



August 25, 2006

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Food and Drug Administration  
Division of Dockets Management  
Office of Management Programs  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

ATTENTION: Ms. Jennie C. Butler  
Director

**Re: Request for Assessment of Safety and Effectiveness  
Mepivacaine Hydrochloride Injection USP, 3% (1.8 mL Dental Cartridge)**

### **CITIZEN PETITION**

Hospira, Inc. ("Hospira") hereby submits this petition under section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act and 21 CFR §10.30 and 21 CFR § 314.93 to request the Commissioner of the Food and Drug Administration to provide a determination that the discontinued formulation of Carbocaine® Injection, 3%, supplied in 1.8 mL cartridge, is suitable for submission as an Abbreviated New Drug Application (ANDA).

#### **A. Action Requested**

The petitioner requests the Commissioner of the Food and Drug Administration to provide a determination that the discontinued formulation of Carbocaine® Injection, 3%, supplied in 1.8 mL cartridge (NDA 12-125 held by Eastman Kodak Company), was not discontinued for safety and efficacy reasons. The petitioner particularly requests the FDA to make a determination that the proposed generic product referring to the originally approved formulation (now discontinued) would not render the product less safe or effective than the currently marketed innovator's product, Carbocaine® Injection, 3%, supplied in 1.7 mL cartridge. The petitioner further requests the FDA to accept

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2006P-0360

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Abbreviated New Drug Application (ANDA) for Mepivacaine Hydrochloride Injection USP, 3%, supplied in 1.8 mL dental cartridge (hereinafter referred to as "proposed generic product") for the reasons discussed herein below.

**B. Statement of Grounds**

**I. Background**

Carbocaine<sup>®</sup> Injection, 3% for dental use (NDA 12-125 held by Eastman Kodak Company) is listed in the current edition of the "Orange Book" as the Reference Listed Drug (RLD). The proposed generic product was developed based the originally approved innovator's product insert dated November 2004. A recently obtained innovator's product insert dated July 2005 lists a different concentration for sodium chloride. In addition, hydrochloric acid is no longer listed as a pH adjuster. A revision to the HOW SUPPLIED section was also noted.

Originally Approved Formulation for Carbocaine<sup>®</sup> Injection, 3%

According to the innovator's product labeling (11/04) for Carbocaine<sup>®</sup> Injection, 3%, the concentration of Sodium Chloride is listed as 3 mg per milliliter. Sodium Hydroxide or Hydrochloric Acid is listed as pH adjuster. The product is supplied in 1.8 mL cartridge.

A copy of the originally approved labeling (11/04) is provided herewith as Exhibit I.

Second Formulation for Carbocaine<sup>®</sup> Injection, 3%

Based on recently obtained innovator's product labeling (07/05) for Carbocaine<sup>®</sup> Injection, 3%, the concentration of Sodium Chloride is now listed as 6 mg per milliliter. Hydrochloric Acid is no longer listed as a pH adjuster. The product is supplied in 1.7 mL cartridge.

A copy of the recently obtained labeling (07/05) is provided herewith as Exhibit II.

## II. Referencing Discontinued Labeling

It is known from the Code of Federal Regulations that when an ANDA makes a reference to a discontinued label of a drug, FDA may still approve the ANDA upon determination that the formulation was not withdrawn for reasons of safety or effectiveness (21 U.S.C. Section 355 (j)(6) and 21 CFR § 314.122 and 21 CFR § 314.161).<sup>1</sup> Similarly FDA is also authorized to approve an ANDA that omits in its labeling an indication or other aspects of the listed drug. The regulation 21 CFR § 314.94(a)(9)(iii)<sup>2</sup> permits ANDA application to seek approval for parenteral products that differ in inactive ingredient. The proposed generic product for Mepivacaine Hydrochloride Injection is identical with the discontinued formulation of Carbocaine® Injection.

### Proposed Generic Product

The proposed generic product is identical with currently approved Carbocaine® Injection with respect to indication, active ingredient, strength, dosage form, and route of administration.

The petitioner is not aware of any documentation which establish that the originally approved formulation for Carbocaine® Injection was discontinued for safety or efficacy reasons. The formula comparison of the originally approved innovator's product (including the proposed generic product which is the subject to this petition) and the currently marketed innovator's product is provided in Table I.

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<sup>1</sup> Although the regulations are consistent with relief sought, this citizen petition is submitted pursuant to section 505(j)(2)(C) of the Federal Food Drug, and Cosmetic Act ("The FDC Act") and 21 CFR § 314.93.

<sup>2</sup> 21 CFR § 314.94(a)(9)(iii): "Inactive ingredient changes permitted in drug products intended for parenteral use". An applicant may seek approval of a drug product that differs from the reference listed drug in preservative, buffer, or antioxidant provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed generic drug product.



**Table I: Comparative Innovator's Labeling Information**

	Reference Listed Drug * (Originally Approved Formulation for Carbocaine® Injection, Per Package Insert 11/04)	Reference Listed Drug (Second Formulation for Carbocaine® Injection, Per Package Insert 07/05)
Conditions of Use:	For production of local anesthesia for dental procedures by infiltration or nerve block in adults and pediatric patients.	For production of local anesthesia for dental procedures by infiltration or nerve block in adults and pediatric patients.
Active Ingredient(s):	Mepivacaine Hydrochloride	Mepivacaine Hydrochloride
Inactive Ingredient(s):	Each milliliter contains 3 mg Sodium Chloride in Water for Injection. The pH is adjusted between 4.5-6.8 with Sodium Hydroxide or Hydrochloride Acid.	Each milliliter contains 6 mg Sodium Chloride in Water for Injection. The pH is adjusted between 4.5-6.8 with Sodium Hydroxide.
Route of Administration:	Injection	Injection
Dosage Form:	Injectable	Injectable
Strength:	3% (30 mg/mL)	3% (30 mg/mL)
How Supplied:	1.8 mL dental cartridge	1.7 mL dental cartridge
* Proposed generic product (Mepivacaine Hydrochloride Injection USP).		

### III. Conclusion

For all the reasons stated above in this statement grounds, the petitioner seeks FDA to provide a determination that the discontinued formulation of Carbocaine® Injection was not voluntarily withdrawn by Eastman Kodak Company for reasons of safety or effectiveness and that the use of that labeling by the proposed generic product would not render the proposed generic product less safe or effective and would be therapeutically equivalent to the currently marketed product for Carbocaine® Injection.

#### C. Environmental Impact

This petition is entitled to a categorical exclusion under 21 CFR § 25.30 and 21 CFR § 25.31.



**D. Economic Impact**

Pursuant to 21 CFR 10.0(b), the petitioner agrees to provide an economic impact analysis if requested by the agency.

**E. Certification**

The undersigned certifies that to the best knowledge and belief of the undersigned, this petition includes all information and reviews upon which the petitioner relies, and that it includes representative data and information known to the petitioner, which is unfavorable to the petition.

We trust that this submission is complete. If you require any clarification or further information, please feel free to contact the undersigned.

Sincerely,

HOSPIRA, INC.

A handwritten signature in black ink, appearing to read "Melissa A. Nguyen", followed by the date "8-25-06" written in a similar script.

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