



Food and Drug Administration
Rockville MD 20857

JAN 12 2009

JAN 14 2009

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

REF: 1-09-001-K

Dear Ms. Long:

Thank you for your recent efforts to update the USP Glycerin Monograph to include in the test for *Identification* a limit of NMT 0.10% DEG/EG. Consistent with this revision, the agency will recommend that the USP monographs for Propylene Glycol and Sorbitol Solution also be revised to include a limit test for diethylene glycol contamination. There have been several incidents over the years that involved DEG contamination of glycerin, propylene glycol, and sorbitol solution. Very recently, there have been news reports from Nigeria of the deaths of young children caused by DEG contamination of propylene glycol used in the manufacture of a children's medication.

Thank you for your prompt attention to this matter. Attached below for your reference is a list of USP monographs that our CDER Office of Compliance has previously evaluated for revision of their ID tests to detect DEG. Please note that both propylene glycol and sorbitol solution were categorized by FDA as "high-priority" for this type of revision. Again, thank you for your continued interest and we look forward to working with you further.

We hope these comments will be helpful to USP and the Excipient Monographs 1 Expert Committee. Please feel free to contact Kay Kim at 301-796-1552 if there are any questions. Please use the reference number provided above on any ensuing correspondence.

Sincerely,

Chris Watts
Team Leader
Standards and Technology Team
Office of Pharmaceutical Science
Center for Drug Evaluation & Research

cc: Ms. Catherine M. Sheehan

Attachment

The following assessment is based on an FDA evaluation of a list of excipients was reported by USP as high-risk with regard to adulteration with DEG or EG in a 6/26/2008 email to Larry Ouderkirk. The assessment performed by USP appears to be strictly based on the conclusion that the monograph might need to be revised to improve the ability to detect DEG or EG contamination.

The compendial articles listed below can be categorized as follows:

- 1- Sugar alcohols
- 2- Propane diols and triols
- 3- Polyols (polyethylene glycol)
- 4- Derivatives of categories 1-3

The risk levels for undetectable DEG/EG contamination are categorized as follows:

H - high
M - medium
L - low

Lactitol (1) (L)
Maltitol (1) (L)
Maltitol Solution (1) (H)
Sorbitol (1) (L)
Sorbitol Solution (1) (H)
Sorbitol sorbitan solution (1) (H)
Noncrystallizing sorbitol solution (1) (H)
Propylene glycol (2) (H)
Propylene glycol dilaurate (4) (M)
Polyethylene glycol (3) (M)
Polyethylene glycol monomethyl ether (4) (L)
Diethylene glycol monoethyl ether (4) (L)
Diethylene glycol stearates (4) (L)