Scientific Workshop on

Female Sexual Interest/Arousal Disorder

October 28, 2014

7:00 am **Registration**

8:00 am **Welcome**
Marsha Henderson, MCRP
Assistant Commissioner for Women's Health
FDA

8:10 am **Background and Meeting Goals**
Christina Chang, M.D., M.P.H.
Clinical Team Leader
Division of Bone, Reproductive and Urologic Products (DBRUP)
Office of Drug Evaluation III (ODE III)
Office of New Drugs (OND)
Center for Drug Evaluation and Research (CDER)
FDA

8:20 am **Current Regulatory Framework**
Marcea Whitaker, M.D.
Medical Officer
DBRUP, ODE III, OND
CDER, FDA

8:30 am **Female Sexual Response**
Rosemary Basson, M.D.
Professor, Psychiatry
Director, Sexual Medicine Program
University of British Columbia

8:50 am **Transitioning from DSM-IV-TR to DSM-5: Diagnostic Challenges**
Cindy Meston, Ph.D.
Professor, Clinical Psychology
Director, Female Sexual Psychophysiology Lab
University of Texas at Austin

9:10 am **Assessing Patient Reported Outcomes: Clinician's Perspective**
Leonard DeRogatis, Ph.D.
Associate Professor, Department of Psychiatry, Johns Hopkins University
Director, Maryland Center for Sexual Health
Member, Board of Directors, the Institute for Sexual Medicine, Inc.

9:30 am **Assessing Patient Reported Outcomes: FDA Perspective**
Ashley Slagle, Ph.D.
Endpoints Reviewer

Study Endpoints and Labeling Development (SEALD)
OND
CDER, FDA

9:50 am **Clarifying Questions to the Speakers**

10:20 am **Break**

10:35 am **Panel Discussion Topic 1 – Diagnostic Challenges**

Moderator: Christina Chang, M.D., M.P.H., (tentative)
Clinical Team Leader, DBRUP, ODEIII, OND
CDER, FDA

Questions to the Panel:

The Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 has the following diagnostic criteria for female sexual interest/arousal disorder (FSIAD):

A. Lack of, or significantly reduced, sexual interest/arousal for a minimum duration of approximately 6 months as manifested by at least 3 of the following indicators:

   a. Absent/reduced frequency of interest in sexual activity
   b. Absent/reduced frequency of sexual/erotic thoughts or fantasies
   c. Absent/reduced initiation of sexual activity and is typically unreceptive to a partner's attempts to initiate
   d. Absent/reduced sexual excitement/pleasure during sexual activity in all or almost all (approximately 75%) sexual encounters
   e. Absent/reduced sexual interest/arousal in response to any internal or external sexual/erotic cues (e.g., written, verbal, visual, etc.)
   f. Absent/reduced genital and/or nongenital sensations during sexual activity in all or almost all (approximately 75%) sexual encounters

B. The problem causes clinically significant distress

C. The sexual dysfunction is not:
   a. Better explained by a non-sexual psychiatric disorder
   b. A consequence of severe relationship distress (e.g., partner violence) or other significant stressors
   c. Attributable to the effects of a substance/medication
   d. Attributable to another medical condition.

1. What do you view as the strengths and weaknesses of these diagnostic criteria when used in clinical practice?

2. What do you view as the strengths and weaknesses of these diagnostic criteria when used for defining inclusion and exclusion criteria for clinical trials that will test drug products?

3. How would you precisely define and quantify each of the 6 indicators of absent or reduced interest/arousal? For example:
   a. How would you define and quantify "reduced frequency?" How much reduction in frequency is needed to meet the criteria for FSIAD?

b. How would you define other terminologies, such as "sexual activity", "interest", "arousal", "sexual excitement/pleasure during sexual activity", "internal sexual/erotic cues", "nongenital sensations"?

4. How would you define or quantify "significant distress?"

5. How would you define or quantify "severe relationship stress" in patients who are not experiencing partner violence?

6. Is input from the sexual partner needed or useful?

11:35 am **Audience Questions to the Panel**

12:05 pm **Lunch**

1:00 pm **Panel Discussion Topic 2 – Clinical Trial Endpoints: Current Challenges and Future Directions**

Moderator: Hylton V. Joffe, M.D., M.M.Sc. (tentative)
Director, DBRUP, ODEIII, OND
CDER, FDA

Questions to the Panel:

1. For a drug intended to improve female sexual desire, FDA has recommended that the drug show improvement compared to placebo in two co-primary efficacy endpoints (satisfying sexual events and sexual desire) and one key secondary efficacy endpoint (distress because of low sexual desire). What would you recommend as the key endpoints for assessing the efficacy of drugs intended to treat FSIAD or aspects of FSIAD? Possibilities include, but are not limited to:
    a. Improvement in satisfying sexual events
    b. Improvement in sexual desire
    c. Improvement in sexual arousal
    d. Reduction in distress experienced because of low desire or arousal
    e. Others

2. What are the strengths and weaknesses of each of the efficacy endpoints above as well as any others that you are recommending?

3. What should be the appropriate recall period in a clinical trial for measuring:
    a. Satisfying sexual events?
    b. Sexual desire?
    c. Sexual arousal?
    d. Distress?
    e. Other endpoints that you are recommending?

4. Should the recall period be the same for all of the efficacy endpoints?

5. Some drugs may be intended for use on an as-needed basis whereas others may be intended for daily administration. Should the recall periods discussed above depend on whether the product is intended for use on an as-needed basis or for daily use?

2:00 pm **Audience Questions to the Panel**

2:30 pm **Break**

2:45 pm **Panel Discussion Topic 3 – Clinical Trial Instruments and Other Design Features: Current Challenges, Future Directions, and Generalizability to Clinical Practice**

Moderator: Hylton V. Joffe, M.D., M.M.Sc. (tentative)
Director, DBRUP, ODEIII, OND
CDER, FDA

Questions to the Panel:

1. What do you view as the strengths and weaknesses of the following instruments for use as key efficacy endpoints in clinical trials that will test drug products?
    a. The Female Sexual Function Index (FSFI) to assess desire or arousal
    b. The Female Sexual Distress Scale – Revised (FSDS-R) to assess distress

2. Do you see a role for evaluating sex or behavioral therapy as an adjunctive treatment to drug therapy?

3. FDA has a long-standing interest of encouraging sponsors to include subjects in their clinical trials who are representative of the patient population who will use the drug in clinical practice. Otherwise, unnecessary exclusions can raise concerns about the generalizability of the findings. The presence of certain diseases or conditions (for example, depression or other medical conditions that may be associated with sexual dysfunction) may confound our assessment of the treatment effect in FSIAD clinical trials. How should this issue be handled during the clinical development program of a drug product intended to treat FSIAD?

4. To qualify for clinical trials evaluating a drug for female sexual dysfunction, subjects undergo structured clinical interviews conducted by clinicians with expertise in the diagnosis and treatment of female sexual dysfunction. The subject also completes instruments that are designed to capture her own assessment of her symptoms, which are then used as the baseline when assessing response to treatment. When applying findings from clinical trials to the population at large, what challenges do you see for clinicians who will be trying to make an accurate diagnosis and assessment of response to treatment in a busy primary care or outpatient setting? What approaches do you recommend for addressing these challenges?

3:45 pm **Audience Questions to the Panel**

4:15 pm **Open Public Comment Period**

4:45 pm **Closing Remarks**
Audrey Gassman, M.D.
DBRUP, ODE III, OND
CDER, FDA

5:00 pm **Adjourn**