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The United States Pharmacopeial  
Convention, Inc.  
12601 Twinbrook Parkway  
Rockville, MD 20852

REF: 6-97-001-R

Dear Dr. Valentino:

This letter is in regard to the USP 23 monograph for Conjugated Estrogens.

We are sure that USP is aware that on May 5, 1997, Janet Woodcock, M.D., Director, CDER, issued a lengthy memorandum that stated:

1. The available scientific evidence indicates that delta-8,9 dehydroestrone sulfate is an estrogenically active component of Conjugated Estrogens, USP;
2. Conjugated Estrogens, USP, have been inadequately characterized by the sponsor of the approved NDA; and
3. Abbreviated applications that rely on synthetic Conjugated Estrogens are not approvable in the absence of information that assures that the active ingredients are the same as the active ingredients of the listed drug.

From the above, it can be concluded that the USP definition of Conjugated Estrogens needs to be revised by, at the minimum, removing references to any source other than equine urine and by elevating delta-8,9 dehydroestrone sulfate from an impurity to an active component with appropriate lower and upper limits on its content. Clearly, it is impossible to make the second change at this time because, to date, there is insufficient information about the actual content of delta-8,9 dehydroestrone sulfate in the bulk triturate.

Since FDA has determined that synthetic conjugated estrogens are not the same as natural conjugated estrogens, we are working very quickly to fully characterize equine urine-derived Conjugated Estrogens. We intend to have this task completed before the end of 1997.

We will provide the USP with a revised definition of Conjugated Estrogens as soon as we establish it. This will establish the composition standards which potential generic applicants must meet to demonstrate the "sameness" of their product as the innovator's.

We are enclosing a copy of Dr. Woodcock's May 5, 1997, memorandum for USP's information and use. We hope this will be helpful to USP.

Sincerely,



Yana Ruth Mille

Chief

Compendial Operations Staff, HFD-354  
Office of Pharmaceutical Science  
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Enclosure