DEPARTMENT OF HEALTH & HUMAN SERVICES

DEC 11 2001

Food and Drug Administration
Rockville MD 20857

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CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Stuart J. Land
Donald O. Beers
Arnold & Porter
555 12th St., NW
Washington, D.C. 20004-1206

Re: Docket No. 94P-0429/CP1 &
Docket No. 94P-0430/PSA1

Dear Mr. Land and Mr. Beers:

According to the records of the Food and Drug Administration's (FDA's) Dockets Management Branch, the petitions referenced above, submitted on November 30, 1994, are still formally unresolved.

As part of the Agency's efforts to reduce the backlog of unresolved petitions, the Center for Drug Evaluation and Research (CDER) has reviewed the petitions and other matters assigned to it for action. One goal of this review is to identify petitions initiated more than five years ago that, as a result of subsequent events, no longer raise significant and current public health issues. CDER believes that responding to these petitions the Agency's capacity to address in a timely fashion petitions and other matters that raise more significant and current public health issues, as well as its capacity to perform its many other duties.

In your first petition, 94P-0429/CP1, you requested that (1) FDA determine that sodium Δ8,9-dehydroestrone sulfate (DHES) is a "concomitant component" in conjugated estrogens drug products, (2) FDA recommend that the United States Pharmacopeia (USP) amend the monograph for conjugated estrogens drug products to include DHES as a concomitant component comprising at least 2 percent but not more than 6 percent of the estrogens in conjugated estrogens drug products, and (3) FDA not accept for filing or approve any new drug application (NDA) or abbreviated new drug application (ANDA) for a conjugated estrogens drug product that does not include DHES in the proportion cited. You also submitted a related petition for stay of action requesting that FDA stay any decision to receive or approve any NDA or ANDA for conjugated estrogens until FDA responds to your request to recognize DHES as a concomitant component in conjugated estrogens drug products.

As you are aware, on May 5, 1997, the Center for Drug Evaluation and Research (CDER) made public a memo explaining its position on the approvability of a synthetic generic version of Premarin. In that document, CDER outlined its current position on Premarin's active ingredients,

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concluding that Premarin is not sufficiently characterized to determine all of its active ingredients. With regard to DHES, CDER stated that available scientific evidence submitted by Wyeth-Ayerst, the sponsor of the approved NDA for Premarin, indicates that DHES is an active estrogen that contributes to the estrogenic potency of Premarin. However, the clinical significance of this contribution has not been determined. CDER stated that investigations to produce the scientific data needed to determine the active ingredients in Premarin are feasible and that such data would allow a determination of which components make a clinically meaningful contribution to its overall effects. Wyeth-Ayerst has committed to characterize the active ingredients of Premarin, and that work is ongoing. CDER concluded that DHES must be included in generic copies of Premarin unless scientific data are presented that demonstrate that the estrogenic activity of DHES is not clinically meaningful. This memo is available on CDER's website at: http://www.fda.gov/cder/news/celetterjw.htm.

CDER has proposed deleting the term "concomitant component" from the USP monograph for conjugated estrogens. However, high-pressure liquid chromatography (HPLC) and gas chromatography (GC) quantitative "fingerprint" identification tests, including a quantitative requirement for DHES, are proposed for conjugated estrogens. This "fingerprint" methodology has been submitted to the USP in a letter outlining proposed revisions to the monograph for conjugated estrogens. Copies of the transmittal letter and the proposed monograph are available on CDER's website at: http://www.fda.gov/cder/regulatory/ initiatives/cestrogens/ce.pdf.

Your petitions were submitted over 6 years ago. Because of the above-outlined policy changes, we are requesting that you respond to Docket Nos. 94P-0429/CP1 and 94P-0430/PSA1, Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, if you wish to keep these petitions active. If we do not receive a written response from you within 30 days, a copy of this letter will be filed in both dockets with instructions that these petitions be considered voluntarily withdrawn without prejudice to resubmission. If you have any questions, please contact me at 301-594-5400.

Sincerely,

Jane A. Axelrad

Jane A. Axelrad
Associate Director for Policy
Center for Drug Evaluation and Research