Michigan State University
Human Research Protection Program

**Subject:** Risk Benefit Ratio

**Section:** 6-3

This policy and procedure supersedes those previously drafted.

**Approved by:** Vice President of Research and Graduate Studies, 3-3-2005. Revision 1 approved by VP Research & Graduate Studies on 3-9-2008. Revision 2 approved by VP Research & Graduate Studies on 7-21-2011.

**Related Sections:** 6-2-A

“(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(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.” 45 CFR 46.111, 21 CFR 56.111

Risks are the harm or injury (e.g., physical, psychological, social, economic, legal) that could occur as a result of participation in a research study. Benefits are valued or desired outcomes or an advantage. Risks to subjects posed by participation in research should be justified by the anticipated benefits to the subjects themselves, to other persons with similar conditions or with similar needs, or at least to society generally. One of the major responsibilities of the Institutional Review Board (IRB) is to assess the risks and benefits of proposed research.

In research where no direct benefits to the subject are anticipated, the IRB must evaluate whether the risks presented by procedures performed solely to obtain generalizable knowledge are ethically acceptable. There should be a limit to the risks society (through government and research institutions) asks individuals to accept for the benefit of others, but the IRB should not be overprotective. In research involving an intervention that could provide a direct benefit to the subjects, a certain amount of risk is justifiable. In studies designed to evaluate therapies for life-threatening illnesses, risk of serious adverse effects may be acceptable. In any trial of a new or not-yet-validated treatment, however, the ratio of risks to benefits should not exceed those presented by any available alternative therapy. See the Human Research Protection Program Manual 6-2-A “Sound Research Design.”

As indicated in the Belmont Report (April 1979):

“Assessment of the justifiability of research should reflect at least the following considerations”: 
“(i) Brutal or inhumane treatment of human subjects is never morally justified.”

“(ii) Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by giving careful attention to alternative procedures.”

“(iii) When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject – or, in some rare cases, to the manifest voluntariness of the participation).”

“(iv) When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits”

“(v) Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process.”

In the process of evaluating the risk/benefit ratio, the IRB considers the following:

- Risks to subjects associated with the research
- Extent to which the risks to subjects involved are minimized by the research design
- Degree of risk (i.e., minimal risk, more than minimal risk)
- Possible benefits to be derived from the research
- Reasonableness of the risks in relation to the possible benefits
- Whether the subjects are provided with an accurate and fair description of the risks and anticipated benefits
- Appropriate intervals for continuing review