Appendix C

OHRP Procedures for a 407 Panel Process for Multi-Site Research

1) The funding agency and the principal investigator of the study should be informed of OHRPs receipt of a request for review under the 407 process. Any decision on the part of the sponsor or the principal investigator to eliminate a study site should not influence the 407 process.

2) OHRP may seek information from other study sites to determine whether the 407 designation is appropriate. However, if after feedback the IRB requests review under the 407 process, OHRP should determine whether it is appropriate to proceed.

3) OHRP should determine whether, pending completion of the 407 process, suspension or termination of enrollment at other sites may be harmful to currently enrolled participants or to the gathering of information vital to the welfare of children.

4) Whether enrollment has or has not begun, when OHRP determines that review under the 407 process should commence, it may be appropriate to postpone enrollments if the IRB requesting review under the 407 process has raised concerns that:
   a) A study judged by other IRBs to have no prospect for direct benefit poses more than a minor increment over minimal risk; *or*
   b) A study judged by other IRBs as approvable under HHS regulations at 45 CFR 46.405, does not in fact offer a prospect of direct benefit.

   The final decision to suspend or terminate enrollment in a study should rest with OHRP, not the agency supporting the research.

5) If OHRP has determined that enrollment at other sites should be suspended or terminated, OHRP should first attempt to convince the IRBs, the investigators, and the supporting agencies to voluntarily suspend enrollment pending the completion of the 407 process. If the IRBs, Principal Investigators, and/or the funding agency nevertheless refuse to suspend or terminate enrollment, despite consultation with OHRP, OHRP should exercise its appropriate legal authority to effectuate the suspension or termination of enrollment.

6) Regardless of whether or not enrollment is stopped, OHRP should make determinations regarding the provision of additional information to the parents or guardians of already enrolled subjects. The IRBs should decide the process by which that information will be conveyed to the parents or guardians.

7) When OHRP determines that enrollment should be suspended pending completion of the 407 process, each IRB should determine the most appropriate way to communicate this information to parents or guardians whose children are study participants.

8) When OHRP determines that enrollment should *not* be suspended pending completion of the 407 process, parents or guardians should be informed if it is reasonable to assume that knowledge that a review is being conducted would raise legitimate parental or guardian

concerns about withdrawing participation in light of a recalculation of risk and prospective benefits. For example:

a) A protocol approved under HHS regulations at 45CFR6.405 may *not* provide direct benefit; or
b) A protocol approved under HHS regulations at 45CFR46.406 may present more than minor increment over minimal risk.

9) If enrollment is permitted to continue, but *the Secretary has determined* that the risk-benefit calculus has significantly changed as a result of a 407 review, re-consent should be required for continued subject participation.

10) If *the Secretary rules that the study should be disapproved*, but *previously enrolled* participants are permitted to continue until being transitioned off the study, parents or guardians of the subjects should be informed that new enrollments have stopped *and their re-consent for the period which the child remains on the study should be obtained.*

11) If a child has completed participation in a study, it may be necessary to notify the child's parents or guardians. This determination should be based on whether the review under the 407 process has produced new information pertinent to the continued welfare of the child.