McGuireWoods LLP
1230 Peachtree Street, N.E.
Suite 2100
Atlanta, GA 30309-3534
Phone: 404.443.5500
Fax: 404.443.5599
www.mcguirewoods.com

Robert L. Florence
Direct: 404.443.5726

McGUIREWOODS

rflorence@mcguirewoods.com
Fax: 404.443.5777

2013 SEP 26 A 9:47

September 25, 2013

Via Federal Express:

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

The undersigned hereby submits this Citizen Petition (the "Petition"), in quadruplicate, pursuant to section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act and 21 C.F.R. §§ 10.30 and 314.93, on behalf of a client requesting the Commissioner of the Food and Drug Administration provide approval to file an Abbreviated New Drug Application ("ANDA") for Ropivacaine Hydrochloride Injection, including Ropivacaine 2mg/mL in a 500mL infusion bag.

The reference-listed drug ("RLD") is NAROPIN® (Ropivacaine Hydrochloride) Injection, NDA 020533 by FRESENIUS KABI USA as listed in the current edition of *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"). NAROPIN ® is currently marketed as a sterile injection product with the presentations shown in Table 1.

Table 1

NAROPIN® Presentations	Volume
NAROPIN®2mg/mL	100mL
NAROPIN®2mg/mL	200mL
NAROPIN®5mg/mL	100mL
NAROPIN®5mg/mL	200mL

A copy of the NDA 020533 Detail Record from the current electronic edition of the Orange Book is included herewith as **Attachment A**.

2013-8052
CP

FDA-2013-P-1203

A. Action Requested

The petitioner respectfully requests the Commissioner of Food and Drugs to determine that Ropivacaine Hydrochloride Injection 2mg/mL (0.2%) with a new fill volume of 500 mL in an infusion bag is suitable for submission as an ANDA.

The active ingredient, dosage form, indications and route of administration of the proposed product are the same as those of the RLD. The proposed product would differ only in total fill volume/total amount of drug (500 mL containing 2mg/mL (0.2%) for a total amount of 1000 mg of Ropivacaine HCl per infusion bag) from the RLD (200 mL containing 2mg/mL (0.2%) for a total amount of 400 mg of Ropivacaine HCl per infusion bag) approved under NDA 020533. Please note that there is no change to the concentration of the product (i.e., the drug content per mL is identical to the RLD), and the difference in the proposed total fill volume is clearly contemplated by the dosing information in the approved labeling for the RLD as detailed in the Statement of Grounds below. In summary, the petitioner seeks a determination for an ANDA that provides for an infusion bag containing 500 mL of an approved dosage strength 2mg/mL (i.e., total drug content 1000 mg) which is a different presentation only with regard to fill volume from that of the RLD.

B. Statement of Grounds

Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act provides for submission of an ANDA for a drug product that differs from an RLD, provided that FDA has approved a petition seeking permission to file such an application. This Petition requests agreement to submit an ANDA for the new fill volume as supported by the following:

1. The strength of the proposed product is identical to that of the RLD when the directions listed on the product insert are followed.

   The formulation of the RLD and the proposed product Ropivacaine Hydrochloride Injection are compared in the following table:

Ingredient	RLD: NAROPIN® Injection	Proposed Ropivacaine Hydrochloride Injection
Ropivacaine HCl	2mg/mL	2mg/mL
Water for Injection, USP	q.s. to 200 mL	q.s. to 500 mL

   The above table shows that the drug content per mL of the proposed product is identical to that of the RLD.

2. As the active ingredient is identical to the approved product on the market, there is no obvious difference in the safety and efficacy between the proposed Ropivacaine Hydrochloride Injection and RLD.

3. The dosage and administration of the proposed drug product is the same as that for the RLD, as recommended in the DOSAGE AND ADMINISTRATION Section of the proposed package insert.

Draft labeling for the proposed drug product is provided herewith as **Attachment B**, and the approved labeling for the RLD is provided as **Attachment C**.

There is no alteration to the active ingredient, route of administration, indications or dosage form. The proposed drug product is intended for use as described in the Indications and Dosage and Administration sections of the currently approved labeling for the RLD. The labeling for the proposed drug product only differs from the RLD with respect to the proposed fill volume (total amount of drug in the infusion bag) and manufacturer-specific information. The proposed change in total fill volume per infusion bag is the only reason for this Citizen Petition.

As continuous epidural infusion rates up to 28 mg per hour for 72 hours (i.e., 2016 mg) has been shown to be well tolerated in adults as evidenced in the package insert of the RLD, and as the largest volume of the RLD commercially available is limited at 200 mL, for patients requiring continuous infusion for prolonged blocks, hospital pharmacists currently either prepare a larger volume (0.2%) admixed product or administer multiple infusion bags/bottles. The petitioner requests an additional fill volume of a (0.2%) 500 mL infusion bag to eliminate the need for a hospital pharmacy admixture, and in order to provide hospital personnel with the safety and convenience of administering a single pre-filled infusion bag to patients requiring prolonged continuous infusions. In addition, this new increased fill volume (500 mL) presentation has the potential to reduce the risk of human error and contamination during admixture and/or administration, while reducing pharmacy work time and the amount of medical waste that is presently being generated with admixture preparation or utilizing multiple containers.

The proposed fill volume does not pose questions of safety or effectiveness because the dosing information contained in the labeling for the RLD clearly contemplates the proposed presentations of the product. Specifically, the FDA approved labeling for the RLD shows that the product is indicated for continuous infusion (see relevant portions of the package insert of the RLD below):

INDICATIONS AND USAGE:

> Naropin is indicated for the production of local or regional anesthesia for surgery and for acute pain management.

> Surgical Anesthesia: epidural block for surgery including cesarean section; major nerve block; local infiltration
>
> Acute Pain Management: epidural ***continuous infusion*** or intermittent bolus, eg, postoperative or labor; local infiltration. (emphasis added).

DOSAGE AND ADMINISTRATION:

> When prolonged blocks are used, either through ***continuous infusion*** or through repeated bolus administration, the risks of reaching a toxic plasma concentration or inducing local neural injury must be considered. ***Experience to date indicates that a cumulative dose of up to 770 mg Naropin administered over 24 hours is well tolerated in adults when used for postoperative pain management: i.e., 2016 mg.*** (emphasis added).

As noted above, the indications and dosage and administration section of the proposed new fill volume is the same as that of the RLD.

Applicability of Pediatric Research Equity Act ("PREA")

The PREA, which was signed into law on December 2, 2003, requires that all applications for approval of a new active ingredient, indication, dosage form, dosing regimen or route of administration contain a pediatric assessment unless the applicant has obtained a waiver or deferral under Section 505B. If the pediatric assessment requires the conduct of clinical studies, the application will be ineligible for submission as an ANDA. This petition is being submitted in support of a new fill volume for use in accordance with the conditions prescribed in the approved labeling for the RLD. It does not encompass a new dosing regimen or any of the other eligibility criteria for the conduct of pediatric studies. Accordingly, the product that is the subject of this petition is exempt from the requirement for a pediatric assessment pursuant to 21 U.S.C. § 505B(a)(1)(A).

For the foregoing reasons, the petitioner respectfully requests that the Commissioner find that Ropivacaine Hydrochloride Injection, 2mg/mL in 500 mL fill volume (corresponding to strength of 1000 mg) raises no questions of safety or effectiveness, and approve this petition accordingly.

C. Environmental Impact

An Environmental Impact Analysis Report for the action requested (i.e., the determination that Ropivacaine Hydrochloride Injection 2mg/mL (0.2%) in a 500 mL infusion bag is suitable for ANDA status) is not required as cited under 21 C.F.R. § 25.31(a).

D. Economic Impact

The petitioner does not believe that information regarding economic impact is necessary for approval of this Petition, but will provide such information upon request.

E. Certification

The petitioner certifies that, to the best knowledge and belief of the undersigned, this Petition includes all information and views on which the petitioner relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the Petition.

Respectfully Submitted,

Robert L. Florence

RLF

Attachments:

1. Attachment A: NDA 020533 Detail Record from the current electronic edition of the Orange Book (three (3) pages total, including attachment cover page);
2. Attachment B: Draft Proposed Labeling (twenty-four (24) pages total, including attachment cover page); and
3. Attachment C: RLD Labeling (seven (7) pages total, including attachment cover page),

cc: Martin Shimer, Regulatory Support Branch Chief, Office of Generic Drugs

From: (404) 443-5500
Robert L. Florence
McGuireWoods LLP
1230 Peachtree Street N.E.
Suite 2100 Promenade
Atlanta, GA 30309

Origin ID: QFEA

FedEx Express

J132013062803 26

Ship Date: 25SEP13
ActWgt: 0.5 LB
CAD: 103720223/WSXI2750

Delivery Address Bar Code

SHIP TO: (404) 443-5667 BILL SENDER

Division of Dockets Management
Food and Drug Administration
Dept of Health & Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Ref # 2057836-0018
Invoice #
PO #
Dept #

THU - 26 SEP 10:30A
PRIORITY OVERNIGHT

TRK# 0201 7967 7245 7552

ASR
20852
MD-US
IAD

XC NSFA

51AG1/9256/1AQE

FOLD on this line and place in shipping pouch with **bar code and delivery address** visible

1. Fold the first printed page in half and use as the shipping label.
2. Place the label in a waybill pouch and affix it to your shipment so that the barcode portion of the label can be read and scanned.
3. Keep the second page as a receipt for your records. The receipt contains the terms and conditions of shipping and information useful for tracking your package.