Advisory Committee for Reproductive Health Drugs
September 29, 2003

Questions

1. **Please discuss what enrollment criteria should be used to adequately capture the population to be studied for ovulation induction, and for ART.**

2. **Should enrollment be stratified by age for ovulation induction, and for ART?**

3. **Should we stratify by use of adjunct procedures, such as donor oocyte or ICSI?**

4. **Should studies be blinded or not? If blinded, discuss the merits of blinding the assessor, the patient, or both.**

5. **Discuss the merits of having placebo and/or active control arms in studies. If an active control is used, discuss how you would define the non-inferiority margin.**

6. **Discuss the advantages and disadvantages of single versus multiple treatment cycles.**

7. **Discuss the advantages and disadvantages of powering studies to detect a difference in live birth rate, or in ongoing pregnancy rate.**

8. **If studies can not be powered to demonstrate differences in live birth rate or ongoing pregnancy rate, discuss the clinical relevance of the following surrogates.**

   Rate of patients with:
   > **Presence of fetal heartbeat**
   > **Presence of gestational sac**
   > **Positive ß-hCG**
   > **Ovulation rate**
   > **Follicular development rate**

9. **Is an intent-to-treat analysis appropriate for ovulation induction? If not, should cycles be analyzed per patient given hCG?**

10. **Is an intent-to-treat analysis appropriate for ART? If not, should cycles be analyzed per retrieval, or per embryo transfer?**

11. **Please discuss which safety endpoint(s) should be evaluated.**

12. Drug manufacturers conducting studies for female infertility currently obtain the following indications:

    a. Induction of ovulation and pregnancy
    b. Multiple follicular development in ART

Please comment on the appropriateness of these indications given your discussions of endpoints and analyses.

13. Should manufacturers who obtain approval for ovulation induction or ART maintain a pregnancy registry? If yes, what information should be collected? At what point should the registry be terminated?