to study the natural course of the disease.

Due to these concerns, the federal regulations require that research design include diverse populations. Investigators submitting protocols for SHIRB review which do not call for heterogeneous study populations are required to justify, in writing, in their submissions, why a homogeneous study population has been chosen.

After a heterogeneous population has been chosen, investigators should pay careful attention to the following two issues:

1. **Special vulnerabilities:** The DHHS recognizes that certain subject populations may require additional protections because they are economically or educationally disadvantaged. The SHIRB will attempt to safeguard every subject's rights and welfare by making sure that any possible coercion or undue influence is eliminated (e.g., compensation that is not commensurate with risk, discomfort, or inconvenience involved, or recruiting in institutional settings where voluntary participation might be compromised). Investigators should address these issues specifically when submitting protocol information to the SHIRB for review.
2. **Consent Form Presentation:** Effort should always be made to ensure that the consent process and the relationship between the investigator and prospective subjects are safeguarded. The federal regulations require the translation of consent documents into the language which is most easily understood by research subjects; the possibility of illiteracy should be accounted for, as should the need for

communicating in non-English languages. The FDA indicated in October 1995, that non-English speaking subjects must have informed consent form information presented in a written language that they understand. [21 CFR 50.20 – 27 and *FDA Information Sheets*, October 1, 1995, p 49] A potential subject's inability to read or to understand English is not an appropriate basis for exclusion from most research.

The SHIRB approved informed consent document should be available in English and other languages as appropriate to the subject population(s). For investigators proposing to use non-English language consent documents, quality assurance procedures should be developed such as translation of the consent document from English to the second language and then back to English, to ensure that the information is correctly conveyed. The SHIRB is required to review all non-English consent forms and recruitment tools. The role of cultural norms of subjects should also be addressed. This information should be provided in a clearly identifiable form to the SHIRB for review.

## **CHILDREN**

The legal mandate of the SHIRB is to protect the rights and welfare of human subjects. The task becomes more difficult when considering children and minors as research subjects. The federal regulations provide for "Additional Protections for Children Involved as Subjects of Research: [\[45 CFR 46 Subpart D\]](#).

### ***Parental Permission and Research of Minimal Risk:***

Parental permission is required in most circumstances for children participating in research. Investigators are required to gain parental permission from at least one of the child's parents or guardians if the research involves only minimal risk. (*Chapter 4, "Informed Consent Requirements: Assent and Parental Permission for the Participation of Children in Research"*)

### ***Parental Permission and Research of More than Minimal Risk:***

- a. If the research poses more than minimal risk and no direct benefit to the child, the investigator is required to gain permission from both parents or the child's guardian in order for the child to participate in the research.
- b. If the research poses more than minimal risk but may directly benefit the child, only one of the child's parents or guardian need given permission.
- c. The investigator is not required to gain permission from both parents, if one of the parents is not reasonably available, deceased, unknown, legally incompetent, or from a parent who does not have legal responsibility for the care and custody of the child. This caveat does not exempt the investigator from obtaining the permission from at least one parent who has legal responsibility for the child.

The SHIRB is required to make additional considerations for the inclusion of children in research who are wards of the state or any other agency or institution. For research that involves more than minimal risk with no prospect of direct benefit to the individual subjects or for research that requires approval of the HHS Secretary, the study must

either be (1) related to the subject's status as a ward, or (2) be conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards. [\[45 CFR 46.406-409\]](#) The SHIRB is required to appoint an advocate for each child who is a ward. The advocate is required to have the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way with the research, the investigator, or the guardian organization. The requirement for an advocate is in addition to gaining permission from any other person acting on behalf of the child as guardian or *in loco parentis*.

Subpart D of the federal regulations requires the SHIRB to classify research involving children into one of four categories relating to the risks and benefits of the proposed research:

- 1. Research involving no greater than minimal risk**
- 2. Research involving greater than minimal risk, but presenting the prospect of direct benefit to individual subjects.** Research in this category is approvable by the SHIRB, provided: (a) the risk is justified by the anticipated benefit to the subjects; (b) the relationship of risk to benefit is at least as favorable as any alternative approach; and (c) adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.
- 3. Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield *important generalizable knowledge about the subject's disorder or condition*.** Research in this category is approvable by the SHIRB, provided: (a) the risk represents a minor increase over minimal risk; (b) the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations; (c) the intervention or procedures is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and (d) adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.
- 4. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.** This section provides a mechanism for the approval of research not falling under categories 1-3. The research must be approved by the Secretary of the Department of Health and Human Services (DHHS) if it is to be funded by the DHHS, after consultation with a panel of experts, and the panel must find that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a significant problem affecting the health and welfare of children.

When assessing risk to children and evaluating a research project proposing to involve children the SHIRB will consider the following issues:

- Is the participation of children as research subjects justified in this particular instance?
- If this research question can be addressed initially in adults, has this work been conducted?
- Have the results from any adult research indicated that the proposed research would benefit, or at least would not be harmful to children?
- Has every effort been made to ensure that a parent is present when the research intervention is conducted? This will not only comfort the child but will enable the parent to exercise the right to end the child's participation in the research project at any time. Investigators should note that in some cases (*e.g.* research into sensitive personal matters, physical examination of adolescents, research into abuse, etc.) it may not be appropriate to have a parent present. If a parent will not be present during the course of the project, has the investigator clearly stated why in the protocol?
- Are the personnel involved in the research, and the facility in which the research will be conducted, knowledgeable about and sensitive to the physical and psychological needs of the children and their families?
- Have the investigators taken into account the child-subject's previous experience with illness and medical interventions? Some children may be able to cope with stresses of research better than others as a result of previous experiences with medicine. Younger, "less experienced" children may be unprepared for participation in medical research.
- How the investigator determined the number of children to be enrolled for the study. Investigators should justify the number of subjects they propose to study. Biomedical investigators should always plan to involve the fewest number of children necessary to obtain statistically significant data from which valid conclusions can be drawn.
- Whether the proposed techniques are the least invasive (physically and psychologically) in order to obtain the information for the study.
- Have the investigators clearly defined how the assent of the child-subjects will be obtained?
- For research involving medical interventions the SHIRB will consider previous research with animals. The investigator should indicate whether the animal research is completed and the results to date.

All personnel working with children should be familiar with State laws requiring reports of suspected child abuse or neglect.

The SHIRB cannot approve research that exposes children as subjects to more than minimal risk and does not satisfy the conditions outlined above. The federal regulations, however, provide a process for seeking approval for such research from the DHHS

Secretary. Please contact the Sunrise Health Office of Research Compliance (SHORC) at 702-731-8559 for more information about this process.

### **TERMINALLY ILL PATIENTS**

Patients with a terminal illness may be willing to “try anything” that might offer hope of either a cure or a slowing of the disease process. Others, aware that nothing further can be done to cure their disease, might fear abandonment by the medical establishment and agree to participate in research as a means of maintaining contact with physicians expert in treating their condition. On the other hand, many terminally ill individuals are willing to submit to considerable discomfort and risk for the possible benefit of future patients suffering from the same condition, and will volunteer for Phase 1 clinical trials or basic research about their particular condition in hopes of helping other, similarly situated patients in the future.

Investigators should be sensitive to these matters and explain with care and clarity the likelihood (or lack thereof) that research subjects will experience any personal medical benefit from their participation in a particular study. This is especially important in Phase 1 drug studies, since the research is designed to evaluate a potential treatment for their illness and as a result, may obscure the fact that the dosage subjects will be given is not expected to produce a therapeutic result.

At the same time, it is important not to treat terminally ill patients as incompetent or incapable of autonomous decision-making, just because they are critically ill.

### **PRISONERS**

Prisoners are considered vulnerable because they are in a restrictive, institutional environment that affords little opportunity for making choices, earning money, communicating with outsiders, or obtaining medical care. The National Commission for the Protection of Human Subjects found that prisoners often volunteer for medical research as a means of access to a competent medical examination, because health care is woefully inadequate in most prisons.

Because their autonomy is limited, prisoners may participate only in certain categories of research, and special precautions are needed to assure that their consent to participate in the research is both knowing and voluntary.

An IRB that reviews research involving prisoners is required to have at least one member who is either a prisoner, or a prisoner representative; and a majority of the IRB members cannot be in any way associated with the prison(s) involved.

The Sunrise Health Institutional Review Board does not currently have a member who is a prisoner or prisoner representative and therefore does not currently review research involving prisoners as subjects.