DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-830/S-008

B.Braun Medical Inc.
Attention: Ms. Jeanne Lanahan
2525 McGaw Avenue
Irvine, CA 92614-5895

Dear Ms. Lanahan:

Please refer to your supplemental new drug application dated December 30, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lidocaine Hydrochloride in 5% Dextrose Injection in EXCEL Plastic Container.

This "Changes Being Effected in 30 days" supplemental new drug application provides for final printed labeling revised as follows:

1. A new part number has been assigned to the labeling.

2. A barcode has been added to the labeling.

3. The "**Rx only**" prescription legend has been moved from the **HOW SUPPLIED** section to the area below the name at the top of the labeling.

4. Under **DESCRIPTION**, the following paragraph has been added prior to the paragraph that begins "The plastic container…":

   The EXCEL Container is Latex-free, PVC-free, and DEHP-free.

5. Under **CLINICAL PHARMACOLOGY**, "(see Drug Interactions)" at the end of the third paragraph has been removed and replaced with the following text:

   …in patients without cardiac or hepatic failure. In clinical studies, patients over 65 years showed decreased lidocaine clearance. This was partly due to the tendency of elderly patients to have lower body weight and the increased risk of cardiac failure in these patients.

6. The revision date has been updated.

7. Under **WARNINGS**, "children" has been replaced with "pediatric patients."

8. Under **PRECAUTIONS**, a new subsection titled "General" has been added.

9. Under **PRECAUTIONS**, a new subsection titled "Laboratory Tests" has been added after the "General" subsection. The following text has been relocated within the PRECAUTIONS section so that it now appears under the "Laboratory Tests" subsection:

Clinical evaluation and periodic laboratory determinations are necessary to monitor changes in fluid balance, electrolyte concentrations, and acid-base balance during prolonged parenteral therapy or whenever the condition of the patient warrants such evaluation.

10. Under **PRECAUTIONS**/***Drug Interactions***, "amiodarone" has been added to the list of drugs in the first sentence of the third paragraph.

11. Under **PRECAUTIONS**, the following new subsection has been added after the Drug Interactions subsection:

    Carcinogenesis, Mutagenesis, and Impairment of Fertility
    Long term animal studies have not been performed to evaluate carcinogenic potential, mutagenic potential or the effect on fertility of lidocaine hydrochloride.

12. Under **PRECAUTIONS**, the "***Usage in Pregnancy*** – Pregnancy Category B" subsection title has been changed to "***Pregnancy*** – Teratogenic Effects – Pregnancy Category B."

13. Under **PRECAUTIONS**, the following three new subsections have been added to the end of the section:

    Nursing Mothers
    It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Lidocaine Hydrochloride and 5% Dextrose Injection USP is administered to a nursing woman.

    Pediatric Use
    The safety and effectiveness of lidocaine has not been established in pediatric patients (neonates to adolescents). (See WARNINGS and DOSAGE AND ADMINISTRATION).

    Geriatric Use
    Lidocaine is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION).

14. Under **DOSAGE AND ADMINISTRATION**, "Children and Infants" in the Rate of Administration chart has been replaced with "Pediatric Patients."

15. Under **DOSAGE AND ADMINISTRATION**, the title of the "***Usage in Children and Infants***" subsection has been changed to "***Pediatric Use***."

16. Under **DOSAGE AND ADMINISTRATION**, a new ***Geriatric Use*** subsection has been added after the ***Pediatric Use*** subsection and reads as follows:

    Geriatric Use
    Patients with reduced hepatic function or diminished hepatic blood flow (as in heart failure and after cardiac surgery), or those over 70 years of age should receive half the usual loading dose and also should be given lower maintenance levels of intravenous lidocaine. Patients over 65 years may benefit from dosing based upon body weight (see CLINICAL PHARMACOLOGY and PRECAUTIONS, Geriatric Use).

17. Under **HOW SUPPLIED**, the following new text has been added:

EXCEL is a registered trademark of B. Braun Medical Inc.
Made in USA

18. The Canadian distribution address has been updated and now reads as follows:

    B. Braun Medical Inc.
    Scarborough, Ontario M1H 2W4

The container labels for all products have been revised as follows:

1. The following text has been added to the container labels just after the Rx only legend:

   Latex-free; PVC-free; DEHP-free
   EXCEL is a registered trademark of B. Braun Medical Inc.

2. The Canadian distribution address has been updated and now reads as follows:

   In Canada, distributed by:
   B. Braun Medical Inc.
   Scarborough, Ontario M1H 2W4

3. The following text has been added after the patent number:

   Made in USA

4. New part numbers have been assigned to the container labels for each of the five products.

We have completed our review of this supplemental new drug application. It is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on April 23, 2004. At the time of your next printing, please make the following changes to the labeling:

1. Under **PRECAUTIONS**, the ***Carcinogenesis, Mutagenesis, and Impairment of Fertility*** subsection should be changed from:

   Carcinogenesis, Mutagenesis, and Impairment of Fertility
   Long term animal studies have not been performed to evaluate carcinogenic potential, mutagenic potential or the effect on fertility of lidocaine hydrochloride.

   To:

   Carcinogenesis, Mutagenesis, Impairment of Fertility
   Long term animal studies have not been performed to evaluate the carcinogenic potential of lidocaine; nor have studies been conducted to assess the mutagenic potential of lidocaine or its potential to affect fertility.

2. Under **PRECAUTIONS**/***Pregnancy*** – Teratogenic Effects – Pregnancy Category B, the first sentence should be changed from:

   Reproduction studies have been performed in rats at doses up to 5 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to lidocaine hydrochloride.

   To:

Reproduction studies have been performed in rats at doses up to 5 times the human dose and have revealed no evidence of harm to the fetus due to lidocaine hydrochloride.

3. Under **PRECAUTIONS**/***Nursing Mothers***, "Lidocaine Hydrochloride and 5% Dextrose" should be changed to "Lidocaine Hydrochloride in 5% Dextrose."

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
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, please contact:

Mr. Russell Fortney
Regulatory Health Project Manager
(301) 594-5311

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Acting Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Norman Stockbridge

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