Date:
CPHS#:

OPHS WORKSHEET PERMISSIBLE RESEARCH WITH CHILDREN

For any protocol involving children/minors, the Committee for the Protection of Human Subjects must determine which of the regulatory categories of permissible research, if any, apply to that study. OHRP recommends that the Committee/IRB document the rationale for this choice.

The HHS regulations at 45 CFR 46, Subpart D and the FDA regulations at 21 CFR 50, Subpart D permit IRBs to approve three categories of research involving children, and describe a fourth category requiring a special level of HHS review, as follows (check the applicable box below).

Note: Along with determination of risk category, the IRB should also make a finding regarding parental permission/consent requirements as appropriate. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under 46.404/50.51 or 46.405/50.52. Where research is covered by 46.406/50.53 and 46.407/50.54 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

☐ **I. Research not involving greater than minimal risk to the children (*45 CFR 46.404 and 21 CFR 50.51*)**

To approve this category of research, the IRB must make the following determinations:
- the research presents no greater than minimal risk to the children;
  AND
- adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in HHS regulations at 45 CFR 46.408 or FDA regulations at 21 CFR 50.55.

☐ **II. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child subjects involved in the research (*45 CFR 46.405 and 21 CFR 50.52*).**

To approve research in this category, the IRB must make the following determinations:
- the risk is justified by the anticipated benefits to the subjects;
- the relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by available alternative approaches;
  AND
- adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in HHS regulations at 45 CFR 46.408 or FDA regulations at 21 CFR 50.55.

☐ **III. Research involving greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research, but likely to yield generalizable knowledge about the subject's disorder or condition (*45 CFR 46.406 and 21 CFR 50.53*).**

To approve research in this category, the IRB must make the following determinations:
- the risk of the research represents a minor increase over minimal risk;
- the intervention or procedure presents experiences to the child subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations;
- the intervention or procedure is likely to yield generalizable knowledge about the

subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition;
AND

- adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in HHS regulations at 45 CFR 46.408 or FDA regulations at 21 CFR 50.55.

A fourth category of research requires a special level of HHS review beyond that provided by the IRB.

☐ **IV. Research that the IRB believes does not meet the conditions of 45 CFR 46.404, 46.405, or 46.406 and of 21 CFR 50.51, 50.52, or 50.53, but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children (*45 CFR 46.407 and 21 CFR 50.54*).**

If the IRB believes that the research does not meet the requirements of 45 CFR 46.404, 46.405, or 46.406 or of 21 CFR 50.51, 50.52, or 50.53, but finds that it presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, it may refer the protocol to HHS for review. The research may proceed only if the Secretary, HHS, or his or her designee, after consulting with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following an opportunity for public review and comment, determines either: (1) that the research in fact satisfies the conditions of 45 CFR 46.404, 46.405, or 46.406, or (2) the following*:

- the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- the research will be conducted in accordance with sound ethical principles; ***AND***
- adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in HHS regulations at 45 CFR 46.408.

*If FDA regulations apply: The Commissioner of Food and Drugs, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, determines either: (1) that the clinical investigation in fact satisfies the conditions of 21 CFR 50.51, 50.52, or 50.53, or (2) that the following conditions are met:

- the clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- the clinical investigation will be conducted in accordance with sound ethical principles; ***AND***
- adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in FDA regulations at 21 CFR 50.55.