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

Include pregnant women?

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

Is risk acceptable?
General Principles

• No testing protocol will eliminate the chance of a pregnant woman 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