# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

# 20-478 / S -007

# APPROVABLE LETTER (S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-478/S-007

Hospital Products Division
Abbott Laboratories
200 Abbott Park Road D-37K AP30
Abbott Park, IL 60064-6157

Attention: Surendera K. Tyagi
Manager, Regulatory Affairs

Dear Mr. Tyagi:

Please refer to your supplemental new drug application dated August 18, 2000, received August 21, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ultane (sevoflurane).

We acknowledge receipt of your submission dated March 28, 2001 which constituted a complete response to our December 20, 2000, action letter.

This supplement proposes changes in the label, packaging, and the DESCRIPTION section of the package insert regarding the presence of water.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit final printed labeling revised as follows.

Please note that the Agency's revisions are indicated by strikeovers and underlined text.

1. Revise the DESCRIPTION Section of the Package Insert as follows:

Sevoflurane is a clear, colorless, ~~stable~~ liquid ~~containing no additives or chemical stabilizers~~. Sevoflurane is nonpungent. It is miscible with ethanol, ether, chloroform, and ~~petroleum~~ benzene, and it is slightly soluble in water. Sevoflurane is stable when stored under normal room lighting conditions according to instructions.

~~Sevoflurane is chemically stable. No discernible degradation occurs in the presence of strong acids or heat.~~ The only known degradation reaction in the clinical setting is through direct contact with $CO_2$ absorbants (soda lime and Baralyme®) producing pentafluoroisopropenyl fluoromethyl ether....

2. The removal of references to ULTANE Quik Fil, proposed changes in the HOW SUPPLIED section and other proposed minor editorial changes of the Package Insert are acceptable.

3. Revise the Carton Label and Immediate Container Label as follows:

Contains sevoflurane, 250 mL~~

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

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 20 paper copies of the FPL, ten of which individually mounted on heavy weight paper or similar material.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

If you have any questions, call Lisa Basham-Cruz, Regulatory Project Manager, at (301) 827-7420.

Sincerely,

*{See appended electronic signature page}*

Cynthia McCormick, M.D.
Director
Division of Anesthetic, Critical Care, and
Addiction Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

/s/

Cynthia McCormick
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