Appendix A

ALGORITHM FOR SUBPART D ANALYSIS (45 CFR 46 AND 21 CFR 50)

Apply the general criteria of 45 CFR 46.111 and 21 CFR 56.111

§46.111(a)(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.
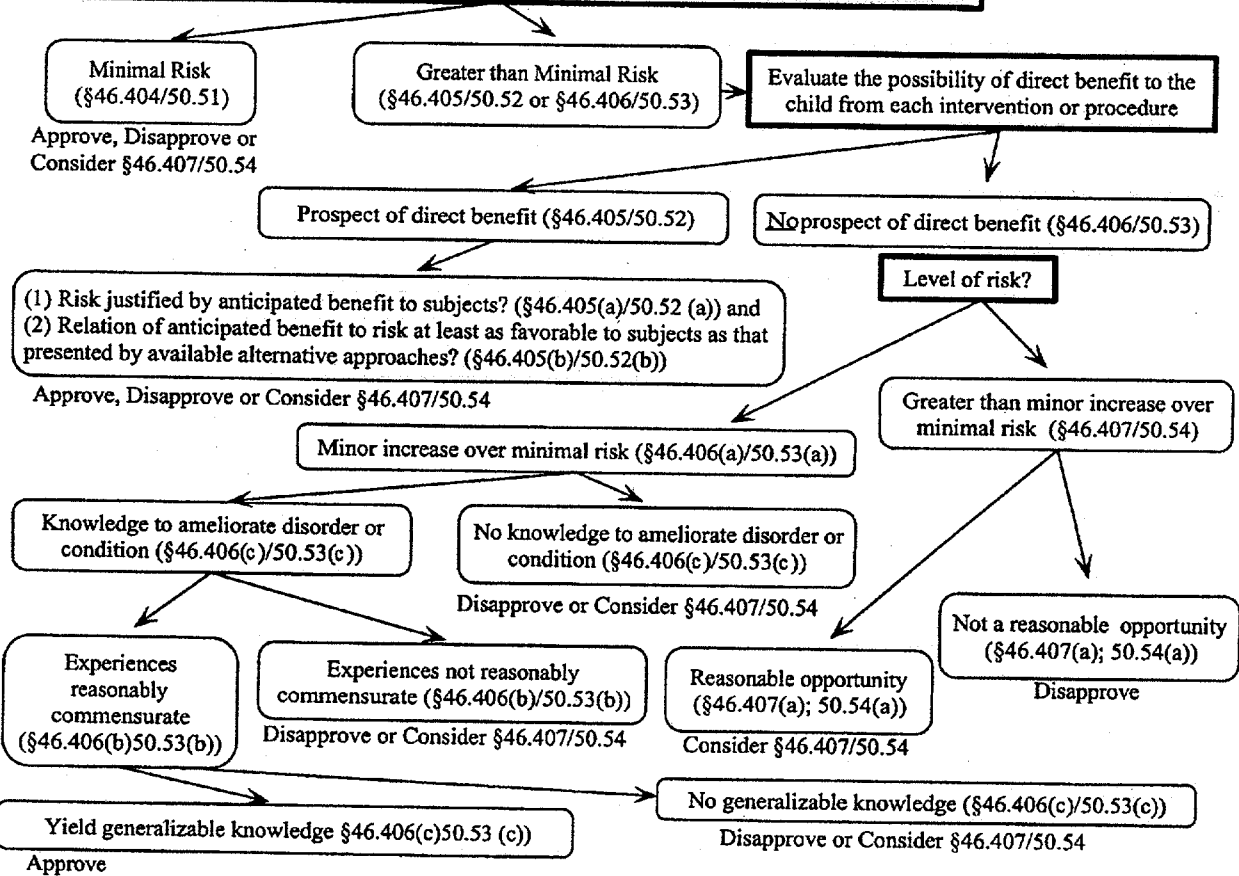
§46.111(a)(3) Selection of subjects is equitable, taking into account the purposes of the research and the setting in which the research will be conducted. The research requires the use of children to answer the scientific question.

Evaluate the balance of risk to benefit and/or knowledge, in general, and applying the categories of Subpart D.

§46.111(a)(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.

§46.111(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, ... additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Assess the level of risk presented by each intervention or procedure in the proposed research.

- Minimal Risk (§46.404/50.51) — Approve, Disapprove or Consider §46.407/50.54
- Greater than Minimal Risk (§46.405/50.52 or §46.406/50.53)
- Evaluate the possibility of direct benefit to the child from each intervention or procedure

Prospect of direct benefit (§46.405/50.52)

Noprospect of direct benefit (§46.406/50.53)

(1) Risk justified by anticipated benefit to subjects? (§46.405(a)/50.52 (a)) and (2) Relation of anticipated benefit to risk at least as favorable to subjects as that presented by available alternative approaches? (§46.405(b)/50.52(b))

Approve, Disapprove or Consider §46.407/50.54

Level of risk?

Minor increase over minimal risk (§46.406(a)/50.53(a))

Greater than minor increase over minimal risk (§46.407/50.54)

Knowledge to ameliorate disorder or condition (§46.406(c)/50.53(c))

No knowledge to ameliorate disorder or condition (§46.406(c)/50.53(c)) — Disapprove or Consider §46.407/50.54

Experiences reasonably commensurate (§46.406(b)50.53(b))

Experiences not reasonably commensurate (§46.406(b)/50.53(b)) — Disapprove or Consider §46.407/50.54

Reasonable opportunity (§46.407(a); 50.54(a)) — Consider §46.407/50.54

Not a reasonable opportunity (§46.407(a); 50.54(a)) — Disapprove

No generalizable knowledge (§46.406(c)/50.53(c)) — Disapprove or Consider §46.407/50.54

Yield generalizable knowledge §46.406(c)50.53 (c) — Approve

For all categories, consider the requirements for parental permission and child assent (§46.408;50.55)

§46.111(a)(4,5) Informed consent will be sought (and appropriately documented) from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116 and §46.117.

§46.111(a)(6) When appropriate, there are adequate provisions for monitoring the data collected to ensure the safety of subjects.

§46.111(a)(7) When appropriate, there are adequate provisions to protect subject privacy and to maintain data confidentiality.