Dear Healthcare Professional:

This letter is to inform you about changes to the prescribing information for Fluothane (halothane, U.S.P.). Many of these changes are intended to highlight and expand upon information already present in the labeling for Fluothane. Much of this information is well-known to persons familiar with the administration of halothane. However, important new information has been included to reflect current scientific opinion, accepted standards of care, and safety information in an effort to ensure the anesthesia care provider remains informed in making treatment decisions regarding the administration of Fluothane.

Arrhythmias in Children Undergoing Halothane Anesthesia for Out-patient Dental Surgery

In a prospective randomized trial conducted in the United Kingdom, the efficacy and safety of halothane and sevoflurane were compared in children undergoing dental surgery in an out-patient setting. It should be noted that in this study general inhalational anesthesia was administered by "nasal masks", and patients were not intubated. Patient end-tidal CO_2, if measured in this study, was not reported. The trial demonstrated a strong association between halothane and ventricular arrhythmias, especially ventricular tachycardia.[1]

Q-T Interval Prolongation and Arrythmias

Halothane has been reported to cause prolongation of the Q-T interval. Q-T interval prolongation constitutes a risk of ventricular tachycardia, including torsade de points. This should be taken into consideration when contemplating the use of halothane in patients with existing Q-T prolongation or in patients receiving other drugs known to prolong the Q-T interval.

These reports confirm the pro-arrhythmic potential of halothane.

Revisions to Prescribing Information for Fluothane

The prescribing information for Fluothane has been revised to include information on circumstances under which Fluothane may be administered. This information is found in the beginning of the **Warnings** section of the revised Fluothane prescribing information.

> Fluothane should be administered only by persons trained in the administration of general anesthesia. Facilities for maintenance of a patent airway, artificial ventilation, oxygen enrichment, and circulatory resuscitation must be immediately available. Unless recognized standards for anesthesia care are adhered to and qualified personnel present and equipment and drugs are on hand to manage emergencies, halothane should not be administered.

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[1]Blayney M., et al Cardiac arrythmias in children during out-patient general anesthesia for dentistry: A prospective randomized trial. Lancet, 1999; 354; 1864-66.

The decision to administer halothane should include an assessment of the individual patient and the safety profile of halothane (e.g., pro-arrhythmic properties, hepatotoxicity, malignant hyperthermia).

Halothane administration is commonly associated with arrhythmias, some of which may be fatal. The risk of arrhythmias during halothane anesthesia may be increased in certain procedures (e.g., dental surgery), clinical states (metabolic abnormalities, hypoxia and/or hypercapnia, pre-existing Q-T prolongation or history of arrhythmias), and populations (e.g., children).

The new prescribing information for Fluothane contains several other revisions in the **Contraindications**, **Warnings**, **Precautions**, **Adverse Reactions**, **Overdosage**, and **Dosing and Administration** sections. Many of these revisions have been made to reflect current scientific opinion and accepted standards of care. The major revisions include the following:

- The **Contraindications** section has been modified and expanded to include patients with known sensitivity to halothane or other halogenated anesthetics; patients with known or suspected susceptibility to malignant hyperthermia; obstetrical anesthesia except when uterine relaxation is required; and patients who have developed jaundice or acute hepatic damage from previous exposure to halothane unless other causes of liver damage were demonstrated.

- The **Warnings** section has been modified and expanded to include information moved from the previous **Precautions** section on hepatotoxicity and malignant hyperthermia. Cases of halothane-associated liver toxicity ("halothane hepatitis"), in some instances leading to liver failure and death, have been described in the literature and in spontaneous reports. Repeat exposure to halothane within a short period of time is not recommended. This expanded information on hepatotoxicity and malignant hyperthermia reflects current recommendations on diagnosis, monitoring, and treatment.

- The **Precautions** section has been modified and expanded to include new information on PEDIATRIC USE, additional information on DRUG INTERACTIONS and new subsections on GERIATRIC USE and LABORATORY TESTS.

If you are aware of any serious adverse events associated with the administration of Fluothane, we encourage you to report such information to Wyeth-Ayerst Laboratories at 1-800-934-5556 or to the Food and Drug Administration MedWatch Program by telephone at 1-800-FDA-1088, by facsimile at 1-800-FDA-0178, by internet at www.FDA.gov/medwatch, or by mail to the following address: MedWatch, HF-2, FDA, 5600 Fishers Lane, Rockville, MD 20857.

A copy of the revised Fluothane prescribing information is included with this letter. If you have any questions regarding the information discussed in this letter, please call 1-800-934-5556 or write to: Wyeth-Ayerst Laboratories, Global Product Information and Labeling Division, 150-B1 Building, P.O. Box 8299, Philadelphia, PA 19101-8299.

Sincerely,

David M. Humphrey, M.D.
Director, Clinical Affairs
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