

7.4 Criteria for IRB Approval of Research

In order for the IRB to approve human subjects research, either through expedited review or by the convened IRB, it must determine that the following requirements are satisfied. These criteria apply to all categories of IRB reviews including initial reviews, continuing reviews, and modifications of previously approved research.

- (1) Risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) 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 the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should 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 is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
- (4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by the Federal Regulations [45 CFR 46.116].
- (5) Informed consent will be appropriately documented, in accordance with, and to the extent required by the Federal Regulations [45 CFR 46.117].
- (6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- (7) When appropriate, 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, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

7.4.1 Risk/Benefit Assessment

The goal of the assessment is to ensure that the risks to research subjects posed by participation in the research are justified by the anticipated benefits to the subjects or society. Toward that end, the IRB must:

- Judge whether the anticipated benefit, either of new knowledge or of improved health or other direct benefit for the research subjects, justifies asking any person to undertake the risks; and
- Disapprove research in which the risks are judged unreasonable in relation to the anticipated benefits.

The assessment of the risks and benefits of proposed research involves a series of steps:

1. **Identify the risks** associated with the research, as distinguished from the risks of activities, diagnostic tests, treatments, or therapies the subjects would receive even if not participating in research;
2. **Determine whether the risks will be minimized** to the extent possible by evaluating the necessity of procedures that impart risk and whether the data could be gained by procedures that are already being performed for other purposes or by alternative procedures that impart less risk;
3. **Identify the anticipated benefits** to be derived from the research, both direct benefits to subjects and possible benefits to society, science and others;
4. **Determine whether the risks are reasonable in relation to the benefits**, if any, and assess the importance of the knowledge to be gained;

In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research - as distinguished from risks and benefits subjects would receive even if not participating in the research.

In addition to evaluation of the risks in the research, the IRB determines, based on the materials submitted by the investigator, that research studies have the resources necessary to protect participants, such as adequate time for the researchers to conduct and complete the research, adequate number of qualified staff, adequate facilities, access to a population that will allow recruitment of the necessary number of participants, availability of medical or psychosocial resources that participants might need as a consequence of the research.

The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks and benefits that fall within the purview of its responsibility.

7.4.1.1 Scientific or Scholarly Review

In order to assess the risks and benefits of the proposed research, the IRB must determine that:

- The research uses procedures consistent with sound research design; and
- The research design is sound enough to reasonably expect the research to answer its proposed question.

In making this determination, the IRB may draw on its own knowledge and expertise, or the IRB may draw on the knowledge and expertise of others, such as reviews by a funding agency, or departmental review. When scientific or scholarly review is conducted by an individual or entity external to the IRB, documentation that the above questions were considered must be provided to the IRB for review and consideration. Scientific or scholarly review is documented and provided to the IRB via written documentation.

Scientific or scholarly review can be delegated to a departmental or other appropriate review committee.

7.4.2 Equitable Selection of Subjects

The IRB determines by reviewing the application, protocol/research plan and other materials that the selection of subjects is equitable with respect to gender, age, class, etc. The IRB will not approve a study that does not provide adequately for the equitable selection of subjects or has not provided an appropriate scientific and ethical justification for excluding classes of persons who might benefit from the research. In making this determination, the IRB evaluates:

- The purposes of the research;
- The setting in which the research occurs;
- Scientific and ethical justification for including vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons;
- The scientific and ethical justification for excluding classes of persons who might benefit from the research; and
- The inclusion/exclusion criteria, and the procedures/materials intended for use for the identification and recruitment of potential subjects.

7.4.2.1 Recruitment of Subjects

The investigator will provide the IRB with a plan for recruitment of all potential subjects for approval. All recruiting materials will be submitted to the IRB, including advertisements, flyers, scripts, letters, information sheets and brochures. The IRB should ensure that the recruitment plan and materials appropriately protect the rights and welfare of the prospective subjects (e.g., do not present undue influence). See Section 7.5.10 for a discussion of IRB review of advertisements and Section 7.5.11 for a discussion of IRB review of payments.

7.4.3 Informed Consent

The IRB will ensure that informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20. In addition, the IRB will ensure that informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117 and 21 CFR 50.27. The IRB will ensure, as part of its review, that the information in the consent document and process is consistent with the research plan, and, when applicable, the HIPAA authorization. See Section 11 below for detailed policies on informed consent.

7.4.4 Data and Safety Monitoring

For all research that is more than minimal risk, the investigator should submit a data and safety monitoring plan. The initial plan submitted to the IRB should describe the procedures for safety monitoring, reporting of unanticipated problems involving risks to subjects or others, descriptions of interim safety reviews and the procedures planned for transmitting the monitoring results to the IRB. This description should include information regarding an independent Data and Safety Monitoring Board (DSMB), if one exists, or an explanation why an independent data safety monitor is not necessary.

The IRB reviews the safety monitoring plan and determines if it makes adequate provision for monitoring the reactions of subjects and the collection of data to ensure the safety of subjects and address problems that may arise over the course of the study. If a plan was not submitted, the IRB determines whether or not a plan is required, and, depending on the circumstances, what the plan should include. The overall elements of the monitoring plan may vary depending on the potential risks, complexity, and nature of the research study.

The factors the IRB will consider in determining whether the safety monitoring plan is adequate for the research are as follows:

1. Monitoring is commensurate with the nature, complexity, size and risk involved.
2. Monitoring is timely. Frequency should be commensurate with risk. Conclusions are reported to the IRB.
3. For low risk studies, continuous, close monitoring by the study investigator or an independent individual may be an adequate and appropriate format for monitoring, with prompt reporting of problems to the IRB, sponsor and regulatory bodies as appropriate.
4. Data and Safety Monitoring plans should specify:
 - The entity or person(s) who will perform the monitoring, and the independence or affiliation that the entity or person(s) has with the sponsor or investigator
 - The safety information that will be collected and monitored, including serious adverse events and unanticipated problems
 - The frequency or periodicity of review of safety data

- The procedures for analysis and interpretation of the data
 - The procedures for review of scientific literature and data from other sources that may inform the safety or conduct of the study
 - The conditions that trigger a suspension or termination of the research (i.e., stopping rules), if applicable
 - The procedures for reporting to the IRB, including a summary description of what information, or the types of information, that will be provided
5. For a Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC), the plan should describe:
- The composition of the board or committee. Generally, a DSMB should be composed of experts in all scientific disciplines needed to interpret the data and ensure subject safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease/condition and treatment under study should be part of the monitoring group or be available if warranted.
 - Frequency and content of meeting reports
 - The frequency and character of monitoring meetings (e.g., open or closed, public or private)
 - The Charter should be provided, when one exists

In general, it is desirable for a DSMB or DMC to be established by the study sponsor for research that is blinded, involves multiple sites, involves vulnerable subjects, or employs high-risk interventions. For some studies the National Institutes of Health (NIH) require a DSMB. The IRB has the authority to require a DSMB or DMC as a condition for approval of research where it determines that such monitoring is needed. When DSMBs or DMCs are used, IRBs conducting continuing review of research may rely on a current statement, or the most recent report, from the DSMB or DMC which indicates that it has and will continue to review study-wide adverse events, study wide interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

7.4.5 Privacy and Confidentiality

The IRB will determine whether adequate procedures are in place to **protect the privacy** of subjects and to **maintain the confidentiality of the data**.

7.4.5.1 Definitions

Privacy. Having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. It is the state or condition of being free from unauthorized intrusion, being observed or disturbed by other people.

Confidentiality. Methods used to ensure that information obtained by investigators about subjects is not improperly divulged.

Private information. Information that has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Sensitive Information. data or information, on any storage media or in any form or format, which requires protection due to the risk of harm that could result from inadvertent or deliberate disclosure, unauthorized access, misuse, alteration, or loss or destruction of the information (e.g., could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, or reputation).

Identifiable information. Information where the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

7.4.5.2 Privacy

The IRB must determine whether the activities in the research appropriately protect the privacy of potential and actual subjects. In order to make that determination, the IRB must obtain information regarding how the investigators plan to access subjects or subjects' private, identifiable information and the subjects' expectations of privacy in the situation. Investigators must have appropriate authorization to access the subjects or the subjects' information.

In developing strategies for the protection of subjects' privacy, consideration is given to:

1. Methods used to identify and contact potential participants
2. Settings in which an individual will be interacting with an investigator
3. Appropriateness of all personnel present for research activities
4. Methods used to obtain information about participants, and the nature of the requested information including minimizing the information obtained to achieve the aims of the research
5. Information that is obtained about individuals other than the "target subjects," (e.g., a subject provides information about a family member for a survey) and whether such individuals meet the regulatory definition of "human subject"

7.4.5.3 Confidentiality

The IRB must determine if appropriate protections are in place to minimize the likelihood that information about subjects will be inappropriately divulged. Safeguards designed to protect confidentiality should be commensurate with the potential of harm from unauthorized, inappropriate or unintentional disclosure.

At the time of initial review, continuing review and with any requests for modification, the IRB assesses whether there are adequate provisions to protect data confidentiality. The IRB does this through the evaluation of the methods used to obtain, record, share, and store information about individuals who may be recruited to participate in studies and about subjects. The investigator will provide the IRB with a plan regarding the procedures to be taken to protect the confidentiality of research data and sensitive information. Additionally, the investigator will

provide information regarding information security procedures and plans to address the protection of paper documents, other physical media (e.g., audio or videotapes), and electronic data and information including the use, maintenance, storage, and transmission of information. The IRB will review all information received from the investigator and determine whether or not the confidentiality of research data is sufficiently protected. In some cases, the IRB may also require that a Certificate of Confidentiality be obtained to additionally protect research data (See Section 25.8) and/or obtain approval from the University of Virginia Information Security Office (InfoSec).

In reviewing confidentiality protections, the IRB shall consider whether or not the data or other information accessed or gathered for research purposes is sensitive and the nature, probability, and magnitude of harms that would be likely to result from a disclosure of collected information outside the research. The IRB in consultation with the InfoSec staff shall evaluate the effectiveness of proposed de-identification techniques, coding systems, encryption methods, methods of transmission, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections. In reviewing confidentiality protections, the IRB and the InfoSec staff shall also consider regulations and organizational requirements and policies regarding the use of information and information security.

Research regulated by the FDA that involves the use of electronic data collection/storage systems must comply with the requirements of 21 CFR Part 11.

7.4.6 Vulnerable Populations

Certain individuals, by nature of their age or mental, physical, economic, educational, or other situation, may be more vulnerable to coercion or undue influence than others. At the time of initial review the IRB will consider the scientific and ethical reasons for including vulnerable subjects in research. The IRB may determine and require that, when appropriate, additional safeguards be put into place for vulnerable subjects, such as those without decision-making capacity.

For an extensive discussion about the IRB's review and approval process for individual populations of vulnerable subjects, please refer to Section 12.