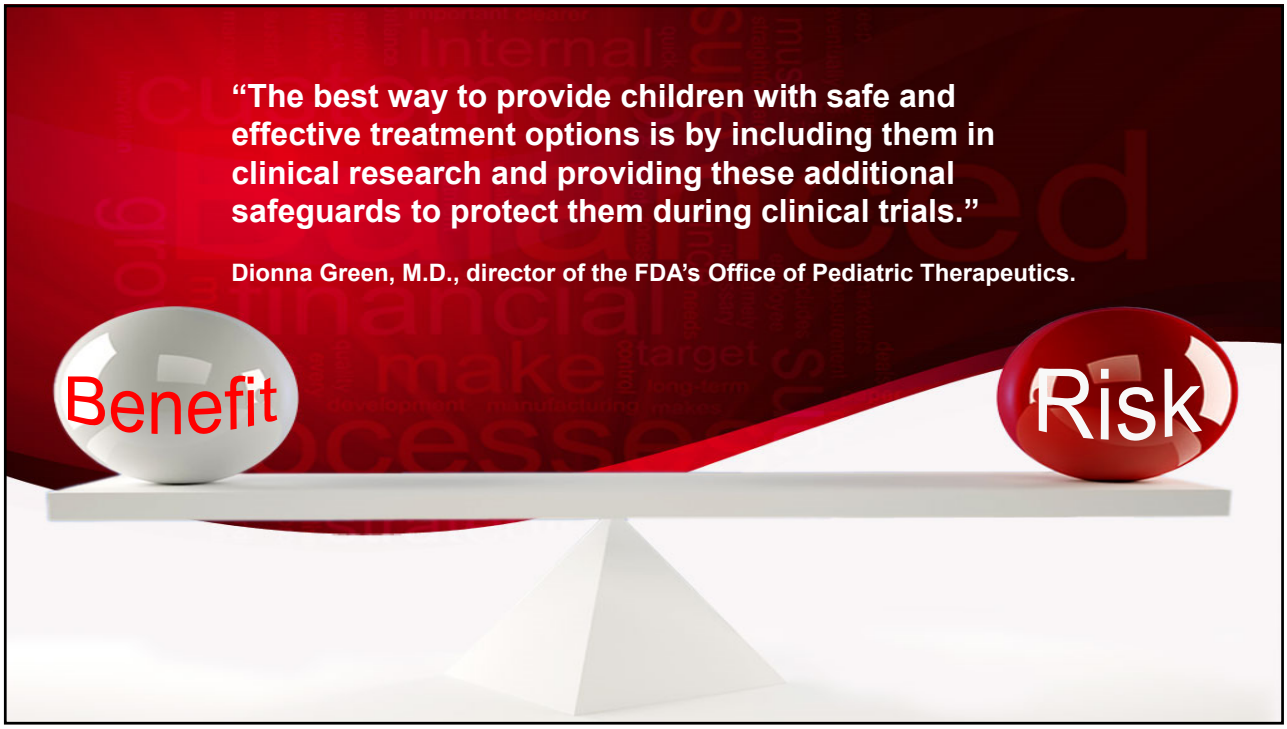

IRB
Mini
training

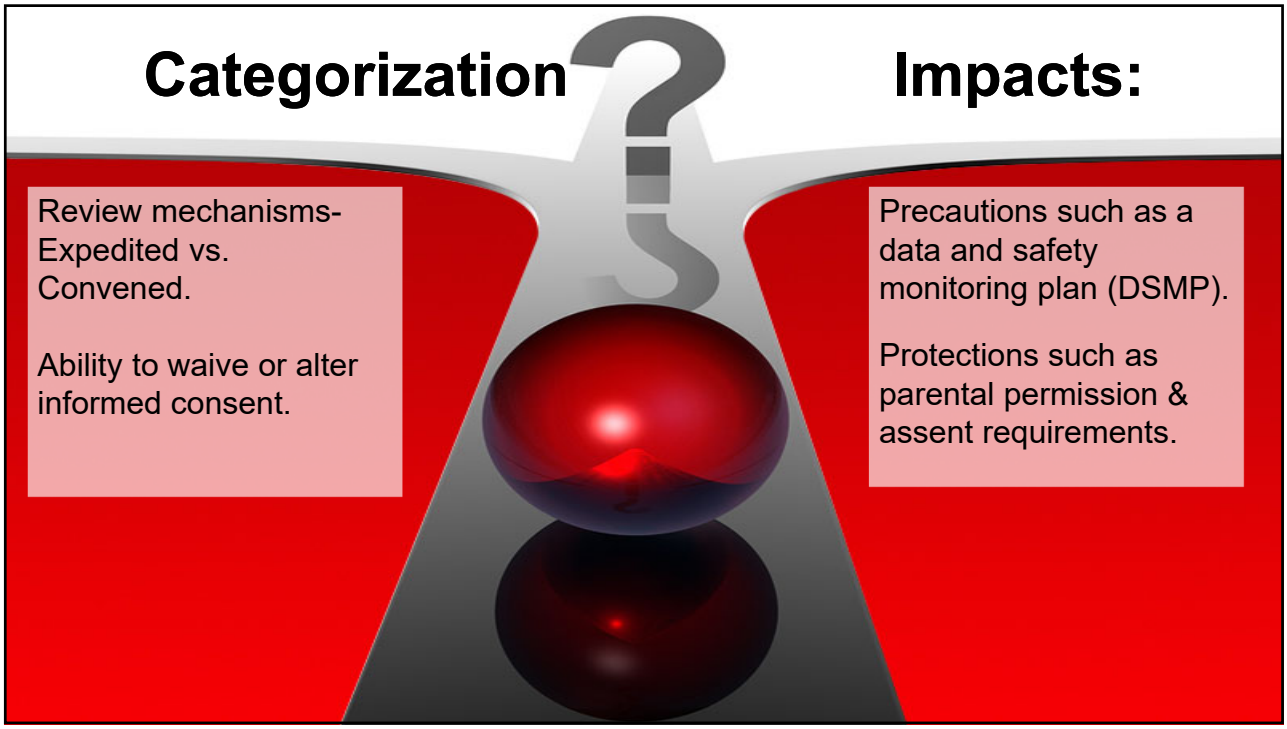
1


Subpart D – Categorizing Risk in Children's Research
Risk
NE
NW
2023

2


"The best way to provide children with safe and effective treatment options is by including them in clinical research and providing these additional safeguards to protect them during clinical trials."
Dionna Green, M.D., director of the FDA's Office of Pediatric Therapeutics.
Benefit
Risk

3


Categorization
Impacts:
Review mechanisms- Expedited vs. Convened.
Ability to waive or alter informed consent.
Precautions such as a data and safety monitoring plan (DSMP).
Protections such as parental permission & assent requirements.

4

Subpart D Category Criteria
404 Category 1 – no greater than minimal risk
405 Category 2 – risk justified by prospect of direct benefit; risk justified by anticipated benefit; & benefit as favorable as available alternatives
406 Category 3 - risk is minor increase over minimal risk & no prospect of direct benefit; & research is commensurate with expected medical situations; & likely to yield generalizable knowledge of importance to condition
407 Category 4 – research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children – Review by HHS Secretary or FDA Commission after consultation with a panel of experts and public comment.

5

Prospect of Direct Benefit

- Per FDA, effectiveness in adults does not need to be established before studies in children may begin. Prospect of direct benefit refers to the potential benefit to the individual child from exposure to the investigational intervention.
- FDA considers placebo-controlled trials to offer no prospect of direct benefit to placebo arm. A placebo-controlled clinical trial must be categorized under either Category 1, 3, or 4.

6

Minimizing Probability or Magnitude of Risk

- Alternatives (*lower risk procedure*)
- Precautions (*screen out "at risk"; DSMP)*
- Contingencies (*comparative effectiveness research*)
- Safeguards (*confidentiality breach*)

7

Case

Condition of Study: Neonatal Abstinence Syndrome

Study Design: Non-interventional study

Study Population: Birth – 2 month – recruited in NICU

Tests: Urine & stool from diaper & three 1 ml blood draw heel stick with standard lab draw when possible

8

Subjects: Neonatal Abstinence Syndrome

Study: Non-interventional study

Tests: Urine & stool from diaper & three 1 ml blood draw with standard lab draw when possible

Investigator Chose Category 3: Greater than minimal risk, no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.

☒ The permission of one parent even if the other parent is alive, known, competent, or not reasonably available or when only one parent has legal responsibility for the care/custody of child.

9

Poll

Do you agree with risk categorization & parental permission request?

10

Category Criteria	Parental Permission
404 Category 1 – no greater than minimal risk	
405 Category 2 – risk justified by prospect of direct benefit; risk justified by anticipated benefit; & benefit as favorable as available alternatives	
406 Category 3 - risk is minor increase over minimal risk & no prospect of direct benefit; & research is commensurate with expected medical situations; & likely to yield generalizable knowledge of importance to condition	
407 Category 4 – research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children – Review by HHS Secretary or FDA Commission after consultation with a panel of experts and public comment.	

11

Children's Form RIS Edit Request

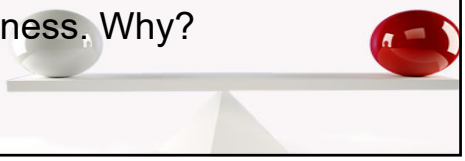
I am requesting

- The permission of both parents 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 (**required for Risk Category 3 or Category 4 Research**).
- The permission of one parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child (**permitted for Risk Category 1 or Category 2 Research**).

12

Assent

- Child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.
- Regulations don't specify the order in which parental permission and child assent should be sought.
- Unless IRB waived assent, if the child dissents from participating in research, even if his or her parents or guardian have granted permission, the child's decision prevails.
- Assent process should emphasize voluntariness. Why?
- Assent should be a continuing concept.



13

Assent required unless

- the capability of some or all of the children is so limited that they cannot reasonably be consulted;
- the intervention or procedure involved in the research holds out the prospect of direct benefit to the health or well-being of the children and is available only in the context of the research; or
- the research meets the same conditions as those for waiver informed consent in research involving adults.

Regulations don't require signatures;
UK policy generally requires unless IRB waives requirement .

14