Where Do We Go From Here?
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?
General Principles

Exclude pregnant women?

Is risk acceptable?

What is the risk of pregnancy or prolonged exposure to study drug with a given testing scheme?
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.
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
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
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)
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
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
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?
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)
Products

• “White paper”
  – Review and input from CTTI members
  – Review and input from public
• Peer-review publication of model
• Resources for researchers