

## Overview

This Standard defines the policies and procedures Rutgers University IRB follows to evaluate risks and potential benefits of proposed research.

- A) [Risk-benefit review of initial and continuing research](#)
- B) [Sources of risk and measures to minimize risk](#)
- C) [Data and safety monitoring](#)
- D) [Risks to vulnerable populations](#)
- E) [Suspension or termination of previously approved research](#)

### REFERENCES:

AAHRPP Standard II-4. The Research Review Unit, including IRBs, systematically evaluates risks to participants and potential benefits as part of the initial review and ongoing review of research.

ORSP Policies and Procedures Manual

### A. Risk-benefit review of initial and continuing research

Benefits of research include direct benefits to individual participants and to the population from which they are drawn, and generalizability of results *to knowledge or practice*. Research subjects must neither be excluded due to special risks, nor included *only* for reason of availability and convenience.

#### **What do Investigators and the IRB consider in evaluating the balance of risks and benefits?**

The Application for Review requires investigators to evaluate the risks and benefits of the proposed study. The IRB considers the following elements:

- Are the risks and benefits adequately identified, evaluated and described?
- Are the potential risks minimized and likelihood of benefits maximized?
- Is the risk/benefit ratio clearly addressed and articulated by the investigator and deemed acceptable for proceeding with the research?
- If vulnerable populations are involved, which regulatory category of risk/benefit does the protocol fall within and are all criteria within the category adequately addressed? Topic D. [Risks to vulnerable populations](#) below includes points to consider for each category of vulnerable subjects, excerpted from the OHRP's detailed *IRB Guidebook*.

#### **How does the IRB consider risk in regard to issues of inclusion?**

IRB discussion centers on issues of justice, beneficence, appropriate levels of inclusion, generalizability of study results, and liability of sponsors. The exclusion of certain populations (such as women or cognitively impaired individuals) from studies raises considerations of justice because exclusion deprives them from the possibility of benefiting individually from participation.

Exclusion or inappropriate representation further raises issues of generalizability: If certain populations are excluded or are not appropriately represented, the data generated by the study may not be generalizable beyond the study population or generalizable only to the group being targeted for ultimate benefit; the excluded group as a class will therefore not benefit.

#### **What additional factors does the IRB take into account in continuing review?**

The balance of risk and benefits to the subjects of a study may change over time as a result of the study or outside developments. The application for continuing review requires the investigator to evaluate study data to date as well as other circumstances (including, for example, the published outcomes of related research) to ensure that the balance of risks to benefits has not shifted to the disadvantage of subjects.

**REFERENCES:**

AAHRPP II-4.A. The RRU has and follows written policies and procedures for conducting initial and continuing review of the risks and potential benefits of research, including criteria for frequency of continuing review and procedures for handling modifications to protocols.

## B. Sources of risk and measures to minimize risk

### **What are potential sources of risk in social, behavioral and medical research?**

The IRB evaluates the risk and benefit analysis described in the research protocol, and also ensures that the Informed Consent process adequately describes the risks. Following are examples of risks to human subjects that must be described, if they are present:

- **Physical** - pain, physical discomfort, injury, illness or disease brought about by the methods and procedures of the research
- **Psychological** - anxiety, fear, stress, confusion, embarrassment, depression, guilt, shock, loss of self-esteem, and/or altered behavior, occurring during the research situation or later, as a result of participation
- **Social** - alterations in relationships with others that are to the disadvantage of the subject, including embarrassment, loss of respect of others, labeling with negative consequences, or diminishing the subject's opportunities and status in relation to others
- **Economic** - cost to subjects for procedures, loss of wages or income, damage to employability or insurability
- **Legal** - risk of criminal prosecution or civil lawsuit when research methods reveal that the subject has or will engage in conduct for which the subject or others may be criminally liable
- **Loss of confidentiality and privacy** - confidentiality is presumed and must be maintained unless the investigator obtains the express permission of the subject to do otherwise. Risks include invasion of privacy, as well as the social, economic, and legal risks outlined above.

### **What measures can be taken to ameliorate risks?**

In the protocol submitted to the IRB, the PI describes the measures that will be taken to ameliorate the identified risks. For example, if there appears to be psychological risk, the investigator should describe debriefing and other supportive processes and might arrange for counseling to be available. *If there appears to be physical risk, the investigator should describe ways in which the discomfort to subjects is minimized, ideally using procedures already being performed on the participants for diagnostic or treatment purposes. The IRB should determine that the least invasive/harmful procedures are being used and that post-procedure care and support is available.* To avoid social, economic and legal risks, the IRB encourages investigators to perform studies anonymously whenever feasible, and to demonstrate procedures to ensure the security of the data if anonymity is not feasible. The IRB evaluates the proposed measures to ensure that they are adequate to the specific nature and degree of risks to which subjects will be exposed.

### **Additional considerations for evaluating research that proposes deception**

The IRB considers the following criteria when evaluating research that proposes deception:

- The proposed subject population must be suitable for the purposes of the study. For example individuals with diminished mental capacity or those with paranoid tendencies may not be suitable subjects for a protocol that involves deception, whereas the IRB may approve the same study if it uses a subject population with normal mental capacity and no history of mental illness.
- The consent process and document should not be part of the deception. Information actually provided in the informed consent process and documentation must be truthful, even if some details of the research are withheld. Subjects should not be asked to sign a lie, nor should information be withheld that would materially affect their decision to participate. Conversely, the investigator should provide as much information as feasible.
- The IRB must decide whether the study is so designed that the subjects will be adequately protected without having given fully informed consent, and if a waiver of some or all of the elements of informed consent can be approved. In deciding whether to waive or alter consent requirements, IRBs must consider the risks to which subjects will be exposed. To receive a waiver of consent requirements, the study must present **no more than minimal risk**.
- To grant a waiver, the IRB must find that the proposed process will not adversely affect the rights and welfare of subjects, and that the deception is essential to the ability to carry out the research.
- *The IRB must determine that the cost of the deception to the subjects being made is outweighed by the benefits the research may provide to the study population and the generalizability of the results to knowledge and practice.*
- *A debriefing statement that informs the subjects of the true nature of the study is required for most studies that involve deception. Debriefing is appropriate if it contributes to the subject's welfare, for example by reducing stress or correcting misconceptions about themselves that resulted from participation in the study.*
- There are some instances in which debriefing may cause more harm than good, and is therefore not recommended (for example if the study results would provide subjects with information that is disturbing about themselves).
- After debriefing, the subject must be given the opportunity to confirm or rescind their consent. In essence, this is the actual informed consent for the subject's participation in the study, and should be prepared, presented and documented in accordance with the guidelines for informed consent. Further referential

information may be found in the American Psychological Association's Code of Ethics at: < <http://www.apa.org/ethics/code2002.html> >.

REFERENCES:

AAHRPP II-4.B. The RRU has and follows written policies and procedures for identifying and analyzing potential sources of risk and measures to minimize risk, including physical, psychological, social, legal, or economic risks. The analysis of risk includes a determination that the risks to participants are reasonable in relation to potential benefits to participants and to society.

Laurie Sloan, Jay Hull & Robert J. Amdur (2003). Deception of Research Subjects. In Amdur, R. *The Institutional Review Board Member Handbook*. Sudbury MA: Jones and Bartlett Publishers, Chapter 3-6.

### C. Data and safety monitoring

*In the research proposal, the Investigator should describe how data and safety monitoring is to be carried out. All studies should have procedures for data and safety monitoring whether it be the Investigator who performs this service, or some independent group like a data safety monitoring board (DSMB). The IRB must make a determination that the procedure set forth is adequate enough to ensure the subjects' safety and confidentiality during the course of the study.*

#### ***When is a DSMB necessary?***

*The IRB should consider the following criteria when determining if a DSMB is necessary.*

- *Is the study a phase III clinical trial.*
- *Is there a large study population where many subjects could be harmed before problems are recognized.*
- *Is the study using multiple sites where no one investigator treats more than a fraction of the subjects*
- *Are highly toxic therapies or dangerous procedures being used. This is a critical determinant of how frequently and intensely subjects should be monitored for adverse effects.*
- *Is there a high expected rate of mortality or morbidity in the study population where problems related to natural history of disease or aging may obscure adverse events caused by the research.*
- *Is a high chance of early termination due to safety, futility, or efficacy.*

#### ***What is the role of the DSMB?***

*The DSMB should review unblinded data at predetermined intervals during the course of the study in order to ensure the safety of research participants. During the review, the DSMB may suggest stopping the research for one of the following reasons.*

- *The study question can be answered with the data that has already been collected.*

- *The study question will not be answered upon completion of the study because too many subjects have been lost, for example, because subjects did not come back for follow-ups or stopped the intervention.*
- *The risks to the subjects are too great.*

***Who should make up a DSMB?***

*The DSMB should be a multidisciplinary group independent of any ties, affiliations, or interests that might unduly influence the members. The DSMB should consist of three to six experts in at least two areas: medical issues (the disease, drug, device, procedure, or outcome measures) and methodological issues (clinical trials design, data management, and statistical analysis).*

***What should the interaction be between the IRB and DSMB?***

*The DSMB will have much greater access to experimental data than the IRB and the DSMB should inform the IRB of all its findings and recommendations to aid the IRB with its oversight responsibility. If the IRB makes a determination that a DSMB is necessary, the IRB should provide in writing to the PI explicit reasons for requesting the establishment of the DSMB explaining the features of the study that require establishment of the DSMB, the specific reports the IRB wants from the DSMB, and additional information required by the IRB such as rules for stopping the study.*

**REFERENCES:**

AAHRPP II-4.C. The RRU reviews the plan for data and safety monitoring in research protocols, when applicable, and determines that the plan provides adequate protection for participants.

*McCutchan, Allen J. (2003). Data and Safety Monitoring. In Amdur, R. The Institutional Review Board Member Handbook. Sudbury MA: Jones and Bartlett Publishers, Chapter 7-4.*

*National Institutes of Health. NIH policy for data and safety monitoring, 10 Jun 1998. Access date 14 Nov 2004. World Wide Web <http://grants2.nih.gov/grants/guide/notice-files/not98-084.html>*

#### D. Risks to vulnerable populations

Benefits of research include direct benefits to individual participants, the population from which they are drawn, and generalizability of results. Research subjects must neither be excluded due to special risks, nor included only for reason of availability and convenience.

IRB discussion centers on issues of justice, beneficence, appropriate levels of inclusion, and generalizability of study results. The exclusion of certain populations (such as women or cognitively impaired individuals) from studies raises considerations of justice because exclusion deprives them from the possibility of benefiting individually from participation.

Exclusion or inappropriate representation further raises issues of generalizability: If certain populations are excluded or are not appropriately represented, the data generated by the study may not be generalizable beyond the study population; the excluded group as a class will therefore not benefit.

#### **Fetuses and Human In Vitro Fertilization**

*New Jersey state law protects the rights of researchers to conduct research on fetuses, including stem cell research ([New Jersey Stem Cell Act](#)). There are four basic categories of research involving human embryos or fetuses with distinct regulations the IRB must take under consideration when evaluating the risks and benefits of this type of research. For all of these categories the IRB must first make a determination that no inducements, including monetary, will be offered to terminate a pregnancy, that the individuals engaged in the research will have no part in any decision regarding the timing, method, or procedures used to terminate a pregnancy, and that these same individuals have no part in determining the viability of a neonate. The four categories, research on the fetus itself, research on pregnant women which indirectly involves the fetus, research on viable neonates, and research on nonviable neonates will be considered in turn. For the federal definitions of fetus, pregnancy, neonate, viable, and nonviable please consult [45 CFR 46.202](#).*

#### ***What are the responsibilities of the IRB when research is proposed that directly involves human fetuses?***

*The IRB may approve research directly involving human fetuses if it makes one of the following determinations and only after preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted to provide data for assessing potential risks to pregnant women and fetuses.*

- *The IRB determines that the purpose of the research is to meet the health needs of the particular fetus and the fetus will be placed at risk to the minimal extent necessary to meet such needs.*
- *The IRB determines that the risk to the fetus is minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.*

***What are the responsibilities of the IRB when research is proposed that will have the fetus as an indirect subject?***

*The IRB may approve research directly involving human fetuses if it makes one of the following determinations and only after preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted to provide data for assessing potential risks to pregnant women and fetuses.*

- *The IRB determines that the purpose of the activity is to meet the health needs of the mother, and the fetus will be placed at risk to the minimum extent necessary to meet such needs.*
- *The IRB determines that the risk to the fetus is minimal.*

***What are the responsibilities of the IRB when research is proposed that will use nonviable neonates?***

*Before approving research involving nonviable neonates, the IRB must determine that all of the following conditions have been satisfied.*

- *Where appropriate, preclinical and clinical studies have been conducted providing data for assessing potential risks to neonates.*
- *Individuals engaged in the research play no role in determining the viability of a neonate.*
- *The vital functions of the neonate will not be artificially maintained.*
- *The research will not terminate the heartbeat or respiration of the neonate.*
- *There will be no added risk to the neonate resulting from research.*
- *The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means.*
- *Consent from both parents of the neonate is obtained and each parent is fully informed regarding the foreseeable impact of the research on the neonate. Consent can be waived for one parent if that parent is reasonably unavailable,*

*incompetent, or temporary incapacitated except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.*

***What are the responsibilities of the IRB when research is proposed that may involve neonates of uncertain viability?***

*Before approving research involving neonates of uncertain viability, the IRB must determine that all of the following conditions have been satisfied:*

- *Where appropriate, preclinical and clinical studies have been conducted providing data for assessing potential risks to neonates.*
- *Individuals engaged in the research play no role in determining the viability of a neonate.*
- *The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective; or the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research.*
- *Consent from both parents of the neonate is obtained and each parent is fully informed regarding the foreseeable impact of the research on the neonate. Consent can be waived for one parent if that parent is reasonably unavailable, incompetent, or temporary incapacitated except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.*

***What are the responsibilities of the IRB when research is proposed involving viable neonates?***

*When determining the risk and benefits of research on viable neonates, the IRB should follow the procedures set forth for [children and minors](#) in Subpart D..*

**Women**

In considering the inclusion of women in the study, IRBs should note the limitations on generalizability that may result from study size or other factors. The ability to evaluate gender differences may depend on sample sizes that the investigator cannot reasonably attain.

Women of child-bearing potential may be excluded from studies not only because of concern for the welfare of the fetus, but also because of possible legal liability

of sponsors and investigators for harm caused by investigational agents or other research activities. Consideration of the liability issue requires balancing the protection of women and potential fetuses against the benefits that would result from their inclusion (*i.e.*, direct benefits and the generalizability of data).

Until a consensus is reached on this question, IRBs should continue to consider representation of women in study protocols in their deliberations on the adequacy of protections of the safety and welfare of subjects with an eye toward the principle of justice per the Belmont Report.

The IRB Guidebook offers suggestions for considering safety of women who are pregnant or lactating (and their infants); and safety in research studies related to conception.

**Points to consider**

1. For all studies, is there reason to exclude pregnant or lactating women? If so, how strict should the screening measures be?
2. For all studies involving pregnant women, have appropriate studies on animals and nonpregnant humans been conducted? Is any special monitoring of the informed consent process needed?
3. For studies directed toward maternal health, is the risk to the fetus the least possible consistent with the research objectives? Will the mother be adequately informed of the potential risk to the fetus and of alternative treatments and their risks and benefits?
4. For studies of pregnancy, labor, or delivery, is the risk to the fetus "minimal"? Is the father's consent required?
5. For studies of lactating women, is the supply and content of breast milk adequately protected?
6. For studies of conception or contraception, are the risks, benefits, reversibility, and alternatives adequately explained? In contraceptive studies, is there adequate explanation of possible failure and of the options available for dealing with unintended pregnancies?
7. Will women be appropriately represented in the study? Does the study need to be designed to allow evaluation of gender differences?

Note that the exemptions from IRB review provided for in 45 CFR 46.101(b) do not apply to research involving pregnant women [*Federal Register* 56 (June 18, 1991): 28013, note 1].

## **Children and Minors**

Federal guidelines refer to state law in the definition of children and minors who are research subjects:

**Children:** Persons who have not attained the legal age for consent to treatment or procedures involved in the research, as determined under the applicable law of the jurisdiction in which the research will be conducted [45 CFR 46.402(a)].

**Emancipated Minor:** A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law, but who are entitled to treatment as if they had by virtue of assuming adult responsibilities, such as self-support, marriage or procreation. (*See also: Mature Minor.*)

**Guardian:** An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care [45 CFR 46.402(3)].

**Mature Minor:** Someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain purposes (*e.g.*, consenting to medical care). Note that a mature minor is not necessarily an emancipated minor. (*See also: Emancipated Minor.*)

### ***What do Investigators and the IRB consider in evaluating the balance of risks and benefits when children are proposed as subjects?***

The IRB must assess the justification of using children as research subjects in light of the expected benefits to the child-subject or to society as a whole. In calculating the degree of risk and benefit, the IRB should weigh the circumstances of the subjects under study, the magnitude of risks that may accrue from the research procedures, and the potential benefits the research may provide to the subjects or class of subjects.

The IRB is required to classify research involving children into one of four categories and to document their discussions of the risks and benefits of the research study. The four categories of research involving children that may be approved by the IRB providing that adequate provisions have been made for soliciting the assent of children and the permission of their parents or guardians are as follows:

- Research not involving greater than minimal risk [45 CFR 46.404].
- Research involving greater than minimal risk that presents the prospect of direct benefit to an individual subject when the risk is justified by the anticipated benefit to the subject and the relationship of risk to benefit is at least as favorable as any available alternative approach [45 CFR 46.405].
- *Research involving greater than minimal risk with no direct benefit to the subject where the research will yield generalizable and vital knowledge about the*

*subject's disorder or condition when the risk is only a minor increase over minimal risk and the intervention or procedures used are reasonably similar to those inherent in the subject's actual or expected medical, dental, psychological, social, or educational settings [45 CFR 46.406].*

- *If the IRB cannot fit the research into one of these three categories, then the IRB must either disapprove the research or refer the research to the Secretary of the DHHS provided that the research presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. [45 CFR 46.407].*

### ***What constitutes minimal risk?***

Procedures that usually present no more than minimal risk to a healthy child include: urinalyses, obtaining small blood samples, EEGs, allergy scratch tests, minor changes in diet or daily routine, and/or the use of standard psychological or educational tests. The assessment of the probability and magnitude of the risk, however, may be different in children who are physically or psychologically sick and may vary depending on the diseases or conditions the subjects may have. For example, obtaining blood samples from a hemophiliac child may present more than minimal risk to the child. On the other hand, IRBs may consider that children suffering from chronic illnesses who are accustomed to invasive procedures are placed at minimal risk by involvement in similar research procedures, in contrast to children who have not had such experiences. The IRB must also consider the extent to which research procedures would be a burden to any child, regardless of whether the child is accustomed to the proposed procedures.

Procedures that exceed the limits of minimal risk may be difficult to define in the abstract, but should not be too difficult to identify on a case-by-case basis. Riskier procedures might include biopsy of internal organs, spinal taps, or the use of drugs whose risks to children have not yet been established. Behavioral interventions likely to cause psychological stress may also exceed minimal risk.

### ***What should the IRB consider when discussing possible benefits?***

The IRB should consider the variability in health and mental health statuses among potential subjects. For example, a potential subject might be a normal, healthy child, or a child who has been exposed to a disease or a toxin (*e.g.*, meningococcus or lead) where it is known that a percentage of the children exposed will actually experience untoward consequences. A child may also be in an early state of disease, *e.g.*, an HIV-infected child, or may actually suffer from disease or other significant medical condition. Thus the IRB must take into account the current health and mental health status of a child and the likelihood of progression to a worsened state without research intervention.

### **Points to consider**

1. Does the research have an identifiable prospect of direct benefit to the individual child participant? Can that benefit be achieved through alternative means?

2. Does the research have an identifiable prospect of risk to the individual child participant? What safeguards are proposed to minimize these risks? When procedures involving greater than minimal risk to children are anticipated, are convincing scientific and ethical justifications given?
3. Is the inclusion of normal volunteers justified?
4. Do studies involving placebo controls place the child at greater risk by withholding from selected subjects potentially therapeutic research drugs or interventions?
5. When possible, have appropriate studies been conducted on animals and adults first? When possible, will older children be enrolled before younger ones?
6. What is the age of majority in the state? Can a child consent to medical care for certain conditions, and, if so, at what age? What legal limits are there on the right of parents to consent on behalf of their children?
7. Is permission of both parents necessary? Under what conditions may permission of one parent be deemed sufficient? (See standard II-7).
8. Will efforts be made to ensure that parents' permission to involve their children in research studies is free from coercion, exploitation, and/or unrealistic promises?
9. Are mechanisms in place to ensure that children are involved as research subjects in ways that do not undermine their dignity as young persons? Are provisions made that show respect for the developing rights of children, such as: (a) obtaining their assent, and, where appropriate, honoring their dissent; and (b) protecting their need for privacy and the confidentiality of information regarding them?
10. Are there special problems that call for the presence of a monitor or advocate during consent procedures? Specifically, is the consent procedure related to the children or parents in their language of greatest comfort/knowledge?
11. Are special needs of adolescents such as counseling and confidentiality accounted for in the research design?
12. Are there any special problems such as confidentiality and reporting that might arise in sensitive research about child abuse or sexual practices of teenagers?
13. If conditions present in children have implications for other family members' health statuses, are appropriate mechanisms proposed for dealing with the larger family unit (*e.g.*, genetic risks or HIV infection)?

14. Should parents be required to be present during the conduct of the research? (Are proposed subjects to be very young? Are the procedures involved painful? Must subjects stay overnight in the hospital when they otherwise would not have to?)

### **Cognitively Impaired Persons**

*There is no clear consensus existing on the acceptable degree of risk when developmentally delayed and mentally compromised persons are involved in research. This topic is still up for debate but the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research made the following recommendations for approving research with cognitively impaired persons when the risk involved is greater than minimal risk which the IRB should consider when discussing the risks and benefits of using this subject population in research.*

- Research that proposes more than minimal risk should involve mentally compromised persons only if they will derive a direct and significant benefit from participation.
- Research involving institutionalized mentally disabled persons that shows a minor increase over **minimal risk** may be permitted only where the research is designed to evaluate an intervention of foreseeable benefit to their care.
- For research that does not involve beneficial interventions and that presents more than minimal risk, the National Commission recommended that the anticipated knowledge sought should be of vital importance for understanding or eventually alleviating the subject's disorder or condition.
- Finally, the National Commission recommended that there be additional ethical review at the national level for research projects the IRB believes should be supported - because the knowledge to be gained may be of major significance to the prevention, diagnosis, or treatment of mental disorders - but that would not otherwise be approved at the local level. The American College of Physicians has similarly recommended the creation of a national board to review research that involves more than minimal risk and that carries no direct benefit for the subjects [1989, p. 846]. Since the mechanism of a national board is not currently available, IRBs reviewing such research should consider obtaining assistance from expert consultants.

### ***What are the procedures the IRB should consider in limiting risk to cognitively impaired persons involved in research?***

IRBs must be sure that investigators have included a description of appropriate psychological or medical screening criteria to prevent or reduce the chances of adverse reactions to the therapeutic and research procedures. When appropriate, IRBs might want to require that other health care providers be consulted to ensure that proposed research

procedures will not be detrimental to ongoing therapeutic regimens. Specific diagnostic, symptomatic, and demographic criteria for subject recruitment should be described in the research proposal.

Any plan to hospitalize subjects or extend hospitalization for research purposes should be justified by the investigator. The effects of separation from supportive family or friends, of disruption in schooling or employment, and the question of responsibility for bearing any additional costs should be carefully considered by the IRB. Methods for assuring adequate protections for the **privacy** of the subjects and the **confidentiality** of the information gathered should also be described by the investigator. Individually identifiable information that is "sensitive" should be safeguarded, and requests for the release of such information to others, for research or auditing, should be allowed only when continued confidentiality is guaranteed.

### **Prisoners**

*OHRP defines a prisoner as “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.”* Further, the Rutgers University IRB expands upon this definition by including parolees or probationers in this definition as there is a likelihood that they may become reincarcerated. In addition to problems of coercion and undue inducement [See SOP II-7.B.], involving prisoners in research raises questions of burden and benefit. Prisoners should neither bear an unfair share of the burden of participating in research, nor should they be excluded from its benefits, to the extent that voluntary participation is possible. Prisoners' rights to self-determination (autonomy) should not be circumscribed more than required by applicable regulations. IRBs should refrain from assuming, without cause, that prospective prisoner-subjects will lack the ability to make autonomous decisions about participation in research. To the extent that prisoner-subjects are found able to voluntarily consent to participation, and to the extent allowable under applicable regulations, prisoners should be allowed the opportunity to participate in potentially beneficial research.

### **Points to consider**

1. Does the IRB have the necessary prisoner-related members?
2. Does the proposed research fall within one of the permissible categories of research with prisoners?
3. Is the use of prisoners as subjects justified?

4. Is there any evidence of duress, coercion, or undue influence in the particular prison(s) from which subjects will be recruited? (Does the prison facility meet all of the conditions set forth in applicable regulations?)

5. Are there any applicable state laws with which the IRB must comply? (See NJAC 10A)

***What types of research are permissible using prisoners as subjects?***

*It is important to point out here that the definition of minimal risk when a prisoner is involved is different than when non-vulnerable subjects are involved. Minimal risk for a prisoner is defined by OHRP as “the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons”. The IRB must review all research proposing prisoners as subjects with this definition of minimal risk and upon review may approve research involving prisoners if the research falls under one of the following four categories.*

- *Research that does not constitute greater than minimal risk and no more than inconveniences the subjects that studies the possible causes, effects, and processes of incarceration, and of criminal behavior.*
- *Research that does not constitute greater than minimal risk and no more than inconveniences the subjects that studies prisons as institutional structures or of prisoners as incarcerated persons.*
- *Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is more prevalent in prisons and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) after the Secretary of Health and Human Services has consulted with appropriate experts including experts in penology, medicine, and ethics, published notice, in the Federal Register, of his intent to approve such research.*
- *Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary of Health and Human Services has consulted with appropriate experts including experts in penology, medicine, and ethics, published notice, in the Federal Register, of his intent to approve such research.*

***What are the additional duties the IRB board must perform on top of the normal IRB procedures when research is proposed that involves prisoners?***

*In addition to limiting the research involving prisoners to the [above four categories](#), the IRB must also review the research proposal involving prisoners and find that the following six conditions have been met and then have Rutgers University submit a letter to OHRP certifying that the Rutgers University IRB has reviewed the research proposal and found that the research is one of the [above](#) four categories and that all the following conditions have been met (Note: OHRP certification is only necessary for DHHS sponsored research).*

- *Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired.*
- *The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers.*
- *Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project.*
- *The information is presented in language which is understandable to the subject population.*
- *Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole.*
- *Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.*

***What is the procedure that should be followed when a previously enrolled research subject becomes a prisoner and the relevant research protocol was not reviewed and approved by the IRB?***

*The Investigator should promptly notify the IRB of this event. All research interactions and interventions with, and obtaining identifiable private information about, the now-*

*incarcerated prisoner-subject must cease until the requirements of involving prisoners as subjects has been satisfied except when the Investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated, the IRB Chairperson may determine that the subject may continue to participate in the research until the requirements for using prisoners as subjects has been met.*

*The IRB should promptly re-review the protocol in accordance with the requirements of using prisoners as subjects if the Investigator wishes to have the prisoner subject continue to participate in the research.*

### **Traumatized and comatose patients**

New Jersey law does not permit research in emergency care. Emergency physicians may use investigational drugs or devices at their discretion, but the patient may not be included as a research subject at the time of the intervention or in the future.

### **Terminally ill patients**

*When research is proposed that involves terminally ill patients, the IRB should review the proposal and consider the following points:*

1. Must the research involve terminally ill patients to achieve its objectives?
2. Is a clear explanation of the patient's eligibility for the study provided?
3. Are specific treatment alternatives, including the option of no treatment, described?
4. Are the potential benefits and risks (and their probability) realistically and simply stated?
5. Are the ways in which participation may affect the patient's lifestyle clearly described (e.g., "You will be hospitalized each month for 5-7 days.")?
6. Is the patient assured that he or she can withdraw from the study at any time? If withdrawal from the research will result in a patient's discharge from a research unit or end the patient's access to health care that has been provided in conjunction with the research, is that fully explained?
7. Should a witness or patient advocate be present during consent negotiations?
8. Is there reason to require that the patient's physician not be the clinical investigator?
9. If the research is done under a Treatment IND or other expanded access mechanism, is the lack of conclusive effectiveness data made clear? Are all costs to subjects of receiving a drug or device under an expanded availability mechanism clearly specified?

10. If a drug is administered at the community level, does the subject's physician have access to information about the drug's potential usefulness and potential risks?

### **Elderly/aged persons**

Aside from the regulatory requirement that IRBs provide additional protections for specially vulnerable persons [Federal Policy §\_\_\_\_.111], there are no specific regulations governing research with elderly subjects. It is generally agreed, however, that the elderly are, as a group, heterogenous and not usually in need of special protections, except in two circumstances: cognitive impairment and institutionalization. Under those conditions, the same considerations are applicable as with any other, nonelderly subject in the same circumstances.

Federal guidance for elderly research subjects applies particularly to inclusion (especially in consideration of participation in benefits and generalizability of results), and issues of informed consent.

### **Minorities**

The participation in research by members of racial and ethnic minority groups raises concerns about appropriate levels of inclusion and generalizability of study results; the issues are parallel to those raised with respect to the inclusion of women in studies. [*See* SOPII-4, "[Women](#)"] In addition, the involvement of minorities raises concerns about the selection of subjects, the possibility of special vulnerability on the part of some prospective subjects, and about consent and the relative strengths or weaknesses of vulnerable groups in the consent process.

### **POINTS TO CONSIDER**

1. Is the subject population appropriately drawn? Will minority subjects likely be appropriately and adequately represented? If not, is the homogeneity of the study population justified?
2. Are subject recruitment strategies appropriate for obtaining a diverse subject population?
3. Have the special needs of prospective subjects been addressed (*e.g.*, child care, transportation)?
4. Has the possibility of undue influence or coercion been eliminated?
5. Does the proposed consent process ensure open and effective communication between the researcher and prospective subjects? Are the consent documents written in language that will be easily accessible to subjects? Are documents in foreign languages necessary? Is foreign language facility on the part of the research staff necessary (both for obtaining consent and conducting the research)?

### **Students, employees and normal volunteers**

Involving students, employees, and normal volunteers in research may present special concerns with which the IRB should be familiar. The federal regulations do not provide explicit protections for subjects in these categories.

**Normal Volunteers.** Strange as it may seem at first, special concerns surround the involvement of normal (*i.e.*, healthy) persons who volunteer to participate in research. Primarily, the principles involved are **beneficence** and **respect for persons**. In the *Belmont Report*, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research stated the two general rules that describe beneficent actions as: (1) do not harm; and (2) maximize possible benefits and minimize possible harms. Volunteers for whom no therapeutic benefit can result from participation in research should, therefore, be exposed to risks that are minimized to the greatest extent possible. While the minimization of risks is an important requisite for any research involving human participants, the altruistic motivation of the normal volunteer's agreement to participate (*i.e.*, of contributing to scientific knowledge for the benefit of society) heightens the concern for the risks to which such participants should ethically be exposed.

The risks with respect to students and employees as research subjects are essentially identical: coercion or undue influence, and confidentiality. In reviewing the informed consent process (See Standard II-7.B.), the IRB evaluates steps taken to minimize these risks.

### **International studies**

It is important that all research with human subjects adequately protect the rights and welfare of the subjects. All human subjects research in which American investigators are involved, and which would be subject to the federal regulations if it were conducted wholly within the United States, must comply with the federal regulations for the protection of human subjects in all material respects *except when it has been determined by the relevant federal department or agency head after review of the foreign country's protection policies that these policies afford protection to the subjects that are at least equivalent to those provided in this policy. In this instance, the foreign country's procedures may be substituted for the procedures required by the federal regulations. Notice of actions taken on such reviews is to be published in the Federal Register (or elsewhere, as provided for in department or agency procedures). [Note that the FDA has not adopted this provision for research that it regulates. All FDA-funded research, however, must comply with both DHHS and FDA regulations.]*

*The Rutgers University IRB includes in its review process considerations for the local context of the research and if necessary enlists individuals familiar with that context to advise the IRB in its review.*

*See also the section on vulnerable populations in Informed Consent Standard II-7.*

REFERENCES:

AAHRPP II-4.D. The RRU has and follows written policies and procedures for determining the risks to vulnerable populations as defined in applicable federal regulations, and specifically, for determining the required risk categories in protocols involving children and prisoners.

45 CFR 46

*Green, Ronald M. (2003) Research Involving Fetuses and In Vitro Fertilization. In Amdur, R. The Institutional Review Board Member Handbook. Sudbury MA: Jones and Bartlett Publishers, 373-379.*

*Nelson, Robert M. (2003). Research Involving Children. In Amdur, R. The Institutional Review Board Member Handbook. Sudbury MA: Jones and Bartlett Publishers, 383-388.*

*Prentice, Ernest, D., Gordon, Bruce G., Kratochvil, Christopher, J., and Kotulak, Gail D. (2003). Research Involving Prisoners. In Amdur, R. The Institutional Review Board Member Handbook. Sudbury MA: Jones and Bartlett Publishers, 394-398.*

OHRP [IRB Guidebook, Chapter 6, Special Classes of Subjects](#)

OHRP [Guidance on the involvement of Prisoners in Research](#) Revised 5/23/2003

E. Suspension or termination of previously approved research

**What circumstances might lead the IRB to suspend or terminate previously approved research?**

Delay of continuing review. HHS regulations at 45 CFR 46.109(e) require that continuing review of research be conducted at intervals appropriate to the degree of risk and not less than once per year. The Sponsored Programs Administrator notifies investigators and sends an application for continuing review long enough before the approval expires to allow the PI time to respond. The regulations make no provision for any grace period extending the conduct of the research beyond the expiration date of IRB approval. Beyond that date subject accrual must be suspended pending re-approval of the research by the IRB.

Non-compliance. The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements, that has been associated with unexpected serious harm to subjects [Federal Policy 45 CFR 46.113]. *Non-compliance also includes failure to inform the IRB of any adverse or unexpected events.* If the IRB decides to suspend or terminate its approval of a research project, the IRB must report its decision promptly to the investigator(s), appropriate institutional officials, and the sponsor or the department or agency head (or designated office, such as OHRP), if the research is federally funded. The IRB's report must include a statement of the reasons for the suspension or termination.

Regardless of the schedule for continuing review, the IRB will investigate allegations of non-compliance whenever they are brought to its attention. The IRB has the authority to suspend or terminate approval of research upon determining non-compliance with Federal regulations, including the requirement for IRB review prior to beginning research.

REFERENCES:

AAHRPP II-4.E. The RRU has and follows written policies and procedures for suspending or terminating previously approved research if warranted by findings in the continuing review or monitoring process.

OHRP Guidebook, 2001, Chapter 3 [http://ohrp.osophs.dhhs.gov/irb/irb\\_chapter3.htm](http://ohrp.osophs.dhhs.gov/irb/irb_chapter3.htm)

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