Where Do We Go From Here?

CLINICAL
TRIALS
TRANSFORMATION
INITIATIVE

Goals for the Meeting

- Review
  - Why we do pregnancy testing in clinical research
  - Methods for doing pregnancy testing in clinical research
    - Types of tests
    - When to test
    - How are decisions about methods being made now?
  - “Comparative effectiveness” of different methods
- Feedback and input
  - What important general principles should be considered in designing pregnancy testing protocols?
  - What information/guidance would be most useful to the research community, and, ultimately, research subjects?
  - What resources would be most helpful for helping disseminate information/guidance?
  - Are there major evidence gaps that should be addressed through specific research?

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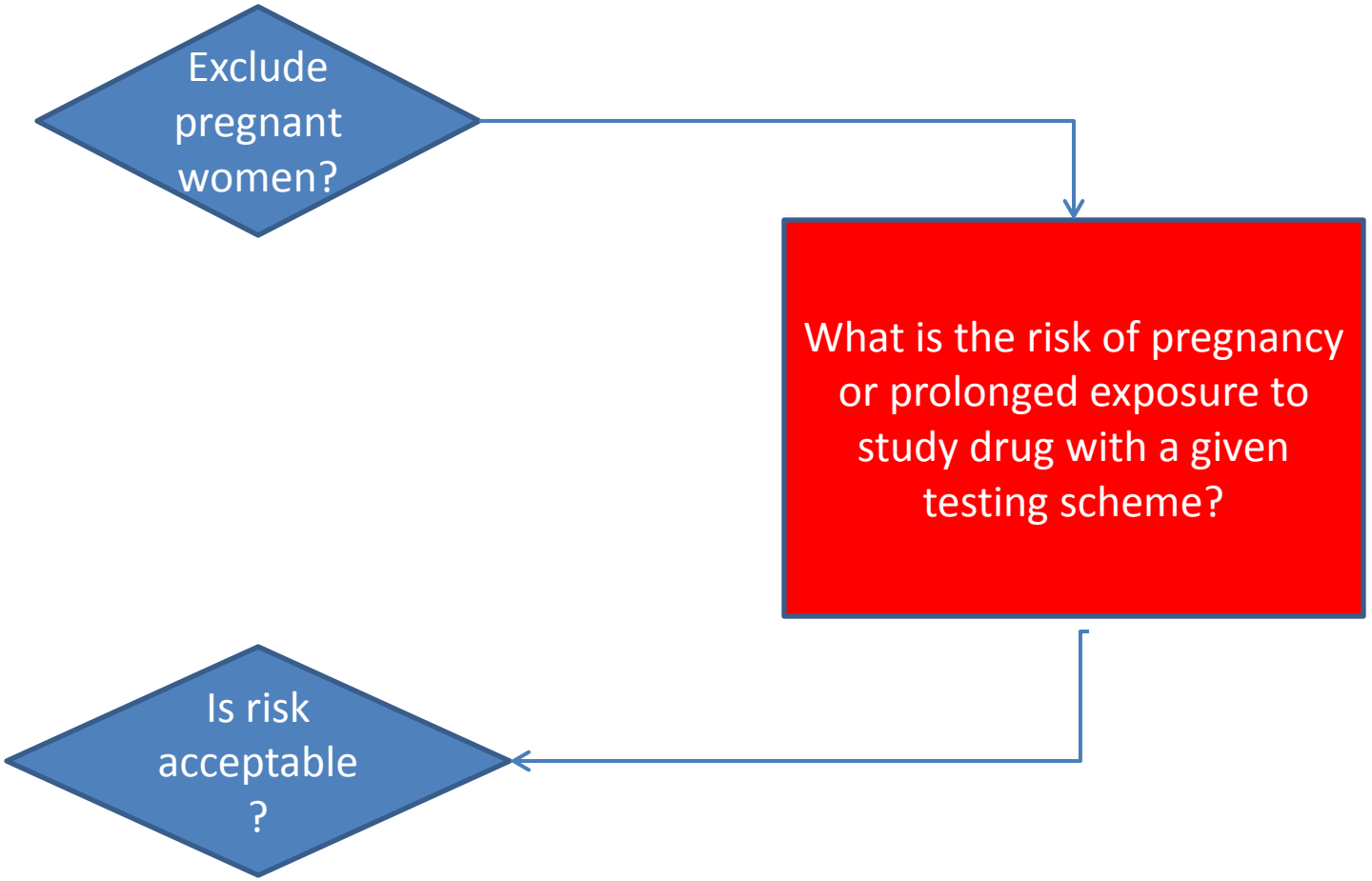
General Principles



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General Principles

- No testing protocol will eliminate the chance of a pregnant women enrolling in a trial or becoming pregnant during the trial
  - A goal of 0 pregnancies is not achievable
- The rationale for the choice of pregnancy testing should be provided in the overall study protocol.
- How positive pregnancy tests are handled should be specified in the protocol.

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General Principles: NPV

- The negative predictive value of pregnancy testing depends on
  - Probability of becoming pregnant
    - Age
    - Contraceptive method
  - Type of pregnancy test
  - Timing of test relative to conception
    - Definition of “negative” test

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General Principles: PPV

- The positive predictive value of a pregnancy testing protocol depends on
  - Probability of pregnancy
  - Probability of other sources of hCG
    - Age
    - Timing during menstrual cycle
    - Interfering antibodies
  - Timing of testing
    - Chemical pregnancies

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General Principles: Trade-offs

- The choice of pregnancy testing protocol should take into account
  - NPV and PPV
  - Burden on subjects
  - Operational feasibility (including potential for errors due to complexity of process)

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General Principles: Comparisons

- Comparisons between estimates of the probability of outcomes with different testing protocols should focus on the absolute difference, particularly for false negative results

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Information/Guidance

- Relevant information on
  - Background risk of miscarriage/congenital anomalies
  - Reproductive biology
  - hCG endocrinology
  - Performance of hCG tests
  - Risks (including uncertainty) about outcomes of pregnancy during study
- Guidance on
  - How to estimate risk
  - Not on whether risk is acceptable, or specific protocol for specific uses

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Resources

- All stakeholders:
  - Access to up-to-date evidence on
    - Relevant reproductive biology and endocrinology
    - Data on performance of different hCG tests relative to a standard relevant for screening in clinical trials
- Protocol designers and regulators
  - Interactive tool for estimating risk of different testing options in different populations
    - Documentation of underlying sources
    - Resources for updating input evidence on regular basis
    - Resources for evaluation—are estimates realistic?

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Evidence Gaps

- Outcomes of currently used pregnancy testing protocols
  - Leverage existing resources from pre-approval studies
  - Identify associations (population characteristics, type of test, timing of test)

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Products

- "White paper"
  - Review and input from CTTI members
  - Review and input from public
- Peer-review publication of model
- Resources for researchers

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