



APR 13 2007

Ms. Angela G. Long
Executive Secretariat
The United States Pharmacopeial
Convention, Inc.
12601 Twinbrook Parkway
Rockville, MD 20852

REF: 4-07-002-O

Dear Ms. Long:

This letter is in regard to the monograph for *Glycerin* in USP 29 and to a recent telephone conversation between our Office of Compliance and Ms. Catherine Sheehan regarding our questions about the tests for *Identification* and *Limit of diethylene glycol and related compounds* in that monograph. As requested by Ms. Sheehan, we are herewith providing written comments for consideration by the USP Excipient Monographs 1 Expert Committee, as follows:

In the *Glycerin* monograph, *Identification - Test B* makes reference to the test for the *Limit of diethylene glycol and related compounds* ("DEG Limit Test") that appears separately in a latter portion of the monograph. The DEG Limit Test describes the preparation of three solutions: (1) a *Resolution solution* containing DEG and *USP Glycerin RS*; (2) a *Standard solution* of DEG; and (3) a *Test solution* of Glycerin. These solutions are injected into the chromatograph to identify Glycerin and to identify the presence of DEG and, if present, to quantify it.

Our concern is that the *Identification* test could be viewed as requiring identification of glycerin only and not necessarily for identifying the presence of and quantifying DEG. Instead, the DEG Limit Test could be interpreted as an impurity test with respect to DEG.

From a regulatory standpoint, it makes a difference whether the detection and quantification of DEG is considered part of the *Identification* test or is considered part of impurity testing. If DEG detection and quantification is part of the *Identification* test, the CGMP regulations at 21 C.F.R. § 211.84(d)(1) would require that manufacturers of drug products detect and quantify any DEG present. Furthermore, manufacturers of glycerin could not deviate from the DEG limit since this would be an aspect of identity. In contrast, if DEG detection and quantification is part of an impurity test, a manufacturer need not include as part of its identity testing the need to detect and quantify DEG in the glycerin. In addition, a manufacturer could deviate from the impurity requirements established in the monograph by labeling the product to indicate that it deviates from the USP test requirements in this regard. The agency would, however, consider such deviation from the impurity test requirements to render the drug adulterated under the Federal Food, Drug, and Cosmetic Act.

We have reviewed this monograph because FDA is developing a guidance for industry on the testing of glycerin to detect DEG contamination. FDA intends to refer manufacturers to the *Identification* tests in the USP monograph. It would be helpful if USP could promptly clarify whether the *Identification* test does indeed require the detection and quantification of DEG. If the USP Expert Committee believes it should, we recommend either moving the entire test for the *Limit of diethylene glycol and related compounds* to *Identification - Test B* or adding language at the end of *Test B* stating that "The absence of diethylene glycol is confirmed by the absence of a chromatographic peak at the retention time of diethylene glycol. If diethylene glycol is present, it should meet the limit specified in the test for *Limit of diethylene glycol and related compounds*."

We hope these comments will be helpful to USP and the Excipient Monographs 1 Expert Committee. Please feel free to contact Monica Caphart of our CDER Office of Compliance at 301-827-9047 if there are any questions of a technical nature. For other questions, please contact me at 301-796-1585. Please use the reference number provided above on any ensuing correspondence.

Sincerely,



Larry A. Ouderkirk

Director

Compendial Operations Staff

Office of Pharmaceutical Science

Center for Drug Evaluation & Research

cc: Ms. Catherine M. Sheehan