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July 14, 2000

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane – Room 1061
Rockville, MD 20852

RE: Draft Guidance: Female Sexual Function: Clinical Development of Drug Products for Treatment Docket # 00D-1278, CDER 9974

Dear Sir or Madam:

I am writing in response to your Draft Guidance on drug products for treatment of female sexual dysfunction. As a practicing gynecologist and reproductive endocrinologist for more than 20 years, I find several significant concerns with your Draft Guidance, and hope that The Division will consider modifying it accordingly.

As a central issue, I believe that the Guidance is entirely too "male" in its concept of female sexual dysfunction. In general, the psychosomatic processes involved in female sexual desire have been neglected and the emphasis on performance (acts with orgasm) has been overstated (see below). My comments are focused specifically on the issue of decreased female sexual desire, and not on the other recognized components, namely sexual arousal, dyspareunia, or orgasmic dysfunction.

The Division's Guidance assumes a direct causal relationship between desire and a sexual activity that follows. It underestimates and significantly undervalues the issues of sexual thoughts, fantasies, dreams and receptivity to a partner's sexual advances, etc.

The Guidance's emphasis on a male paradigm for female sexual dysfunction might be thought of in two ways. First, many women report a decreased receptivity to partner sexual advances as their primary sexual desire disorder. Many postmenopausal women with desire disorders are in long-term marriages and other established relationships. These relationships commonly have an established frequency or pattern of sexual encounters <u>that may be determined by the partner</u>. A reduction in female sexual desire may not convert to a reduction in the frequency or number of sexual acts or encounters, but rather to a change in the women's satisfaction and willingness to initiate

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such activities. As such, the Division's Guidance emphasizing frequency and numbers of sexual acts and behaviors over internal psychological desire, interest and receptivity, misses the essence of Component 1, "decreased sexual desire".

The second male paradigm driven problem with the Guidance is that it overvalues orgasm as a primary endpoint for trials of drug products to treat female sexual dysfunction (VI. Clinical Trial Endpoints). If a new drug is meant to improve decreased sexual desire as its only indicated component for therapy, orgasmic function may not always follow. If the Division accepts that the four listed clinical trial endpoints should be 1) sexual intercourse, 2) oral sex, 3) partner initiated or 4) self-masturbation, these need not, by sole virtue of their frequency, result in orgasm. It is often the act itself and the subject's satisfaction with it that is the endpoint of note. Clinical trial endpoints should include each of these sexual encounters (there may be others). However, orgasm should be separated from the encounter, as yet another endpoint, which may or may not be impacted by the treatment under investigation. Finally, the word "satisfactory" needs to apply to each of these encounters, not only sexual intercourse, and should be listed as a separate issue different from either the frequency or number of sexual encounters or acts (listed above), or the presence or absence of orgasm. It is only a male concept of sex that **always** ends in orgasm.

Finally, satisfaction is "underrated" in the Draft Guidance. As women age, particularly when paired with the same or long-time partners, frequency of sexual encounters may remain the same or may decrease, with little or no difference in sexual satisfaction. Individuals complaining of female sexual dysfunction may still have the same number of encounters, or a number of encounters that under normal circumstances would be satisfactory. However, their experience of these encounters may not be satisfactory because their "head wasn't in it". Measures of satisfaction have taken a secondary place to counting sexual acts and orgasms in the current draft document. Satisfaction needs to have an equal or even greater measure of importance as regards all components of FSD, as it is, in effect, THE goal of treatment.

Thank you for your consideration of these issues.

Sincerely yours,

James A. Simon, M.D.

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