Section One - Subpart A

Evaluate the research proposal and apply the general criteria of Subpart A [45 CFR 46.111; 21 CFR 56.111]

- Ensure that risks to subjects are minimized by using procedures which (i) are consistent with sound research design; (ii) don't expose subjects to unnecessary risk; (iii) are already being performed for diagnostic or treatment purposes. [§46.111(a)(1); §56.111(a)(1)]

- Ensure that selection of subjects is equitable, taking into account the research purpose(s) and the setting in which the research will be conducted. The research should require the use of children to answer the scientific question(s). [§46.111(a)(3); §56.111(a)(3)]

- Evaluate the anticipated benefits, if any, of the research to subjects, and the importance of the knowledge that may reasonably be expected to result.[§46.111(a)(2); §56.111(a)(2)]

- Ensure that additional safeguards have been included to protect the rights and welfare of children. [§46.111(b); §56.111(b)]

Section Three - Parental Permission and Child Assent

Apply the additional safeguards of Subpart D. See Section Two - Subpart D.

Section Three - Parental Permission, Child Assent and Additional Subpart A

- §46.111(a)(4,5) Informed consent sought (and documented), to extent required by §46.116 and §46.117.

- For all Subpart D categories, consider the requirements for parental permission and child assent ($46.408;50.55)

- Waive assent if (a) capability of some or all children so limited that they cannot reasonably be consulted or (b) research intervention or procedure offers prospect of direct benefit that is (i) important to children's health/well-being and (ii) available only in research.

- Permission of one parent sufficient ($46.404/405; §50.51/52); permission of both parents necessary unless one parent deceased, unknown, incompetent, or not reasonably available, or only one parent has legal custody of the child ($46.406/46.407; §50.53/54).

- §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.
ALGORITHM FOR PEDIATRIC PROTOCOL ANALYSIS
(SUBPARTS A AND D - 45 CFR 46 AND 21 CFR 50)

Section Two - Additional Safeguards of Subpart D

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

   - Minimal Risk ($§46.404/50.51$)
     - Approve, Disapprove or Consider $§46.407/50.54$

   - More than Minimal Risk
     - Evaluate the possibility of direct benefit to the child from each intervention or procedure

       - Prospect of direct benefit ($§46.405/50.52$)
         - (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 $§46.407/50.54$

       - No prospect of direct benefit ($§46.406/50.53$)

2. Evaluate level of risk

   - More than Minimal Risk
     - Evaluate prospect of direct benefit ($§46.405/50.52$)
     - Approve, Disapprove or Consider $§46.407/50.54$

3. Evaluate level of risk

   - Minor increase over minimal risk ($§46.406(a)/50.53(a)$)
     - Experiences reasonably commensurate ($§46.406(b)/50.53(b)$)
       - Disapprove or Consider $§46.407/50.54$
     - Understand or ameliorate child's disorder or condition ($§46.406(c)/50.53(c)$)
       - Disapprove or Consider $§46.407/50.54$
     - Yield generalizable knowledge of vital importance ($§46.406(c)/50.53 (c)$)
       - Approve

   - Greater than minor increase over minimal risk ($§46.407/50.54$)
     - Experiences not reasonably commensurate ($§46.406(b)/50.53(b)$)
       - Disapprove or Consider $§46.407/50.54$
     - No understanding or amelioration of child's disorder or condition ($§46.406(c)/50.53(c)$)
       - Disapprove or Consider $§46.407/50.54$
     - No generalizable knowledge of vital importance ($§46.406(c)/50.53(c)$)
       - Disapprove

   - Reasonable opportunity to understand, prevent or alleviate serious problem affecting children's health or welfare ($§46.407(a); 50.54(a)$)
     - Conducted in accord with sound ethical principles ($§46.407(b); 50.54(b)$)
       - Consider $§46.407/50.54$
     - Not conducted in accord with sound ethical principles ($§46.407(b); 50.54(b)$)
       - Disapprove

   - Not a reasonable opportunity ($§46.407(a); 50.54(a)$)
     - Disapprove

If Considering Approval, Return to Section Three.

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