DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 12-223/S-036

Merck & Co., Inc.
Attention: Ms. Virginia G. Snyder
Manager, Regulatory Affairs
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Ms. Snyder:

Please refer to your supplemental new drug application dated January 4, 2001, received January 5, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for AquaMEPHYTON™ (phytonadione) Injection.

We acknowledge receipt of your submission dated February 2, 2001.

This "Changes Being Effected in 30 days" supplemental new drug application provides for revisions to the BOX WARNING, ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION sections of the package insert labeling based on WAES reports regarding severe reactions, including fatalities reported following intramuscular administration. Additionally, the preferred route of administration has been revised to include the subcutaneous route only. The HOW SUPPLIED section has been revised to delete National Stock Numbers and information regarding multiple dose containers.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text and with the minor editorial revision listed below. Accordingly, the supplemental application is approved effective on the date of this letter.

Revise the second sentence in the black box warning to read:

"Severe reactions, including fatalities, have also been reported following INTRAMUSCULAR administration."

The final printed labeling (FPL) must be identical, and include the minor editorial revision indicated, to the submitted draft labeling (package insert submitted January 4, 2001). These revisions are terms of the approval of this application.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999).

Alternatively, you may submit 15 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 12-223/S-036." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Cheryl Perry, R.N., B.S.N., Regulatory Health Project Manager, at (301) 827-7475.

Sincerely,

{See appended electronic signature page}

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research