CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 040837

Name: Lidocaine Hydrochloride Jelly USP, 2%

Sponsor: Hi-Tech Pharmacal Co., Inc.

Approval Date: March 23, 2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040837

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040837

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 040837

Hi-Tech Pharmacal Co., Inc.
Attention: Joanne Curri
Director, Regulatory Affairs
369 Bayview Avenue
Amityville, NY 11701

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated November 20, 2006, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Lidocaine Hydrochloride Jelly USP, 2%.

Reference is also made to your amendments dated June 28, 2007; September 29, 2009; January 15, July 19, and August 19, 2010; and January 20, and March 3, 2011.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Lidocaine Hydrochloride Jelly USP, 2% to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug, Xylocaine® (Lidocaine Hydrochloride Jelly, 2%), of APP Pharmaceuticals, LLC.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS, See 505-1(i).

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/U_CM072392.pdf

The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
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/

LEIGH A SEARS
03/23/2011

ROBERT L WEST
03/23/2011
Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

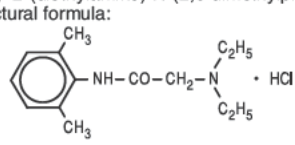
ANDA 040837

LABELING

Lidocaine Hydrochloride Jelly USP, 2%
Rx Only

DESCRIPTION
Lidocaine Hydrochloride Jelly USP, 2% is a sterile aqueous product that contains a local anesthetic agent and is administered topically. (See **INDICATIONS AND USAGE** for specific uses.)

Lidocaine Hydrochloride Jelly USP, 2% contains lidocaine HCl which is chemically designated as acetamide, 2 (diethylamino) *N* (2,6 dimethylphenyl) , monohydrochloride and has the following structural formula:



Lidocaine Hydrochloride Jelly USP, 2% also contains hydroxypropyl methylcellulose, and the resulting mixture maximizes contact with mucosa and provides lubrication for instrumentation. The unused portion should be discarded after initial use.

Composition of Lidocaine Hydrochloride Jelly USP, 2% 30 mL and 5 mL tubes: Each mL contains 20 mg of lidocaine HCl. The formulation also contains hydroxypropyl methylcellulose, methylparaben, propylparaben, purified water, and hydrochloric acid and/or sodium hydroxide to adjust pH to 6.2 to 6.8.

CLINICAL PHARMACOLOGY
Mechanism of Action: Lidocaine stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses, thereby effecting local anesthetic action.

Onset of Action: The onset of action is 3 to 5 minutes. It is ineffective when applied to intact skin.

Hemodynamics: Excessive blood levels may cause changes in cardiac output, total peripheral resistance, and mean arterial pressure. These changes may be attributable to a direct depressant effect of the local anesthetic agent on various components of the cardiovascular system.

Pharmacokinetics and Metabolism: Lidocaine may be absorbed following topical administration to mucous membranes, its rate and extent of absorption depending upon concentration and total dose administered, the specific site of application, and duration of exposure. In general, the rate of absorption of local anesthetic agents following topical application occurs most rapidly after intratracheal administration. Lidocaine is also well absorbed from the gastrointestinal tract, but little intact drug may appear in the circulation because of biotransformation in the liver.

Lidocaine is metabolized rapidly by the liver, and metabolites and unchanged drug are excreted by the kidneys. Biotransformation includes oxidative N dealkylation, ring hydroxylation, cleavage of the amide linkage, and conjugation. N dealkylation, a major pathway of biotransformation, yields the metabolites monoethylglycinexylidide and glycinexylidide. The pharmacological/toxicological actions of these metabolites are similar to, but less potent than, those of lidocaine. Approximately 90% of lidocaine administered is excreted in the form of various metabolites, and less than 10% is excreted unchanged. The primary metabolite in urine is a conjugate of 4 hydroxy 2,6 dimethylaniline.

The plasma binding of lidocaine is dependent on drug concentration, and the fraction bound decreases with increasing concentration. At concentrations of 1 to 4 mcg of free base per mL, 60 to 80 percent of lidocaine is protein bound. Binding is also dependent on the plasma concentration of the alpha 1 acid glycoprotein.

Lidocaine crosses the blood brain and placental barriers, presumably by passive diffusion.

Studies of lidocaine metabolism following intravenous bolus injections have shown that the elimination half life of this agent is typically 1.5 to 2 hours. Because of the rapid rate at which lidocaine is metabolized, any condition that affects liver function may alter lidocaine kinetics. The half life may be prolonged twofold or more in patients with liver dysfunction. Renal dysfunction does not affect lidocaine kinetics but may increase the accumulation of metabolites.

Factors such as acidosis and the use of CNS stimulants and depressants affect the CNS levels of lidocaine required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6 mcg free base per mL. In the rhesus monkey arterial blood levels of 18 to 21 mcg/mL have been shown to be threshold for convulsive activity.

INDICATIONS AND USAGE
Lidocaine hydrochloride jelly USP, 2% is indicated for prevention and control of pain in procedures involving the male and female urethra, for topical treatment of painful urethritis, and as an anesthetic lubricant for endotracheal intubation (oral and nasal).

CONTRAINDICATIONS
Lidocaine is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type or to other components of lidocaine hydrochloride jelly USP, 2%.

WARNINGS
EXCESSIVE DOSAGE, OR SHORT INTERVALS BETWEEN DOSES, CAN RESULT IN HIGH PLASMA LEVELS AND SERIOUS ADVERSE EFFECTS. PATIENTS SHOULD BE INSTRUCTED TO STRICTLY ADHERE TO THE RECOMMENDED DOSAGE AND ADMINISTRATION GUIDELINES AS SET FORTH IN THIS PACKAGE INSERT. THE MANAGEMENT OF SERIOUS ADVERSE REACTIONS MAY REQUIRE THE USE OF RESUSCITATIVE EQUIPMENT, OXYGEN, AND OTHER RESUSCITATIVE DRUGS.

Lidocaine hydrochloride jelly USP, 2% should be used with extreme caution in the presence of sepsis or severely traumatized mucosa in the area of application, since under such conditions there is the potential for rapid systemic absorption.

When used for endotracheal tube lubrication care should be taken to avoid introducing the product into the lumen of the tube. Do not use the jelly to lubricate the endotracheal stylettes. If allowed into the inner lumen, the jelly may dry on the inner surface leaving a residue which tends to clump with flexion, narrowing the lumen. There have been rare reports in which this residue has caused the lumen to occlude. (See also **ADVERSE REACTIONS** and **DOSAGE AND ADMINISTRATION**.)

PRECAUTIONS
General: The safety and effectiveness of lidocaine depend on proper dosage, correct technique, adequate precautions, and readiness for emergencies. (See **WARNINGS** and **ADVERSE REACTIONS**.) The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. Repeated doses of lidocaine may cause significant increases in blood levels with each repeated dose because of slow accumulation of the drug or its metabolites. Tolerance to elevated blood levels varies with the status of the patient. Debilitated, elderly patients, acutely ill patients, and children should be given reduced doses commensurate with their age and physical status. Lidocaine should also be used with caution in patients with severe shock or heart block.

Lidocaine hydrochloride jelly USP, 2% should be used with caution in patients with known drug sensitivities. Patients allergic to para aminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine.

Many drugs used during the conduct of anesthesia are considered potential triggering agents for familial malignant hyperthermia. Since it is not known whether amide type local anesthetics may trigger this reaction and since the need for supplemental general anesthesia cannot be predicted in advance, it is suggested that a standard protocol for management should be available. Early unexplained signs of tachycardia, tachypnea, labile blood pressure, and metabolic acidosis may precede temperature elevation. Successful outcome is dependent on early diagnosis, prompt discontinuance of the suspect triggering agent(s) and institution of treatment, including oxygen therapy, indicated supportive measures and dantrolene (consult dantrolene sodium intravenous package insert before using).

Information for Patients: When topical anesthetics are used in the mouth, the patient should be aware that the production of topical anesthesia may impair swallowing and thus enhance the danger of aspiration. For this reason, food should not be ingested for 60 minutes following use of local anesthetic preparations in the mouth or throat area. This is particularly important in children because of their frequency of eating.

Numbness of the tongue or buccal mucosa may enhance the danger of unintentional biting trauma. Food and chewing gum should not be taken while the mouth or throat area is anesthetized.

Carcinogenesis – Long term studies in animals have not been performed to evaluate the carcinogenic potential of lidocaine.

Mutagenesis – The mutagenic potential of lidocaine has been tested in the Ames Salmonella reverse mutation assay, an *in vitro* chromosome aberrations assay in human lymphocytes and in an *in vivo* mouse micronucleus assay. There was no indication of any mutagenic effect in these studies.

Impairment of Fertility: The effect of lidocaine on fertility was examined in the rat model. Administration of 30 mg/kg, s.c. (180 mg/m^2) to the mating pair did not produce alterations in fertility or general reproductive performance of rats. There are no studies that examine the effect of lidocaine on sperm parameters. There was no evidence of altered fertility.

Use in Pregnancy:
Teratogenic Effects: Pregnancy Category B
Reproduction studies for lidocaine have been performed in both rats and rabbits. There was no evidence of harm to the fetus at subcutaneous doses of up to 50 mg/kg lidocaine (300 mg/m^2 on a body surface area basis) in the rat model. In the rabbit model, there was no evidence of harm to the fetus at a dose of 5 mg/kg, s.c. (60 mg/m^2 on a body surface area basis). Treatment of rabbits with 25 mg/kg (300 mg/m^2) produced evidence of maternal toxicity and evidence of delayed fetal development, including a non significant decrease in fetal weight (7%) and an increase in minor skeletal anomalies (skull and sternebral defect, reduced ossification of the phalanges). The effect of lidocaine on post natal development was examined in rats by treating pregnant female rats daily subcutaneously at doses of 2, 10, and 50 mg/kg (12, 60, and 300 mg/m^2) from day 15 of pregnancy and up to 20 days post partum. No signs of adverse effects were seen either in

dams or in the pups up to and including the dose of 10 mg/kg (60 mg/m^2); however, the number of surviving pups was reduced at 50 mg/kg (300 mg/m^2), both at birth and the duration of lactation period, the effect most likely being secondary to maternal toxicity. No other effects on litter size, litter weight, abnormalities in the pups and physical developments of the pups were seen in this study.

A second study examined the effects of lidocaine on post natal development in the rat that included assessment of the pups from weaning to sexual maturity. Rats were treated for 8 months with 10 or 30 mg/kg, s.c. lidocaine (60 mg/m^2 and 180 mg/m^2 on a body surface area basis, respectively). This time period encompassed 3 mating periods. There was no evidence of altered post natal development in any offspring; however, both doses of lidocaine significantly reduced the average number of pups per litter surviving until weaning of offspring from the first 2 mating periods.

There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery:
Lidocaine is not contraindicated in labor and delivery. Should lidocaine hydrochloride jelly USP, 2% be used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind.

Nursing Mothers:
Lidocaine is secreted in human milk. The clinical significance of this observation is unknown. Caution should be exercised when lidocaine is administered to a nursing woman.

Pediatric Use:
Although the safety and effectiveness of lidocaine hydrochloride jelly USP, 2% in pediatric patients have not been established, a study of 19 premature neonates (gestational age <33 weeks) found no correlation between the plasma concentration of lidocaine or monoethylglycinexylidide and infant body weight when moderate amounts of lidocaine (i.e. 0.3 mL/kg of lidocaine gel 20 mg/mL) were used for lubricating both intranasal and endotracheal tubes. No neonate had plasma levels of lidocaine above 750 mcg/L. Dosages in children should be reduced, commensurate with age, body weight, and physical condition. (See **DOSAGE AND ADMINISTRATION**.)

ADVERSE REACTIONS

To report SUSPECTED ADVERSE REACTIONS, contact Hi Tech Pharmacal Co., Inc. at 1 800 262 9010 or FDA at 1 800 FDA 1088 or www.fda.gov/medwatch.

Adverse experiences following the administration of lidocaine are similar in nature to those observed with other amide local anesthetic agents. These adverse experiences are, in general, dose related and may result from high plasma levels caused by excessive dosage or rapid absorption, or may result from a hypersensitivity, idiosyncrasy, or diminished tolerance on the part of the patient. Serious adverse experiences are generally systemic in nature. The following types are those most commonly reported:

There have been rare reports of endotracheal tube occlusion associated with the presence of dried jelly residue in the inner lumen of the tube. (See also **WARNINGS** and **DOSAGE AND ADMINISTRATION**.)

Central Nervous System: CNS manifestations are excitatory and/or depressant and may be characterized by lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression, and arrest. The excitatory manifestations may be very brief or may not occur at all, in which case the first manifestation of toxicity may be drowsiness merging into unconsciousness and respiratory arrest.

Drowsiness following the administration of lidocaine is usually an early sign of a high blood level of the drug and may occur as a consequence of rapid absorption.

Cardiovascular System: Cardiovascular manifestations are usually depressant and are characterized by bradycardia, hypotension, and cardiovascular collapse, which may lead to cardiac arrest.

Allergic: Allergic reactions are characterized by cutaneous lesions, urticaria, edema, or anaphylactoid reactions. Allergic reactions may occur as a result of sensitivity either to the local anesthetic agent or to other components in the formulation. Allergic reactions as a result of sensitivity to lidocaine are extremely rare and, if they occur, should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.

OVERDOSAGE

Acute emergencies from local anesthetics are generally related to high plasma levels encountered during therapeutic use of local anesthetics. (See **ADVERSE REACTIONS**, **WARNINGS**, and **PRECAUTIONS**.)

Management of Local Anesthetic Emergencies: The first consideration is prevention, best accomplished by careful and constant monitoring of cardiovascular and respiratory vital signs and the patient's state of consciousness after each local anesthetic administration. At the first sign of change, oxygen should be administered.

The first step in the management of convulsions consists of immediate attention to the maintenance of a patent airway and assisted or controlled ventilation with oxygen and a delivery system capable of permitting immediate positive airway pressure by mask. Immediately after the institution of these ventilatory measures, the adequacy of the circulation should be evaluated, keeping in mind that drugs used to treat convulsions sometimes depress the circulation when administered intravenously. Should convulsions persist despite adequate respiratory support, and if the status of the circulation permits, small increments of an ultra short acting barbiturate (such as thiopental or thiamylal) or a benzodiazepine (such as diazepam) may be administered intravenously. The clinician should be familiar, prior to use of local anesthetics, with these anticonvulsant drugs. Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor as directed by the clinical situation (e.g., ephedrine).

If not treated immediately, both convulsions and cardiovascular depression can result in hypoxia, acidosis, bradycardia, arrhythmias, and cardiac arrest. If cardiac arrest should occur, standard cardiopulmonary resuscitative measures should be instituted.

Dialysis is of negligible value in the treatment of acute overdosage with lidocaine.

The oral LD_{50} of lidocaine hydrochloride in non fasted female rats is 459 (346 to 773) mg/kg (as the salt) and 214 (159 to 324) mg/kg (as the salt) in fasted female rats.

DOSAGE AND ADMINISTRATION

When lidocaine hydrochloride jelly USP, 2% is used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind.

The dosage varies and depends upon the area to be anesthetized, vascularity of the tissues, individual tolerance, and the technique of anesthesia. The lowest dosage needed to provide effective anesthesia should be administered. Dosages should be reduced for children and for elderly and debilitated patients. Although the incidence of adverse effects with lidocaine hydrochloride jelly USP, 2% is quite low, caution should be exercised, particularly when employing large amounts, since the incidence of adverse effects is directly proportional to the total dose of local anesthetic agent administered.

For Surface Anesthesia of the Male Adult Urethra: When using lidocaine hydrochloride jelly USP, 2% 30 mL tubes, sterilize the plastic cone for 5 minutes in boiling water, cool, and attach to the tube. The cone may be gas sterilized or cold sterilized, as preferred. Slowly instill approximately 15 mL (300 mg of lidocaine hydrochloride) into the urethra or until the patient has a feeling of tension. A penile clamp is then applied for several minutes at the corona. An additional dose of not more than 15 mL (300 mg) can be instilled for adequate anesthesia.

Prior to sounding or cystoscopy, a penile clamp should be applied for 5 to 10 minutes to obtain adequate anesthesia. A total dose of 30 mL (600 mg) is usually required to fill and dilate the male urethra.

Prior to catheterization, smaller volumes of 5 to 10 mL (100 to 200 mg) are usually adequate for lubrication.

For Surface Anesthesia of the Female Adult Urethra: When using lidocaine hydrochloride jelly USP, 2% 30 mL tubes, sterilize the plastic cone for 5 minutes in boiling water, cool, and attach to the tube. The cone may be gas sterilized or cold sterilized, as preferred. Slowly instill 3 to 5 mL (60 to 100 mg of lidocaine hydrochloride) of the jelly into the urethra. If desired, some jelly may be deposited on a cotton swab and introduced into the urethra. In order to obtain adequate anesthesia, several minutes should be allowed prior to performing urological procedures.

Lubrication for Endotracheal Intubation: Apply a moderate amount of jelly to the external surface of the endotracheal tube shortly before use. Care should be taken to avoid introducing the product into the lumen of the tube. Do not use the jelly to lubricate endotracheal stylettes. See **WARNINGS** and **ADVERSE REACTIONS** concerning rare reports of inner lumen occlusion. It is also recommended that use of endotracheal tubes with dried jelly on the external surface be avoided for lack of lubricating effect.

MAXIMUM DOSAGE: No more than 600 mg of lidocaine hydrochloride should be given in any 12 hour period.

Children: It is difficult to recommend a maximum dose of any drug for children since this varies as a function of age and weight. For children less than ten years who have a normal lean body mass and a normal lean body development, the maximum dose may be determined by the application of one of the standard pediatric drug formulas (e.g., Clark's rule). For example, in a child of five years weighing 50 lbs, the dose of lidocaine hydrochloride should not exceed 75 to 100 mg when calculated according to Clark's rule. In any case, the maximum amount of lidocaine administered should not exceed 4.5 mg/kg (2 mg/lb) of body weight.

HOW SUPPLIED

Lidocaine Hydrochloride Jelly USP, 2% is supplied in

30 mL aluminum tube	Box of 1
5 mL aluminum tube	Box of 1

A detachable applicator cone and a key for expressing the contents are included in the 30 mL carton.

Store at controlled room temperature 20 to 25°C (68 to 77°F) [see USP].

Manufactured by:
Hi Tech Pharmacal Co., Inc.
Amityville, NY 11701

NDC 50383-781-05

Hi·Tech
PHARMACAL

Lidocaine Hydrochloride Jelly USP, 2%

Rx Only **20 mg/mL**
5 mL

Lidocaine Hydrochloride Jelly USP, 2% is a sterile, aqueous solution of lidocaine hydrochloride, hydroxypropyl methylcellulose, methylparaben, propylparaben, purified water, and hydrochloric acid and/or sodium hydroxide to adjust pH.
USUAL DOSAGE: See package insert.
For topical use only. Discard unused portion. Store at controlled room temperature 20 to 25°C (68 to 77°F) [see USP]. See crimp closure for lot number and expiration date.

Hi-Tech Pharmacal Co., Inc.
Amityville, NY 11701

Rev. 781:00 10/10

NDC 50383-781-05

Hi·Tech
PHARMACAL

Lidocaine Hydrochloride Jelly USP, 2%

Rx Only **20 mg/mL**
5 mL

Lidocaine Hydrochloride Jelly USP, 2% is a sterile, aqueous solution o lidocaine hydrochloride, hydroxypropyl methylcellulose, methylparaben, propylparaben, puri ied water, and hydrochloric acid and/or sodium hydroxide to adjust pH
USUAL DOSAGE See package insert
For topical use only Discard unused portion Store at controlled room temperature 20 to 25°C (68 to 77°) [see USP See crimp closure or lot number and expiration date

Hi- ech Pharmacal Co , nc
Amityville, NY 11701

Rev 781 00 10/10

(b) (4)

NDC 50383-781-30

Hi·Tech PHARMACAL

Lidocaine Hydrochloride Jelly USP, 2%

Rx Only **20 mg/mL**
30 mL

Lidocaine Hydrochloride Jelly USP, 2% is a sterile, aqueous solution of lidocaine hydrochloride, hydroxypropyl methylcellulose, methylparaben, propylparaben, purified water, and hydrochloric acid and/or sodium hydroxide to adjust pH.
USUAL DOSAGE: See package insert.
For topical use only. Discard unused portion. Store at controlled room temperature 20 to 25°C (68 to 77°F) [see USP]. See crimp closure for lot number and expiration date.

Hi-Tech Pharmacal Co., Inc.
Amityville, NY 11701

Rev. 781:00 10/10

NDC 50383-781-30

Hi·Tech PHARMACAL

Lidocaine Hydrochloride Jelly USP, 2%

Rx Only 20 mg/mL
30 mL

Lidocaine Hydrochloride Jelly USP, 2% is a sterile, aqueous solution o lidocaine hydrochloride, hydroxypropyl methylcellulose, methylparaben, propylparaben, puri ied water, and hydrochloric acid and/or sodium hydroxide to adjust pH
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For topical use only Discard unused portion Store at controlled room temperature 20 to 25°C (68 to 77°) [see USP See crimp closure or lot number and expiration date

Hi- ech Pharmacal Co , nc
Amityville, NY 11701

Rev 781 00 10/10

(b) (4)

HI-TECH PHARMACAL CO., INC.
Amityville, NY 11701
Rev. 781:00 10/10

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NDC 50383 781 05

Hi-Tech PHARMACAL

Lidocaine Hydrochloride Jelly USP, 2%

Rx Only
5 mL

78105

Lidocaine Hydrochloride Jelly USP 2% is a s erile aqueous solu ion of lidocaine hydrochloride hydroxypropyl me hylcellulose me hylparaben proplyparaben purified wa er and hydrochloric acid and/or sodium hydroxide o adjus pH

USUAL DOSAGE: See package inser **For topical use only** Discard unused por ion

S ore a con rolled room empera ure 20 o 25°C (68 o 77°F) [see USP]

NDC 50383 781 05

Hi-Tech PHARMACAL

Lidocaine Hydrochloride Jelly USP, 2%

Rx Only
5 mL

02409391

(b) (4)

PROPERTY OF

(b) (4)

NO CHANGE OR ALTERATION ALLOWED TO TEMPLATE!

0804O7/N1D

HI-TECH

LIDOCAINE HYDROCHLORIDE 2% JELLY

09/17/2009

1+5/16 x 15/16 x 4+11/32

5.031 x 7+1/4

Printed side

.016 SBS

Grain Direction: horizontal

(b) (4)

- NO CHANGE OR ALTERATION ALLOWED TO TEMPLATE

1+15/32 x1+11/32 x4+15/32

Printed side

8+13/32 x 6+3/32

.016 SBS

(b) (4)

PROPERTY OF HI-TECH

LIDOCAINE HYDROCHLORIDE 2% JELLY

060446O2A

07/10/2006

HI-TECH PHARMACAL CO., INC
Amityville, NY 11701

Rev. 781:00 10/10

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NDC 50383-781-30

Hi-Tech PHARMACAL

Lidocaine Hydrochloride Jelly USP, 2%

Rx Only
30 mL

78130

Lidocaine Hydrochloride Jelly USP, 2%
Rx Only
30 mL

Hi-Tech PHARMACAL

NDC 50383-781-30

NDC 50383-781-30

Hi-Tech PHARMACAL

Lidocaine Hydrochloride Jelly USP, 2%

Rx Only
30 mL

Lidocaine Hydrochloride Jelly USP, 2% is a sterile, aqueous solution of lidocaine hydrochloride, hydroxypropyl methylcellulose, methylparaben, propylparaben, purified water, and hydrochloric acid and/or sodium hydroxide to adjust pH.

USUAL DOSAGE: See package insert. **For topical use only**. Discard unused portion.

Store at controlled room temperature 20 to 25°C (68 to 77°F) [see USP].

02409381

(b) (4)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040837

LABELING REVIEWS

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-837 Date of Submission: November 20, 2006

Applicant's Name: Hi-Tech Pharmacal Co., Inc.

Established Name: Lidocaine Hydrochloride Jelly USP, 2%

Labeling Deficiencies:

1. CONTAINER –30 mL

   a. Please revise the title to " Lidocaine Hydrochloride Jelly USP, 2%"

   b. "hydroxypropyl methylcellulose" rather than "hydroxypropylmethylcellulose" [add a space]

   c. Include "sodium hydroxide" and "hydrochloric acid" in the listing of inactive ingredients as appearing in the DESCRIPTION section of the package insert labeling and/or comment.

   d. Revise the statement "Consult package…information." to read "USUAL DOSAGE: See package insert.".

   e. Revise the storage temperature statement to read "Store at controlled room temperature, (b) (4) [see USP]".

   f. Include the route of administration "For topical use only".

   g. We encourage the inclusion of the text "Discard unused portion." We refer you to the statement "The unused portion should be discarded after initial use." found in your DESCRIPTION section of the package insert labeling.

   h. Revise to read "methylparaben" rather than "methyl-paraben".

   i. Please ensure that the lot number and expiration date are on the label. Refer to 21 CFR 201.17 and 201.18.

2. CARTON – 1s (30 mL)

   Refer to CONTAINER comments.

3. INSERT

   a. GENERAL

      i. Use the term "mcg" rather than "μg".

      ii. Use the term "to" rather than a hyphen when expressing a range.

iii. Delete the terminal zeros when referencing an amount. [e.g., “6 mcg” rather than “6.0 μg”]

iv. Please note that USAN names are common nouns and should be treated as such in the text of labeling (i.e., lower case). Upper case may be used when the USAN name stands alone on labels or in the title of the package insert

b. TITLE

i. Please add the phrase “Rx only” directly below the established name.

ii. Refer to CONTAINER comment a.

c. DESCRIPTION

i. First paragraph:

…”(See INDICATIONS AND USAGE for…)”

ii. We encourage the inclusion of the molecular formula and weight.

iii. Refer to CONTAINER comment b.

d. WARNINGS

Last paragraph, third sentence, revise “...the jelly may be dry...” to “...the jelly may dry...”

e. PRECAUTIONS

i. General

Third paragraph, second sentence, revise to read “Since it is not...”

ii. Carcinogenesis, Mutagenesis, Impairment of Fertility

Refer to enclosed RLD labeling. Please follow the RLD labeling’s format.

iii. Use in Pregnancy

Refer to enclosed RLD labeling.

iv. Nursing Mothers

Refer to enclosed RLD labeling.

v. Pediatric Use

Refer to enclosed RLD labeling.

f. OVERDOSAGE – Management of Local Anesthetic Emergencies:

i. Second paragraph, third sentence, correct the spelling of “thiamylal”.

ii. Let the penultimate sentence of the second paragraph “If not treated…” begin a new third paragraph.

iii. Last paragraph, revise “...lidocaine HCL...” to “...lidocaine hydrochloride...”

g. DOSAGE AND ADMINISTRATION

i. For Surface Anesthesia of the Male Adult Urethra

A) First paragraph, third sentence, revise “...lidocaine HCL...” to “...lidocaine hydrochloride...”

B) Let the last sentence “Prior to catherization…” be the new last paragraph. In the same sentence, revise to read “smaller volumes [plural].

ii. Lubrication for Endotracheal Intubation:

First sentence, revise “on” to “of”.

h. MAXIMUM DOSAGE

Revise “...lidocaine HCL...” to “...lidocaine hydrochloride...”

i. HOW SUPPLIED

i. We note that a detachable applicator cone and a key for expressing the contents are listed in this section for your 30 mL tube package size. However, you did not submit data to support this statement in the container/closure section. Please submit the data/or explain. Also include data that the cone could be boiled for 5 minutes, may be gas sterilized or cold sterilized.

ii. See comment (e) under CONTAINER.

Submit labels and labeling electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – ANDA.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission please provide a side-by-side comparison of your proposed labeling with your last labeling submission with all differences annotated and explained.

NOTES/QUESTIONS TO THE CHEMIST:

1. Email sent to chemist on 4/12/07

Neeru,

I'm sending out some labeling deficiencies. Please note:

i. HOW SUPPLIED

i. We note that a detachable applicator cone and a key for expressing the contents are listed in this section for your 30 mL tube package size. However, you did not submit data to support this statement in the container/closure section. Please submit the data/or explain. Also include data that the cone could be boiled for 5 minutes, may be gas sterilized or cold sterilized.

I didn't see any data in their container/closure Section XIII about the cone.

Ann

FOR THE RECORD:

1. MODEL LABELING – Xylocaine 2% Jelly (Abraxis). This is NDA 08-816/S-032, approved on July 23, 2004 for revised **PRECAUTIONS** section of the package insert. The "**Carcinogenesis, Mutagenesis,Impairment of Fertility"** subsection is revised. Also, all the references to (b) (4) are deleted as these presentations are no longer marketed.

2. This drug product is the subject of a USP monograph.
Packaging and storage— Preserve in tight containers.

3. INACTIVE INGREDIENTS

The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 53 (Volume 1.1).

The inactive ingredients are: hydroxypropyl methylcellulose, methylparaben, propylparaben, sodium hydroxide, hydrochloric acid, water.

Same inactive ingredients but not Q1= Q2. The concentrations of the inactive ingredients, methylparaben and propylparaben are (b) (4) of those found in the formulation of Xylocaine 2% jelly. However, these concentrations were found acceptable by OGD as these concentrations were allowed for other generic products in the past.

5. PATENT DATA

There are no unexpired patents for this product in the Orange Book Database.

[Note: Title I of the 1984 Amendments does not apply to drug products submitted or approved under the former Section 507 of the Federal Food, Drug and Cosmetic Act (antibiotic products). Drug products of this category will not have patents listed.]

Exclusivity Data

There is no unexpired exclusivity for this product.

6. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

Both RLD and the ANDA: CRT

7. PACKAGING CONFIGURATIONS

RLD: 30 mL aluminum tube & 5 mL plastic tube.

ANDA: 30 mL aluminum tube

8. CONTAINER/CLOSURE (p.282, vol.1.1)

Aluminum tube with a white cap. I did not see a detachable cone nor key in Cont/Closure (Section XIII). See comments to the firm.

9. MANUFACTURER

Hi-Tech Pharmacal Co., Inc.
369 Bayview Avenue,
Amityville, NY
(p.127, vol.1.1)

10. Per Chan's old review of 40-433: I spoke with Lisa DeLuca of AstraZeneca on 5/25/01) regarding the packaging configuration of Xylocaine 2% Jelly and how this drug product is being used in the clinical settings. The 30 mL aluminum tube comes with the detachable cone, but not the 5 mL tube. In addition, she sated that the syringe may be accompanied with the catheter attached, but she is not sure. She said she would mail me the sample of these different packaging configurations.
We have received in mail the sample of these different packaging configurations from the innovator. The innovator's syringe of 10 mL & 20mL has a narrow-tube like extension of about 5 mm at the tip of the syringe, which may be used for a catheter.

Note that the innovator is only manufacturing the 30 mL aluminum tube and the 5 mL plastic tube currently.

Date of Review: April 12, 2007 **Date of Submission: November 20, 1006**

Primary Reviewer: Thuyanh Vu **Date:**

Team Leader: **Date:**

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

/s/

Thuyanh Vu
4/12/2007 11:28:18 AM
MEDICAL OFFICER

John Grace
4/13/2007 10:32:59 AM
MEDICAL OFFICER

Telephone Fax

ANDA 40-837

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park
North I
7520 Standish Place
Rockville, MD 20855-2773
301-827-7342

TO: Hi Tech Pharmacal Co., Inc. TEL: 631-789-8228 ext. 4127

ATTN: Joanne Curri FAX: 631-841-4166

FROM: Ann Vu

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lidocaine Hydrochloride Jelly USP, 2%

Pages (including cover): 4_

SPECIAL INSTRUCTIONS:

Labeling Comments

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-837 Date of Submission: June 28, 2007

Applicant's Name: Hi-Tech Pharmacal Co., Inc.

Established Name: Lidocaine Hydrochloride Jelly USP, 2%

Labeling Deficiencies:

1. CONTAINER –30 mL

   Acceptable in final print.

2. CARTON – 1s (30 mL)

   Acceptable in final print.

3. INSERT

   A. HOW SUPPLIED

      You may not delete the cone since it is used for administration of the drug product. Please submit the cone specification data to both labeling and chemistry. Also include data that the cone could be boiled for 5 minutes, may be gas sterilized or cold sterilized.

   B. Please provide a sample of the drug product and cone in order for us to evaluate the directions in the DOSAGE AND ADMINISTRATION section. Forward the sample to:

      ATTN: Thuyanh Vu
      OGD/CDER/FDA
      Document Control Room
      Metro Park, North II
      7500 Standish Place, Room 150
      Rockville, MD 20855-2733

Submit labeling electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – ANDA.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission please provide a side-by-side comparison of your proposed labeling with your last labeling submission with all differences annotated and explained.

{See appended electronic signature page}

_____

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
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/

Charles Hoppes

7/25/2007 10:27:50 AM

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-837 Date of Submission: June 28, 2007

Applicant's Name: Hi-Tech Pharmacal Co., Inc.

Established Name: Lidocaine Hydrochloride Jelly USP, 2%

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I didn't see any data in their container/closure Section XIII about the cone.

Ann

FOR THE RECORD:

1. MODEL LABELING – Xylocaine 2% Jelly (Abraxis). This is NDA 08-816/S-032, approved on July 23, 2004 for revised **PRECAUTIONS** section of the package insert. The "**Carcinogenesis, Mutagenesis,Impairment of Fertility"** subsection is revised. Also, all the references to (b) (4) are deleted as these presentations are no longer marketed.

2. This drug product is the subject of a USP monograph.
Packaging and storage— Preserve in tight containers.

3. INACTIVE INGREDIENTS

The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 53 (Volume 1.1).

The inactive ingredients are: hydroxypropyl methylcellulose, methylparaben, propylparaben,

sodium hydroxide, hydrochloric acid, water.

Same inactive ingredients but not Q1= Q2. The concentrations of the inactive ingredients, methylparaben and propylparaben are (b) (4) of those found in the formulation of Xylocaine 2% jelly. However, these concentrations were found acceptable by OGD as these concentrations were allowed for other generic products in the past.

5. PATENT DATA

There are no unexpired patents for this product in the Orange Book Database.

[Note: Title I of the 1984 Amendments does not apply to drug products submitted or approved under the former Section 507 of the Federal Food, Drug and Cosmetic Act (antibiotic products). Drug products of this category will not have patents listed.]

Exclusivity Data

There is no unexpired exclusivity for this product.

6. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

Both RLD and the ANDA: CRT

7. PACKAGING CONFIGURATIONS

RLD: 30 mL aluminum tube & 5 mL plastic tube.

ANDA: 30 mL aluminum tube

8. CONTAINER/CLOSURE (p.282, vol.1.1)

Aluminum tube with a white cap. I did not see a detachable cone nor key in Cont/Closure (Section XIII). See comments to the firm.

Joanne Curry left message on 7/19/07 stating that HiTech accidently deleted the cone from the HOW SUPPLIED section. However, HiTech did not submit any cone specification data to labeling or chemistry. With this cycle, I requested a sample of the drug product and cone for me to evaluate the directions of use. See comments to the firm.

9. MANUFACTURER

Hi-Tech Pharmacal Co., Inc.
369 Bayview Avenue,
Amityville, NY
(p.127, vol.1.1)

10. Per Chan's old review of 40-433: I spoke with Lisa DeLuca of AstraZeneca on 5/25/01) regarding the packaging configuration of Xylocaine 2% Jelly and how this drug product is being used in the clinical settings. The 30 mL aluminum tube comes with the detachable cone, but not the 5 mL tube. In addition, she sated that the syringe may be accompanied with the catheter attached, but she is not sure. She said she would mail me the sample of these different packaging configurations.
We have received in mail the sample of these different packaging configurations from the innovator. The innovator's syringe of 10 mL & 20mL has a narrow-tube like extension of about 5 mm at the tip of the syringe, which may be used for a catheter.

Note that the innovator is only manufacturing the 30 mL aluminum tube and the 5 mL plastic tube currently.

Date of Review: July 13, 2007 **Date of Submission: June 28, 2007**

Primary Reviewer: Thuyanh Vu **Date:**

Team Leader: **Date:**

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/s/

Thuyanh Vu
7/25/2007 08:38:41 AM
LABELING REVIEWER

Charles Hoppes
7/25/2007 10:26:06 AM
LABELING REVIEWER

LABELING APPROVAL SUMMARY

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-837 Dates of Submission: January 15 and June 30, 2010

Applicant's Name: Hi-Tech Pharmacal Co., Inc.

Established Name: Lidocaine Hydrochloride Jelly USP, 2%

BASIS OF APPROVAL:

☐ Yes ☒ No

REMS acceptable?
☐ Yes ☐ No ☒ n/a

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):
Do you have 12 Final Printed Labels and Labeling? Yes

Container Labels (5 mL and 30 mL): Final printed labels acceptable in 1/15/10 e-submission

Carton Labels (5 mL and 30 mL): Final printed labels acceptable in 1/15/10 e-submission

Professional Package Insert Labeling: Final printed labeling acceptable in 1/15/10 e-submission

SPL: DLDE acceptable in 1/15/10 e-submission

Revisions needed post-approval: No

BASIS OF APPROVAL:
Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Xylocaine Jelly
NDA Number: 08-816
NDA Drug Name: Xylocaine Jelly
NDA Firm: APP
Date of Approval of NDA Insert and supplement #: S-032: approved 7/23/04
Has this been verified by the MIS system for the NDA? YES
Was this approval based upon an OGD labeling guidance? No
Basis of Approval for the Container Labels: side-by-sides
Other Comments

FOR THE RECORD:

1. MODEL LABELING – Xylocaine 2% Jelly (Abraxis). This is NDA 08-816/S-032, approved on July 23, 2004 for revised **PRECAUTIONS** section of the package insert. The "**Carcinogenesis, Mutagenesis, Impairment of Fertility"** subsection is revised. Also, all the references to (b) (4) are deleted as these presentations are no longer marketed.

2. This drug product is the subject of a USP monograph.
Packaging and storage— Preserve in tight containers.

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5. PATENT DATA

There are no unexpired patents for this product in the Orange Book Database.

[Note: Title I of the 1984 Amendments does not apply to drug products submitted or approved under the former Section 507 of the Federal Food, Drug and Cosmetic Act (antibiotic products). Drug products of this category will not have patents listed.]

Exclusivity Data

There is no unexpired exclusivity for this product.

6. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

Both RLD and the ANDA: CRT

7. PACKAGING CONFIGURATIONS

In 1/15/10 chemistry amendment firm submitted additional 5 mL aluminum tube size.

RLD: 30 mL aluminum tube & 5 mL plastic tube.

ANDA: 30 mL and 5 mL aluminum tube

8. CONTAINER/CLOSURE (p.282, vol.1.1)

Aluminum tube with a white cap. I did not see a detachable cone nor key in Cont/Closure (Section XIII). See comments to the firm.

Joanne Curry left message on 7/19/07 stating that HiTech accidently deleted the cone from the HOW SUPPLIED section. However, HiTech did not submit any cone specification data to labeling or chemistry. With this cycle, I requested a sample of the drug product and cone for me to

evaluate the directions of use. See comments to the firm.

Hi-Tech submitted the cone drawing and specifications in the 6/30/10 AF. The cover letter states that the cone (b) (4) materials may be boiled for five minutes, gas sterilized, or cold sterilized.

From Chemist review #3

Proposed Packaging Configuration:

Size	Tube	Cap
30 mL	30 ml 1x4-3/4 Aluminum Tube with End (b) (4) (b) (4)	(b) (4) White supplied by (b) (4)
5 mL	**5 mL, 0.625 x 3.5" white open-ended aluminum tube with** (b) (4)	(b) (4) **White supplied by** (b) (4)

9. MANUFACTURER

Hi-Tech Pharmacal Co., Inc.
369 Bayview Avenue,
Amityville, NY
(p.127, vol.1.1)

10. Per Chan's old review of 40-433: I spoke with Lisa DeLuca of AstraZeneca on 5/25/01) regarding the packaging configuration of Xylocaine 2% Jelly and how this drug product is being used in the clinical settings. The 30 mL aluminum tube comes with the detachable cone, but not the 5 mL tube. In addition, she sated that the syringe may be accompanied with the catheter attached, but she is not sure. She said she would mail me the sample of these different packaging configurations.
We have received in mail the sample of these different packaging configurations from the innovator. The innovator's syringe of 10 mL & 20mL has a narrow-tube like extension of about 5 mm at the tip of the syringe, which may be used for a catheter.

Note that the innovator is only manufacturing the 30 mL aluminum tube and the 5 mL plastic tube currently.

In AF 6/30/10: Hi-Tech will submit samles of the cone and drug product once it becomes available.

Date of Review: November 3, 2010 **Dates of Submission: January 15 and June 30, 2010**

Primary Reviewer: Thuyanh Vu **Date:**

Team Leader: **Date:**

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6 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

THUYANH VU
11/03/2010

JOHN F GRACE
11/04/2010
for Wm Peter Rickman

****LABELING APPROVAL SUMMARY #2****
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40837 Date of Submission: January 20, 2011

Applicant's Name: Hi-Tech Pharmacal Co., Inc.

Established Name: Lidocaine Hydrochloride Jelly USP, 2%

BASIS OF APPROVAL:

☐ Yes ☒ No

REMS acceptable?
☐ Yes ☐ No ☒ n/a

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):
Do you have 12 Final Printed Labels and Labeling? Yes

Container Labels (5 mL and 30 mL): Final printed labels acceptable in 1/20/11 e-submission

Carton Labels (5 mL and 30 mL): Final printed labels acceptable in 1/20/11 e-submission

Professional Package Insert Labeling: Final printed labeling acceptable in 1/20/2011 e-submission

SPL: DLDE acceptable in 1/15/10 e-submission

Revisions needed post-approval: No

BASIS OF APPROVAL:
Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Xylocaine Jelly
NDA Number: 08-816
NDA Drug Name: Xylocaine Jelly
NDA Firm: APP
Date of Approval of NDA Insert and supplement #: S-032: approved 7/23/04
Has this been verified by the MIS system for the NDA? YES
Was this approval based upon an OGD labeling guidance? No
Basis of Approval for the Container Labels: side-by-sides
Other Comments

FOR THE RECORD:

1. MODEL LABELING – Xylocaine 2% Jelly (Abraxis). This is NDA 08-816/S-032, approved on July 23, 2004 for revised **PRECAUTIONS** section of the package insert. The "**Carcinogenesis, Mutagenesis, Impairment of Fertility"** subsection is revised. Also, all the references to (b) (4) are deleted as these presentations are no longer marketed.

2. This drug product is the subject of a USP monograph.
Packaging and storage— Preserve in tight containers.

3. INACTIVE INGREDIENTS

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5. PATENT DATA

There are no unexpired patents for this product in the Orange Book Database.

[Note: Title I of the 1984 Amendments does not apply to drug products submitted or approved under the former Section 507 of the Federal Food, Drug and Cosmetic Act (antibiotic products). Drug products of this category will not have patents listed.]

Exclusivity Data

There is no unexpired exclusivity for this product.

6. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

Both RLD and the ANDA: CRT

7. PACKAGING CONFIGURATIONS

In 1/15/10 chemistry amendment firm submitted additional 5 mL aluminum tube size.

RLD: 30 mL aluminum tube & 5 mL plastic tube.

ANDA: 30 mL and 5 mL aluminum tube

8. CONTAINER/CLOSURE (p.282, vol.1.1)

Aluminum tube with a white cap. I did not see a detachable cone nor key in Cont/Closure (Section XIII). See comments to the firm.

Joanne Curry left message on 7/19/07 stating that HiTech accidently deleted the cone from the HOW SUPPLIED section. However, HiTech did not submit any cone specification data to labeling or chemistry. With this cycle, I requested a sample of the drug product and cone for me to evaluate the directions of use. See comments to the firm.

Hi-Tech submitted the cone drawing and specifications in the 6/30/10 AF. The cover letter states that the cone [redacted] materials may be boiled for five minutes, gas sterilized, or cold sterilized.

From Chemist review #3

Proposed Packaging Configuration:

Size	Tube	Cap
30 mL	30 ml 1x4-3/4 Aluminum Tube with End [redacted]	[redacted] White supplied by [redacted]
5 mL	**5 mL, 0.625 x 3.5" white open-ended aluminum tube with** [redacted]	[redacted] **White supplied by** [redacted]

9. MANUFACTURER

Hi-Tech Pharmacal Co., Inc.
369 Bayview Avenue,
Amityville, NY
(p.127, vol.1.1)

10. Per Chan's old review of 40-433: I spoke with Lisa DeLuca of AstraZeneca on 5/25/01) regarding the packaging configuration of Xylocaine 2% Jelly and how this drug product is being used in the clinical settings. The 30 mL aluminum tube comes with the detachable cone, but not the 5 mL tube. In addition, she sated that the syringe may be accompanied with the catheter attached, but she is not sure. She said she would mail me the sample of these different packaging configurations.
We have received in mail the sample of these different packaging configurations from the innovator. The innovator's syringe of 10 mL & 20mL has a narrow-tube like extension of about 5 mm at the tip of the syringe, which may be used for a catheter.

Note that the innovator is only manufacturing the 30 mL aluminum tube and the 5 mL plastic tube currently.

In AF 6/30/10: Hi-Tech will submit samles of the cone and drug product once it becomes available.

Date of Review: January 28, 2011 **Dates of Submission: January 20, 2011**

Primary Reviewer: Thuyanh Vu **Date:**

Team Leader: **Date:**

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6 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

THUYANH VU
01/28/2011

JOHN F GRACE
01/31/2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040837

CHEMISTRY REVIEWS

ANDA # 40-837

Lidocaine Hydrochloride Jelly USP, 2%

Hi-Tech Pharmacal Co., Inc.

Neeru B. Takiar
Office of Generic Drugs
Division of Chemistry III
Team 12

Table of Contents

Chemistry Review Data Sheet

1. ANDA #: 40-837

2. REVIEW #: 1

3. REVIEW DATE: 9/28/07; 10/18/07

4. REVIEWER: Neeru B. Takiar

5. PREVIOUS DOCUMENTS: N/A

Previous Documents	Document Date

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	November 20, 2006

7. NAME & ADDRESS OF APPLICANT:

Name:	Hi-Tech Pharmacal Co., Inc.
Address:	369 Bayview Avenue Amityville, NY 11701
Representative:	Joanne Curri
Telephone:	631-789-8228
Fax:	631-841-4166

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name:	N/A
b) Non-Proprietary Name (USAN):	Lidocaine Hydrochloride Jelly, 2%

9. LEGAL BASIS FOR SUBMISSION:

Reference Listed Drug:	Xylocaine (Lidocaine HCl) Jelly, 2%
RLD Company:	Abraxis Bioscience, NDA # 008-816
Patents:	None, Pages 7
Exclusivity:	None, Page 8

10. PHARMACOLOGICAL CATEGORY:	Topical Anesthetic
11. DOSAGE FORM:	Jelly (maximum 1200 mg daily)
12. STRENGTH/POTENCY:	2%
13. ROUTE OF ADMINISTRATION:	Topical
14. Rx/OTC DISPENSED:	_X__ Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

Chemistry Review Data Sheet

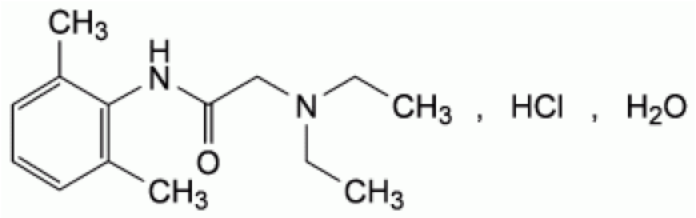
_____SPOTS product – Form Completed

__X__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Lidocaine Hydrochloride

Acetamide, 2-(diethylamino)-*N*-(2,6-dimethylphenyl)-, monohydrochloride, monohydrate.
2-(Diethylamino)-2',6'-acetoxylidide monohydrochloride monohydrate [*6108-05-0*].
$C_{14}H_{22}N_2O \cdot HCl \cdot H_2O$ 288.81



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	**Lidocaine***				*** Review Pending**
(b) (4)	III	(b) (4)	(b) (4)	4			

*** Need clarification (LOA refers to Lidocaine instead of Lidocaine HCl on page 59). See section 22 (Synthesis) for details. Review of DMF is Pending.**

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

18. STATUS:

CONSULTS/ CMC	RECOMMENDATION	DATE	REVIEWER

RELATED REVIEWS			
Microbiology	Pending – Sterile Process		
EES	Acceptable	15-May-2007	
Methods Validation	N/A		
Labeling	**Deficient**		
Bioequivalence	Acceptable	20-August-2007	
EA	Satisfactory	4-October-2007	N. Takiar
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.

_X__ Yes ____ No If no, explain reason(s) below:

The Chemistry Review for ANDA 40-837

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

NOT Approvable. Major amendment (Review #1)

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Product:
The proposed drug product, Lidocaine Hydrochloride 2% Jelly is a sterile, USP product.

The inactive ingredients for the drug product are: Hydroxypropyl methylcellulose, Methylparaben, Propylparaben, and Purified Water. Either (b) (4) sodium hydroxide or (b) (4) hydrochloric acid may be used for pH adjustment.

Drug Substance:
Lidocaine Hydrochloride drug substance is supplied by (b) (4). The firm's specifications are based on the manufacturer's and EP monograph specifications. *Currently, DMF is pending review (LOA provided is for Lidocaine instead of Lidocaine HCl).*

Batch Sizes:
The ANDA batch was produced at (b) (4) The proposed commercial batch size is (b) (4)

Both the drug substance and drug product are compendial items.

B. Description of How the Drug Product is intended to be used

The drug product will be marketed as topical anesthetic, with a proposed strength of 2% (sterile), packaged in 30 mL aluminum tube with (b) (4) cap.

The proposed expiration dating for the product is 24 months; based on three month accelerated data. The recommended storage conditions are 20-25 °C (68-77 °F) [see USP Controlled Room Temperature].

The RLD storage is listed as 20-25 °C (68-77 °F) excursions permitted to (b) (4) [see USP Controlled Room Temperature].

MDD: 1200 mg/day

The drug substance: based on the ICH Guideline Q3A (R)
IT is (b) (4) for any single unknown impurities (unspecified).
QT is (b) (4) for any specified identified or specified unidentified impurity.

The drug product: based on the ICH Guideline Q3B (R)
IT is (b) (4) for any single unknown impurities (unspecified).
QT is 0.20 % for any specified identified or specified unidentified impurity.

C. Basis for Approvability or Not-Approval Recommendation

The application is not recommended for Approval (CMC and labeling are deficient, DMF is pending review; needs clarification).

15 Pages has been Withheld in Full as b4 (CCI/TS) immediately following this page

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-837 APPLICANT: Hi-Tech Pharmacal Co., Inc.

DRUG PRODUCT: Lidocaine Hydrochloride Jelly USP, 2%

The deficiencies presented below represent MAJOR deficiencies.

A. Deficiencies:

1. Please ensure that the amount of Hydroxypropyl methylcellulose ((b) (4)) proposed in the formulation will not impact the suspendability of the drug as compared with the RLD.

2. Throughout your application, you refer to Lidocaine Hydrochloride. However, LOA for drug substance you provided is for Lidocaine only. Please clarify and provide the correct LOA including drug master file number to evaluate any updated information.

3. Regarding drug substance, we have the following comments:

a. (b) (4)

b.

c.

d.

e.

f. (b) (4)

Please provide the revised drug substance specifications and results for the test batch.

4. For drug substance identification, the background check IR spectra on page 71 appears to show peaks at about the same wave numbers as those found in the test sample and the reference standard spectra. Please explain. Please provide UV spectra of active ingredient, Lidocaine hydrochloride to justify the identity and detection wavelength of the molecule.

5. Please provide your in-house as well as the manufacturer's detailed certificate of analysis for hydrochloric acid, because it is listed as one of the ingredients in the composition table to be used for pH adjustment.

6. A comparison of the ANDA manufacturing process versus the proposed commercial process is not included. Please provide a process and equipment comparison with justifications for any changes.

7. Please describe the maximum holding time for the bulk finished drug product prior to packaging in the market containers. Please also clarify that any bulk holding times are included in the calculation of the drug product expiry.

8. Regarding container/closure system, we have the following comments:

   a. The DMF holder (b) (4)) letter on page 284 indicates that the Aluminum tubes are collapsible. However, your component description does not address this. Please clarify.

   b. Please provide composition information on the (b) (4).

   c. Please clarify (b) (4)

   d. Please clarify (b) (4)

   e. We notice that a detachable applicator cone and a key for expressing the contents are included in the 30 mL tube labeling section. However, there is no supporting

composition, test data, COA and manufacturer/DMF information provided in the ANDA under Container/Closure section. Please explain.

9. Please establish specification (b) (4)

10. Regarding finished drug product, we have the following comments:

    a. Please add specification for container appearance to the finished drug product testing protocol.

    b. Please be advised that drug product impurities specifications, based upon ICH Q3B and maximum daily dose, would normally be acceptable. However, (b) (4)

    c. The specification range for (b) (4). Please revise or justify the specification.

11. Please explain how (b) (4)

12. Regarding stability of drug product, we have the following comments:

    a. (b) (4)

    b.

    c.

    d.

e. (b) (4)

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. OGD is changing its CMC review process through our question based review (QbR) initiative, which is described in more detail on the OGD website: http://www.fda.gov/cder/ogd/QbR.htm.

   OGD's QbR was designed with the expectation that ANDA applications would be organized according to the Common Technical Document (CTD), a submission format adopted by multiple regulatory bodies including the FDA. Generic firms are strongly recommended to submit their ANDAs in the CTD format (either eCTD or paper) to facilitate the implementation of the QbR and to avoid undue delays in the review of their applications.

   Because of the increasing number of ANDA submissions OGD receives each year, the Quality Overall Summary (QOS) part of the CTD format is extremely important to making our new review process more efficient. Beginning in January 2007, all ANDA applicants are recommended to provide an electronic copy of a QOS that addresses OGD's QbR questions. The QbR-Quality Overall Summary Outline posted on our webpage http://www.fda.gov/cder/ogd/ contains all the questions to prepare the QOS. The QOS should be submitted in both MS Word and pdf format along with the paper or electronic submission. The QOS should be provided even if the remainder of the application is not in CTD format. OGD has prepared QOS models that can be found on the OGD web site. We ask you to use these as a guide for your submissions.

Sincerely yours,

Vilayat A. Sayeed, Ph.D.
Director
Division of Chemistry III
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 40-837
ANDA DUP
DIV FILE

Endorsements:

HFD-630/NTakiar/10/4/2007; 10/18/2007
HFD-630/RIser/10/19/2007
HFD-617/JSkanchy/10/25/2007
V:\FIRMSAM\HITECH\LTRS&REV\40837R01.doc
F/T by :

TYPE OF LETTER: NOT APPROVABLE - MAJOR

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

/s/

Neeru Takiar
10/31/2007 12:44:37 PM
CHEMIST

Jeanne Skanchy
11/2/2007 02:42:53 PM
CSO

Robert Iser
11/5/2007 08:30:23 AM
CHEMIST

ANDA 40-837

Lidocaine Hydrochloride Jelly USP, 2%

Hi-Tech Pharmacal Co., Inc.

Neeru B. Takiar
Office of Generic Drugs
Division of Chemistry III
Team 12

Table of Contents

Chemistry Review Data Sheet

1. ANDA #: 40-837

2. REVIEW #: 2

3. REVIEW DATE: 6/17/2009

4. REVIEWER: Neeru B. Takiar

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original	November 20, 2006

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Major Amendment	September 29, 2008

7. NAME & ADDRESS OF APPLICANT:

Name:	Hi-Tech Pharmacal Co., Inc.
Address:	369 Bayview Avenue Amityville, NY 11701
Representative:	Joanne Curri
Telephone:	631-789-8228
Fax:	631-789-8429

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name:	N/A
b) Non-Proprietary Name (USAN):	Lidocaine Hydrochloride Jelly, 2%

9. LEGAL BASIS FOR SUBMISSION:

Reference Listed Drug:	Xylocaine (Lidocaine HCl) Jelly, 2%
RLD Company:	Abraxis Bioscience, NDA # 008-816
Patents:	None, Pages 7
Exclusivity:	None, Page 8

10. PHARMACOLOGICAL CATEGORY: Topical Anesthetic

11. DOSAGE FORM: Jelly (maximum 1200 mg daily)

12. STRENGTH/POTENCY: 2%

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: _X__ Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X__ Not a SPOTS product

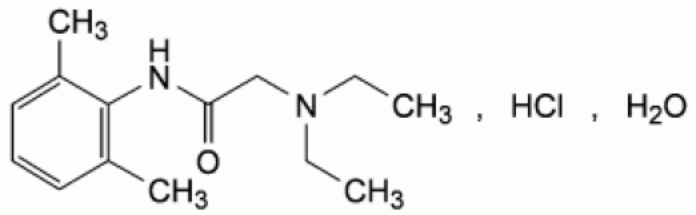
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Lidocaine Hydrochloride

Acetamide, 2-(diethylamino)-*N*-(2,6-dimethylphenyl)-, monohydrochloride, monohydrate.

2-(Diethylamino)-2',6'-acetoxylidide monohydrochloride monohydrate [*6108-05-0*].

$C_{14}H_{22}N_2O \cdot HCl \cdot H_2O$ 288.81



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4) (b) (4)	(b) (4)				**Review Pending ONDQA**
(b) (4)	III	(b) (4)	(b) (4)	4			

* **Correct DMF for Lidocaine Hydrochloride is (b) (4) (Not Lidocaine DMF (b) (4), as submitted in the original ANDA). The drug substance Lidocaine HCl is manufactured by (b) (4) An LOA for DMF (b) (4) is provided in response 2 (Major Amendment 9/29/2008).**

[1] Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 –Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	**Pending – Sterile Process**		
EES	Acceptable	15-May-2007	
Methods Validation	N/A		

Labeling	**Pending**		
Bioequivalence	Acceptable	20-August-2007	Shirley Lu
EA	Satisfactory	4-October-2007	N. Takiar
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ___
Yes __X__ No If no, explain reason(s) below:

ANDA amendment volume 4.1 was not found when review was to start.

The Chemistry Review for ANDA 40-837

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

NOT Approvable [NA-MAJOR].

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Product:
The proposed drug product, Lidocaine Hydrochloride 2% Jelly is a sterile, USP product.

The inactive ingredients for the drug product are: Hydroxypropyl methylcellulose, Methylparaben, Propylparaben, and Purified Water. Either (b) (4) sodium hydroxide or (b) (4) hydrochloric acid may be used for pH adjustment.

Drug Substance:
In the original ANDA, reference provided to DMF ((b) (4)) was for Lidocaine instead of Lidocaine Hydrochloride The correct DMF No. for Lidocaine Hydrochloride drug substance is (b) (4) by (b) (4) (Major amendment 9/29/2008) .

In major amendment dated September 29, 2008, reference to correct DMF ((b) (4) and LOA is provided.

Currently, DMF status is pending ONDQA review.

Batch Sizes:
The ANDA batch was produced at (b) (4) The proposed commercial batch size is (b) (4)

Both the drug substance and drug product are compendial items.

B. Description of How the Drug Product is intended to be used

The drug product will be marketed as topical anesthetic, with a proposed strength of 2% (sterile), packaged in 30 mL aluminum tube with (b) (4) cap.

The proposed expiration dating for the product is 24 months; based on three month accelerated data. The recommended storage conditions are 20-25 °C (68-77 °F) [see USP Controlled Room Temperature].

The RLD storage is listed as 20-25 °C (68-77 °F) excursions permitted to (b) (4) [see USP Controlled Room Temperature].

MDD: 1200 mg/day

The drug substance: based on the ICH Guideline Q3A (R)
IT is (b) (4) for any single unknown impurities (unspecified).
QT is (b) (4) for any specified identified or specified unidentified impurity.

The drug product: based on the ICH Guideline Q3B (R)
IT is (b) (4) for any single unknown impurities (unspecified).
QT is 0.20 % for any specified identified or specified unidentified impurity.

C. Basis for Approvability or Not-Approval Recommendation

The application is not recommended for Approval (CMC and labeling are deficient, DMF is pending review).

20 Pages has been Withheld in Full as b4 (CCI/TS) immediately following this page

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-837 APPLICANT: Hi-Tech Pharmacal Co., Inc.

DRUG PRODUCT: Lidocaine Hydrochloride Jelly USP, 2%

The deficiencies presented below represent MAJOR deficiencies.

A. Deficiencies:

1. Based on your response to comment 12c in major amendment September 29, 2008, the agency has suspended any further review of this ANDA until an amendment containing complete information and data necessary from the new exhibit batch to support your chosen plan of action is submitted for evaluation. The new exhibit batch information should contain all in-process, drug product, and stability data necessary to support the manufacturing changes and a complete summary of process changes with scientific rationale for each change.

2. Please be informed that your drug product should be in compliance with the current USP <467> General Chapter and/or ICH Q3C. Please see the following website, http://www.fda.gov/cder/ogd/residualsolvents.pdf, for additional guidance on required data and information.

Sincerely yours,

Vilayat A. Sayeed, Ph.D.
Director
Division of Chemistry III
Office of Generic Drugs
Center for Drug Evaluation and Research

Endorsements:

HFD-630/NTakiar/6/17/2009
HFD-630/RIser/6/18/2009
HFD-617/JSkanchy/
V:\Chemistry Division III\Team 12\Final Version For DFS Folder\ANDA\40837R02.doc
F/T by :

TYPE OF LETTER: NOT APPROVABLE - MAJOR

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

/s/

Neeru Takiar
6/22/2009 01:48:04 PM
CHEMIST

Jeanne Skanchy
6/26/2009 02:42:53 PM
CSO

Robert Iser
6/29/2009 09:52:55 AM
CHEMIST

ANDA 040837

Lidocaine Hydrochloride Jelly USP, 2%

Hi-Tech Pharmacal Co., Inc.

Neeru B. Takiar
Office of Generic Drugs
Division of Chemistry III
Team 12

Table of Contents

Chemistry Review Data Sheet

1. ANDA #: 040837

2. REVIEW #: 3

3. REVIEW DATE: 3/17/2010

4. REVIEWER: Neeru B. Takiar

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original	November 20, 2006

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Major Amendment	September 29, 2008*
Major Amendment	January 15, 2010

** review was suspended in cycle #2.*

7. NAME & ADDRESS OF APPLICANT:

Name: Hi-Tech Pharmacal Co., Inc.
Address: 369 Bayview Avenue, Amityville, NY 11701
Representative: Joanne Curri
Telephone: 631-789-8228
Fax: 631-789-8429

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Lidocaine Hydrochloride Jelly, 2%

9. LEGAL BASIS FOR SUBMISSION:

Reference Listed Drug: Xylocaine (Lidocaine HCl) Jelly, 2%
RLD Company: Abraxis Bioscience, NDA # 008816
Patents: None, Pages 7
Exclusivity: None, Page 8

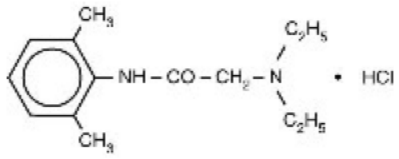
10. PHARMACOLOGICAL CATEGORY: Topical Anesthetic
11. DOSAGE FORM: Jelly (maximum 1200 mg daily)
12. STRENGTH/POTENCY: 2%
13. ROUTE OF ADMINISTRATION: Topical
14. Rx/OTC DISPENSED: _X__ Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X__ Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
Lidocaine Hydrochloride, USP
Chemical Formula: $C_{14}H_{22}N_2O \bullet HCl$
Molecular Weight: 270.8
Chemical Name: Acetamide, 2-(diethylamino)-N-(2,6- dimethylphenyl)-, monohydrochloride



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	Lidocaine Hydrochloride*	1	Adequate	3/17/2010	Review by Neeru Takiar
(b) (4)	III	(b) (4)	(b) (4)	4	N/A		
(b) (4) *	III	(b) (4)	(b) (4)	4	N/A		

* ***Correct DMF for Lidocaine Hydrochloride is*** (b) (4) ***(Not Lidocaine DMF*** (b) (4)***, as submitted in the original ANDA). The drug substance Lidocaine HCl is manufactured by*** (b) (4) ***An LOA for DMF*** (b) (4) ***is provided in response 2 (Major Amendment 9/29/2008).***

***** Added in Major Amendment 9/29/2008 (see response 8e below)***

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

18. STATUS:

CONSULTS/ CMC	RECOMMENDATION	DATE	REVIEWER

RELATED REVIEWS			
Microbiology	**Deficient**	10/1/2008	E. Addeku
EES	Acceptable	15-May-2007	
Methods Validation	N/A		
Labeling	**Deficient**	7/25/2007	A. Vu
Bioequivalence	Acceptable	20-August-2007	Shirley Lu
EA	Satisfactory	4-October-2007	N. Takiar
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. _X__
Yes ____ No If no, explain reason(s) below:

The Chemistry Review for ANDA 040837

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Approvable

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Product:
The proposed drug product, Lidocaine Hydrochloride 2% Jelly is a sterile, USP product.

The inactive ingredients for the drug product are: Hydroxypropyl methylcellulose, Methylparaben, Propylparaben, and Purified Water. Either 10% sodium hydroxide or 10% hydrochloric acid may be used for pH adjustment.

Drug Substance:
In the original ANDA, reference provided to DMF ((b) (4) was for Lidocaine instead of Lidocaine Hydrochloride The correct DMF No. for Lidocaine Hydrochloride drug substance is (b) (4) (Major amendment 9/29/2008) .

In major amendment dated September 29, 2008, reference to correct DMF (b) (4) I) and LOA is provided. DMF (b) (4) is Adequate.

Batch Sizes:
The ANDA batch was produced at (b) (4) The proposed commercial batch size is (b) (4)

New ANDA batch Sizes:
Exhibit batch size (lot # 602-448): (b) (4); Fill Sizes: 5 mL* and 30 mL
Proposed commercial batch: (b) (4) Fill Sizes: 5 mL* and 30 mL

**** added in September 29, 2008 amendment.***

Both the drug substance and drug product are compendial items.

B. Description of How the Drug Product is intended to be used

The drug product will be marketed as topical anesthetic, with a proposed strength of 2% (sterile), packaged in 30 mL aluminum tube with (b) (4) cap.

The firm has add a 5 mL container size in September 29, 2008 amendment.

The proposed expiration dating for the product is 24 months; based on three month accelerated data. The recommended storage conditions are 20-25 °C (68-77 °F) [see USP Controlled Room Temperature].

The RLD storage is listed as 20-25 °C (68-77 °F) excursions permitted to (b) (4) [see USP Controlled Room Temperature].

MDD: 1200 mg/day

The drug substance: based on the ICH Guideline Q3A (R)

(b) (4)

.

The drug product: based on the ICH Guideline Q3B (R)

(b) (4)

C. Basis for Approvability or Not-Approval Recommendation

The application is recommended for Approval. CMC is acceptable.

Labeling and Micro reviews are pending.

20 Pages has been Withheld in Full as b4 (CCI/TS) immediately following this page

Endorsements:

HFD-630/NTakiar/3/17/2010
HFD-630/RIser/3/23/2010
HFD-617/LBradford/3/29/2010
V:\Chemistry Division III\Team 12\Final Version For DFS Folder\ANDA\40837R03.doc

TYPE OF LETTER: APPROVABLE

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-40837	ORIG-1	HI TECH PHARMACAL CO INC	LIDOCAINE HYDROCHLORIDE

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

/s/

LAXMA R NAGAVELLI
04/22/2010
signed on behalf of Neeru Takiar

ROBERT L ISER
04/22/2010
This ANDA was found approvable at the Team level. The review may need an addendum per current OGD policy after review by Division or First Generic Audit Team or after finalization of other discipline reviews or EES.

LEIGH A BRADFORD
04/22/2010

ANDA 040837

Lidocaine Hydrochloride Jelly USP, 2%

Hi-Tech Pharmacal Co., Inc.

Neeru B. Takiar
Office of Generic Drugs
Division of Chemistry III
Team 12

Table of Contents

Chemistry Review Data Sheet

1. ANDA #: 040837

2. REVIEW #: 4

3. REVIEW DATE: 3/14/2011

4. REVIEWER: Neeru B. Takiar

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original	November 20, 2006
Major Amendment	September 29, 2008*
Major Amendment	January 15, 2010

** review was suspended in cycle #2.*

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Telephone Amendment	March 3, 2011

7. NAME & ADDRESS OF APPLICANT:

Name: Hi-Tech Pharmacal Co., Inc.
Address: 369 Bayview Avenue, Amityville, NY 11701
Representative: Joanne Curri
Telephone: 631-789-8228
Fax: 631-789-8429

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Lidocaine Hydrochloride Jelly, 2%

9. LEGAL BASIS FOR SUBMISSION:

Reference Listed Drug: Xylocaine (Lidocaine HCl) Jelly, 2%
RLD Company: Abraxis Bioscience, NDA # 008816
Patents: None, Pages 7
Exclusivity: None, Page 8

10. PHARMACOLOGICAL CATEGORY: Topical Anesthetic
11. DOSAGE FORM: Jelly (maximum 1200 mg daily)
12. STRENGTH/POTENCY: 2%
13. ROUTE OF ADMINISTRATION: Topical
14. Rx/OTC DISPENSED: _X__ Rx ___OTC

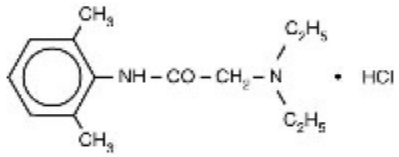
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

Chemistry Review Data Sheet

_____SPOTS product – Form Completed

__X__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
Lidocaine Hydrochloride, USP
Chemical Formula: $C_{14}H_{22}N_2O \bullet HCl$
Molecular Weight: 270.8
Chemical Name: Acetamide, 2-(diethylamino)-N-(2,6- dimethylphenyl)-, monohydrochloride



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	Lidocaine Hydrochloride*	1	Adequate	3/14/2011	Review by Neeru Takiar
(b) (4)	III	(b) (4)	(b) (4)	4	N/A		
(b) (4) *	III	(b) (4)	(b) (4)	4	N/A		

* ***Correct DMF for Lidocaine Hydrochloride is*** (b) (4) ***(Not Lidocaine DMF #*** (b) (4)***, as submitted in the original ANDA). The drug substance Lidocaine HCl is manufactured by*** (b) (4) ***An LOA for DMF*** (b) (4) ***is provided in response 2 (Major Amendment 9/29/2008).***

***** Added in Major Amendment 9/29/2008 (see response 8e below)***

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: **N/A**

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Acceptable	29-September-2010	E. Addeku
EES	Acceptable	8-February-2011	A. Inyard
Methods Validation	N/A		
Labeling	Acceptable	31-January-2011	A. Vu
Bioequivalence	Acceptable	20-August-2007	Shirley Lu
EA	Satisfactory	4-October-2007	N. Takiar
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. _X__
Yes ____ No If no, explain reason(s) below:

The Chemistry Review for ANDA 040837

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Approvable

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Product:
The proposed drug product, Lidocaine Hydrochloride 2% Jelly is a sterile, USP product.

The inactive ingredients for the drug product are: Hydroxypropyl methylcellulose, Methylparaben, Propylparaben, and Purified Water. Either (b) (4) sodium hydroxide or (b) (4) hydrochloric acid may be used for pH adjustment.

Drug Substance:
In the original ANDA, reference provided to DMF ((b) (4) was for Lidocaine instead of Lidocaine Hydrochloride The correct DMF No. for Lidocaine Hydrochloride drug substance is (b) (4) (Major amendment 9/29/2008) .

In major amendment dated September 29, 2008, reference to correct DMF (b) (4)) and LOA is provided. DMF (b) (4) is Adequate.

Batch Sizes:
The ANDA batch was produced at (b) (4) The proposed commercial batch size is (b) (4)

New ANDA batch Sizes:
Exhibit batch size (lot # 602-448): (b) (4) Fill Sizes: 5 mL* and 30 mL
Proposed commercial batch: (b) (4) Fill Sizes: 5 mL* and 30 mL

**** added in September 29, 2008 amendment.***

Both the drug substance and drug product are compendial items.

B. Description of How the Drug Product is intended to be used

The drug product will be marketed as topical anesthetic, with a proposed strength of 2% (sterile), packaged in 30 mL aluminum tube with (b) (4) cap.

The firm has add a 5 mL container size in September 29, 2008 amendment.

The proposed expiration dating for the product is 24 months; based on three month accelerated data. The recommended storage conditions are 20-25 °C (68-77 °F) [see USP Controlled Room Temperature].

The RLD storage is listed as 20-25 °C (68-77 °F) excursions permitted to (b) (4) [see USP Controlled Room Temperature].

MDD: 1200 mg/day

The drug substance: based on the ICH Guideline Q3A (R)
IT is (b) (4) for any single unknown impurities (unspecified).
QT is (b) (4) for any specified identified or specified unidentified impurity.

The drug product: based on the ICH Guideline Q3B (R)
IT is (b) (4) for any single unknown impurities (unspecified).
QT is 0.2% for any specified identified or specified unidentified impurity.

C. Basis for Approvability or Not-Approval Recommendation

The CMC review is currently acceptable per the review team recommendations. ANDA approvability is pending tertiary review at the Division, other disciplines and/or EES. This CMC review may require an addendum based on recommendations made by other review disciplines.

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Endorsements:

HFD-630/NTakiar/3/14/2011
HFD-630/LNagavelli/3/15/2011
HFD-617/LASears/3/15/2011
V:\Chemistry Division III\Team 34\Final Version For DARRTS Folder\ANDA\40837R04.doc

TYPE OF LETTER: APPROVABLE

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

/s/

NEERU B TAKIAR
03/15/2011

LAXMA R NAGAVELLI
03/15/2011

LEIGH A SEARS
03/15/2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040837

BIOEQUIVALENCE REVIEWS

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	40-837
Drug Product Name	Lidocaine Hydrochloride Jelly
Strength	2%
Applicant Name	Hi-Tech Pharmacal
Address	369 Bayview Avenue Amityville, NY 11701
Submission Date(s)	November 20, 2006
Reviewer	Shirley K. Lu, Ph.D.
First Generic	No
Applicant's Point of Contact	Joanne Curri
Contact's Telephone #	631-789-8228
Contact's Fax #	631-841-4166

REVIEW OF A WAIVER REQUEST

I. Executive Summary

Hi-Tech is requesting a waiver of *in vivo* bioequivalence study requirements for Lidocaine Hydrochloride Jelly, 2%. The reference listed drug is Xylocaine®, 2% (NDA #08-816) manufactured by Abraxis Bioscience and is a Drug Efficacy Study Implementation (DESI) effective drug product (coded "AT").

Based on the information submitted, Lidocaine Hydrochloride Jelly, 2% is acceptable as per 21 CFR 320.24(b)(6).

II. Table of Contents

III. Submission Summary

A. Drug Product Information

Test Product	Lidocaine Hydrochloride Jelly, 2%
Reference Product	Xylocaine®, 2%
RLD Manufacturer	Abraxis Bioscience
NDA No.	08-816
RLD Approval Date	3/12/53
Indication	Xylocaine® (lidocaine hydrochloride) is indicated for prevention and control of pain in procedures involving the male and female urethra, for topical treatment of painful urethritis, and as an anesthetic lubricant for endotracheal intubation (oral and nasal).

B. Background/History

Bioavailability	If swallowed, lidocaine is nearly completely absorbed, but it undergoes extensive first-pass metabolism in the liver, resulting in a systemic bioavailability of only 35%. Although lidocaine is not administered orally, some systemic absorption is possible when using oral viscous solutions. Transdermal absorption of lidocaine is related to the duration of application and the surface area over which the patch is applied. Following application of patches over a 420 cm^2 area of intact skin for 12 hours, the absorbed dose of lidocaine was 64 mg resulting in a Cmax of 0.13 mcg/ml.
Food Effect	N/A
T_{max}	2-5 minutes; duration of action: 30-60 minutes
Metabolism	Lidocaine is extensively metabolized in the liver into two active compounds, monoethylglycinexylidide and glycinexylidide, which possess 100% and 25% of the potency of lidocaine, respectively. The major metabolic pathway, sequential N-deethylation to monoethylglycinexylidide and glycinexylidide, is primarily mediated by CYP1A2 with a minor role of CYP3A4. It is not known if lidocaine is metabolized in the skin.
Excretion	Lidocaine and its metabolites are excreted by the kidneys. More than 98% of an absorbed dose of lidocaine can be recovered in the urine as metabolites or parent drug. Less than 10% of lidocaine is excreted unchanged in adults.
Half-life	Initial half-life: 7-30 minutes Terminal half-life: 1.5-2 hours
Relevant OGD or DBE History	There are 4 other generic products listed in the Orange Book for Lidocaine Hydrochloride Jelly, 2%: #80-429 (Polymedica, 4/11/74) #81-318 (Teva, 4/29/93) #86-283 (International Medication, 8/7/79) #40-433 (Akorn, 2/12/03) Note: In addition to #08-816 (Abraxis), currently #80-429 is also designated as an RLD. In verbal consultation with the Orange Book staff, it was determined that the second RLD designation (#80-429) was made in error. The correct RLD is the NDA product (#08-816).
Agency Guidance	See additional attachments section

Drug Specific Issues (if any) The RLD is coded "AT" in the Orange Book. This refers to:
"*All solutions and DESI drug products containing the same active ingredient in the same topical dosage form for which a waiver of in vivo bioequivalence has been granted and for which chemistry and manufacturing processes are adequate to demonstrate bioequivalence are considered therapeutically equivalent…*"

C. Formulation

Location in appendix	Section IV, Page 4
Are inactive ingredients within IIG limits?	Yes
If no, list ingredients outside of limits	
Is the formulation acceptable?	Yes
If not acceptable, why?	

D. Waiver Request(s)

Strengths for which waivers are requested	2%
Regulation cited	21 CFR 320.24(b)(6)
Proportional to strength tested in vivo?	N/A
Waivers granted?	Yes
If not then why?	

E. Comments

1. In the process of reviewing a waiver for ANDA #40-433, it was decided by DBE that non-solution drug products coded "AT" in the Orange Book can be considered bioequivalent to the RLD under 21 CFR 320.24(b)(6) instead of 21 CFR 320.22(b)(3). (See additional attachments section.) The test product for ANDA #40-433 was found acceptable under this regulation.

2. The proposed product is a jelly intended for administration solely by the topical route. The active ingredient, route of administration, dosage form and strength of the test product is the same as that of the reference listed product.

3. The test product has a slight difference in the amount of [redacted] (b) (4) in the formulation (test product contains [redacted] (b) (4) while RLD contains [redacted] (b) (4) However, this change in inactive ingredient would not be expected to significantly affect the absorption of the active drug ingredient.

4. All other excipients used in the test formulation are qualitatively and quantitatively the same as the RLD.

F. Recommendation

The Division of Bioequivalence agrees that the information submitted by Hi-Tech on its drug product, Lidocaine Hydrochloride Jelly, 2% is bioequivalent to the reference listed drug, Xylocaine® and falls under 21 CFR 320.24(b)(6) of the Bioavailability/Bioequivalence Regulations. The test product is acceptable.

G. Appendix

Formulations

TEST- Lidocaine Hydrochloride Jelly, 2% (Hi-Tech)

Component	Function	mg/mL
Lidocaine Hydrochloride, USP	Active	20 mg
Hydroxypropyl Methylcellulose (b) (4)	(b) (4)	(b) (4)
Methylparaben, NF	(b) (4)	(b) (4)
Propylparaben	(b) (4)	(b) (4)
(b) (4) Sodium Hydroxide solution	pH adjuster	pH adjustment*
(b) (4) Hydrochloric Acid solution	pH adjuster	pH adjustment*
Purified Water	(b) (4)	(b) (4)

*Target pH = (b) (4)

REFERENCE-Xylocaine® Jelly, 2% (Abraxis Bioscience)

Component	Function	mg/mL
Lidocaine Hydrochloride	Active	20 mg
Hydroxypropyl Methylcellulose	(b) (4)	(b) (4)
Methylparaben	(b) (4)	(b) (4)
Propylparaben	(b) (4)	(b) (4)
Sodium Hydroxide	pH adjuster	pH adjustment*
Hydrochloric Acid	pH adjuster	pH adjustment*
Purified Water, USP	(b) (4)	(b) (4)

[1]The composition for the RLD was obtained from an amendment review of ANDA #40-433 (submitted 8/10/01) referencing NDA #08-816 annual report for 2001.

H. Consult Reviews

N/A

I. Additional Attachments

(As taken from waiver review of #40-433)

Division of Bioequivalence Director's Meeting

September 18, 2001

Attending: G. Buehler, Bob West D. Conner, R. Patnaik, Lizzie Sanchez, Cecelia Parise, Donald Hare, Barbara Davit, Carol Kim

1. (b) (4)

2. Lidocaine Topical Jelly, 2%. This is a DESI drug and is rated AT. This means that in vivo bioequivalence studies were waived for pre-62 topical drug products. Should a waiver of in vivo bioequivalence continue to be granted for non-solution pre-1962 topical products? A gel is not a solution and does not "fit" under the current waiver regulations. Bioequivalence for topical lidocaine can be demonstrated through a pharmacokinetic study.

   All Pre 1962 topical drugs products were eligible for waivers of in vivo bioequivalence. The regulations in place at the time indicated that the Agency shall grant a waiver for these topical products. Post 1962 non- solution topical drugs are not eligible for waivers of in vivo studies. If OGD and the Division of Bioequivalence decide that pre 1962 topical products require bioequivalence studies, then it will have to request bioequivalence studies for all pre 1962 non-solution topical products that have been approved. This would be a major undertaking, and would most likely require some type of notice to industry. The present product under discussion is qualitatively the same and has some minor quantitative differences in (b) (4) However, these differences are not believed to impact bioequivalence. If an inactive ingredient such as propylene glycol were sufficiently different, such that it may impact absorption of the active ingredient, then the product may need an in vivo study or would have to be reformulated. If the agency believes that there is good reason to require a bioequivalence study for a product that normally would be eligible for a waiver of in vivo studies it can invoke 21 CFR 320.22(f).

   The decision was made to treat newly submitted applications for pre-1962 topical drug products on a case-by-case basis. The regulation 21 CFR 320.24(b)(6) should be cited for the determination of bioequivalence when reviewing pre-62

topical products, since topical products that are not solutions cannot be “waived” under the current regulations. A waiver under 21 CFR 320.22(e) is not appropriate since there is no public health need for this product.

A similar situation exists for Erythromycin 2% topical Gel. This product is not a pre-1962 drug product, but is an antibiotic that was formerly regulated under section 507 of the Act and was approved prior to the implementation of the Waxman-Hatch regulations. This product is rated AT also. It was also determined that since agency did not require an in vivo bioequivalence studies for this product in the past, this practice will continue. The same regulation should be cited for the determination of bioequivalence for this product since it does not fall under the “waiver” provisions (21 CFR 320.24(b)(6)). In addition, if the Division of Bioequivalence believes that there are sufficient reasons not to approve this product without in vivo studies the Division may request that the firm submit an in vivo bioequivalence study, or reformulate the product, whichever is the more suitable option.

BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-837

APPLICANT: Hi-Tech Pharmacal

DRUG PRODUCT: Lidocaine Hydrochloride Jelly, 2%

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalence comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

{See appended electronic signature page}

Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA #: 40-837

BIOEQUIVALENCE - ACCEPTABLE Submission Date: 11/20/06

1. WAIVER (WAI) Strength: 2%
(Topical jelly)

Outcome: AC

Outcome decision: AC - ACCEPTABLE

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/s/

Shirley Lu
8/16/2007 05:33:52 PM
BIOPHARMACEUTICS

Yih Chain Huang
8/16/2007 05:39:00 PM
BIOPHARMACEUTICS

Barbara Davit
8/20/2007 02:12:39 PM
BIOPHARMACEUTICS

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040837

MICROBIOLOGY REVIEWS

Product Quality Microbiology Review

September 22, 2008

ANDA: 40-837

Drug Product Name
Proprietary: N/A
Non-proprietary: Lidocaine Hydrochloride 2 % Jelly
Drug Product Priority Classification: N/A

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
11/20/2006	11/21/2006	N/A	08/18/2008

Submission History (for amendments only)
N/A

Applicant/Sponsor
Name: Hi-Tech Pharmacal Co., Inc.
Address: 369 Bayview Avenue, Amityville, N.Y. 11701
Representative: Joanne Curri
Telephone: 631-789-8228

Name of Reviewer: Eric K. Adeeku

Conclusion: The submission is **not recommended** for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original ANDA

2. SUBMISSION PROVIDES FOR: Initial marketing of the drug product

3. MANUFACTURING SITE:
Hi-Tech Pharmacal Co., Inc.
26 Edison Street,
Amityville, NY 11701

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: 2 % in 30 mL fill, Topical, Jelly, multiple use.

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: Ionic flux inhibitor required for the initiation and conduction of impulses.

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: None

filename: 40-837.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability - This submission is **not recommended** for approval on the basis of sterility assurance. Specific comments and deficiencies are provided in the 'Product Quality Microbiology Assessment'.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology - (b) (4) .

B. Brief Description of Microbiology Deficiencies -
No validation data provided for container/closure integrity testing.
No validation data provided for equipment sterilization using the (b) (4) sterilizer.

C. Assessment of Risk Due to Microbiology Deficiencies -
The safety risk associated with the microbiology deficiencies is considered high.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
Microbiologist: Eric K. Adeeku, Ph.D.
Microbiology Team Leader: Lynne A. Ensor, Ph.D.

C. CC Block
cc: Field Copy

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H. LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS

ANDA: 40-837 APPLICANT: Hi-Tech Pharmacal Co., Inc.

DRUG PRODUCT: Lidocaine Hydrochloride 2 % Jelly

Microbiology Deficiencies:

1. Regarding media fills:
   a. (b) (4)
   b.
   c.
   d.

2. Please provide validation data for the container/closure integrity testing of the packaging components used for the drug product. Please describe how your positive and negative control samples are prepared. If positive controls are prepared by breaching the container/closure system, please describe how they were breached and what was used to breach them.

3. Regarding the (b) (4) of the aluminum containers and caps used to package the drug product:
   a. (b) (4)
   b.
   c.
   d.
   e.

4. Regarding sterilization of (b) (4)

5. Regarding the sterilization of equipment in the (b) (4)
   a. (b) (4)

b.

c.

6. Regarding the building and facility layout, please provide an indication of the flow of material and the product on the floor plan.

7. Regarding antimicrobial effectiveness testing, please provided data to validate antimicrobial effectiveness making sure testing begins with an acceptable population of compendial organism and indicate the concentration of the preservatives contained in the tested lots.

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,

{See appended electronic signature page}

Lynne A. Ensor, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

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/s/

Erik Adeeku
9/29/2008 05:05:54 PM
MICROBIOLOGIST

Mark Anderson
9/29/2008 05:24:27 PM
MICROBIOLOGIST

checked for correct linking

Lynne Ensor
10/1/2008 04:37:09 PM
MICROBIOLOGIST

Product Quality Microbiology Review

August 25, 2010

ANDA: 040837

Drug Product Name
Proprietary: N/A
Non-proprietary: Lidocaine Hydrochloride 2 % Jelly
Drug Product Priority Classification: N/A

Review Number: 2

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
07/19/2010	07/20/2010	N/A	08/02/2010
08/19/2010	08/20/2010	N/A	08/20/2010

Submission History (for amendments only)

Date(s) of previous submission(s)	Microbiology Review #	Date(s) of previous Micro Review(s)
11/20/2006	1	09/22/2008

Applicant/Sponsor
Name: Hi-Tech Pharmacal Co., Inc.
Address: 369 Bayview Avenue, Amityville, N.Y. 11701
Representative: Joanne Curri
Telephone: 631-789-8228

Name of Reviewer: Eric K. Adeeku, Ph.D.

Conclusion: The submission is **recommended** for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original ANDA amendment

2. SUBMISSION PROVIDES FOR: Initial marketing of the drug product

3. MANUFACTURING SITE:
Hi-Tech Pharmacal Co., Inc.
26 Edison Street,
Amityville, NY 11701

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: 2 % in 30 mL fill, Topical, Jelly, multiple use.

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: Ionic flux inhibitor required for the initiation and conduction of impulses.

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS:
The subject amendment provides responses to the microbiology deficiencies conveyed to the applicant in the Agency's 10/01/2008 deficiency letter.

Further data was provided by applicant's representative, Joanne Curry on 08/19/2010 as was requested by reviewer.

filename: 040837a1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability - This submission is **recommended** for approval on the basis of sterility assurance.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology - (b) (4)

B. Brief Description of Microbiology Deficiencies -
None identified.

C. Assessment of Risk Due to Microbiology Deficiencies -
No microbiology deficiencies were identified. The applicant demonstrates an adequate level of sterility assurance for the manufacturing process.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
Microbiologist: Eric K. Adeeku, Ph.D.
Microbiology Team Leader: Lynne A. Ensor, Ph.D.

C. CC Block
cc: Field Copy

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/s/

ERIC K ADEEKU
09/27/2010

MARK D ANDERSON
09/27/2010
checked for correct file and linking; both OK

LYNNE A ENSOR
09/29/2010

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 040837

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

40837

Hi-Tech PHARMACAL Co. Inc.

Ack for filing
505(b)(2)
3/23/07

November 20, 2006

Mr. Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II
HFD-600, Room 150
7500 Standish Place
Rockville, MD 20855-2773

NOTE: MICROBIOLOGICAL (STERILIZATION VALIDATION) INFORMATION ENCLOSED, VOLUMES III-IV

RECEIVED
NOV 21 2006
OGD / CDER

RE: Lidocaine Hydrochloride 2% Jelly

Dear Mr. Buehler:

Pursuant to 21 CFR part 314.92, subpart C and Section 505(j) of the Federal Food, Drug and Cosmetic Act, Hi-Tech is submitting an abbreviated new drug application for Lidocaine Hydrochloride 2% Jelly. This submission, inclusive of a microbiology section, contains an archival copy (four volumes), a review copy (four volumes) and a method validation package (one volume).

The product is a sterile topical solution which contains an active ingredient in the same strength and dosage form, as well as the same inactive ingredients, as the reference listed drug Xylocaine (Lidocaine Hydrochloride) 2% Jelly (Abraxis Bioscience's NDA 08-816).

The proposed labeling of the new drug is the same as that of Abraxis Bioscience's Xylocaine (Lidocaine Hydrochloride) Jelly 2% with the exception of changes that are necessary due to a change in the manufacturer. The comparison of labeling can be found in Section IV of this application.

The certification required by the Generic Drug Enforcment Act of 1992 is submitted in Section XX and Hi-Tech's certification that a true copy of this application has been submitted to the New York District Office is submitted in Section XXI of this

application. The required patent certification information and a completed Form FDA 356h are also included.

If you have any questions concerning the enclosed information, please contact Joanne Curri at 631-789-8228, extension 4127. We look forward to your prompt review of this abbreviated new drug application.

Sincerely,

HI-TECH PHARMACAL CO., INC.

Joanne Curri
Director of Regulatory Affairs

Enc.

ANDA CHECKLIST
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION

ANDA Nbr: 40-837 **FIRM NAME**: HI- TECH PHARMAL CO. INC.

RELATED APPLICATION(S): NA

First Generic Product Received? NO

DRUG NAME: LIDOCAINE HYDROCHLORIDE USP
DOSAGE FORM: JELLY, 02%

Bio Assignments:		
☒ **BPH**	☐ **BCE**	☒ **Micro Review !!!Yes, MICRO Review NEEDED!!!**
☐ **BST**	☐ **BDI**	

Random Queue: 12
Chem Team Leader: Khorshidi, Hossein PM: Jeanne Skanchy Labeling Reviewer: Ann Vu

Letter Date: NOVEMBER 20, 2006 **Received Date**: NOVEMBER 21, 2006

Comments: EC- 1 YES **On Cards:** YES
Therapeutic Code: 6040400 ANESTHETIC/TOPICAL

Archival Format: PAPER **Sections** I **(356H Sections per EDR Email)**
Review copy: YES E-Media Disposition: YES SENT TO EDR
Not applicable to electronic sections
Field Copy Certification (Original Signature) YES

Methods Validation Package (3 copies PAPER archive) **YES (USP)**
(Required for Non-USP drugs)

Cover Letter YES | **Table of Contents** YES

PART 3 Combination Product Category N Not a Part3 Combo Product
(Must be completed for ALL Original Applications) Refer to the Part 3 Combination Algorithm

Reviewing CSO/CST Jeen Min

Date February 17, 2007

Recommendation:

☒ **FILE** ☐ **REFUSE to RECEIVE**

Supervisory Concurrence/Date: S. Middleton for M.S. **Date: 2/23/07**

ADDITIONAL COMMENTS REGARDING THE ANDA:

Top 200 Drug Product:

ACCEPTABLE

Sec. I	**Signed and Completed Application Form (356h)** YES (Statement regarding Rx/OTC Status) RX YES	☒
Sec. II	**Basis for Submission** **NDA# : 008-816** **YES** Ref Listed Drug: XYLOCAINE Firm: ABRAXIS BIOSCIENCE ANDA suitability petition required? NA If Yes, then is change subject to PREA (change in dosage form, route, active ingredient) For products subject to PREA a wavier request must be granted prior to approval of ANDA. Wavier Granted:	☒
Sec. III	**Patent Certification** 1. Paragraph: II **YES** 2. Expiration of Patent: NO Patents A. Pediatric Exclusivity Submitted? B. Pediatric Exclusivity Tracking System checked? **Exclusivity Statement: YES**	☒
Sec. IV	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use **YES** 2. Active ingredients **YES** 3. Route of administration **YES** 4. Dosage Form **YES** 5. Strength **YES**	☒
Sec. V	**Labeling** (Mult Copies N/A for E-Submissions) 1. 4 copies of draft (each strength and container) or 12 copies of FPL **YES** 2. 1 RLD label and 1 RLD container label **YES** 3. 1 side by side labeling comparison with all differences annotated and explained **YES** 4. Was a proprietary name request submitted? **NO** (If yes, send email to Labeling Rvwr indicating such.)	☒
Sec. VI	**Bioavailability/Bioequivalence** **1. Financial Certification** (Form FDA 3454) **and Disclosure Statement** (Form 3455) **N/A no bio** **2. Request for Waiver of In-Vivo Study(ies): YES: Topical** **3. Formulation data same?** (Comparison of all Strengths) (Ophthalmics, Otics, Topicals Perenterals) **YES: same IIG but not Q1=Q2 accoroding COMIS** **4. Lot Numbers of Products used in BE Study(ies):** N/A **5. Study Type: IN-VIVO PK STUDY(IES)** (Continue with the appropriate study type box below)	☒
Study Type	**IN-VIVO PK STUDY(IES)** (i.e., fasting/fed/sprinkle) NA a. Study(ies) meets BE criteria (90% CI or 80-125, Cmax, AUC) N/A b. EDR Email: Data Files Submitted: c. In-Vitro Dissolution: N/A	☐

Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** NO a. Properly defined BE endpoints (eval. by Clinical Team) b. Summary results meet BE criteria (90% CI within +/- 20% or 80-120) c. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) d. EDR Email: Data Files Submitted	☐
Study Type	**TRANSDERMAL DELIVERY SYSTEMS** NO a. In-Vivo PK Study 1. Study(ies) meet BE Criteria (90% CI or 80-125, Cmax, AUC) 2. In-Vitro Dissolution 3. EDR Email: Data Files Submitted b. Adhesion Study c. Skin Irritation/Sensitization Study	☐
Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** NO a. Solutions (Q1/Q2 sameness): 1. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile) b. Suspensions (Q1/Q2 sameness): 1. In-Vivo PK Study a. Study(ies) meets BE Criteria (90% CI or 80-125, Cmax, AUC) b. EDR Email: Data Files Submitted 2. In-Vivo BE Study with Clinical EndPoints a. Properly defined BE endpoints (eval. by Clinical Team) b. Summary results meet BE criteria (90% CI within +/- 20% or 80-120) c. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) d. EDR Email: Data Files Submitted 3. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile)	☐
Study Type	**TOPICAL CORTICOSTEROIDS (VASOCONSTRICTOR STUDIES)** NO a. Pilot Study (determination of ED50) b. Pivotal Study (study meets BE criteria 90%CI or 80-125)	☐

Sec. VII	**Components and Composition Statements** 1. Unit composition and batch formulation **YES**	☒

(b) (4)

[redacted]

Each ml contains:	Hi-Tech	RLD
Lidocaine Hydrochloride ,USP	20 mg	2%
Hydroxypropyl methylcellulose (b) (4)		(b) (4)
Methylparaben, NF		
Propylparaben, NF		
(b) (4) Sodium Hydroxide Solution	pH adjustment	"
Hydrochloric Acid Solution	pH adjustment	"
Purified Water, USP	(b) (4)	

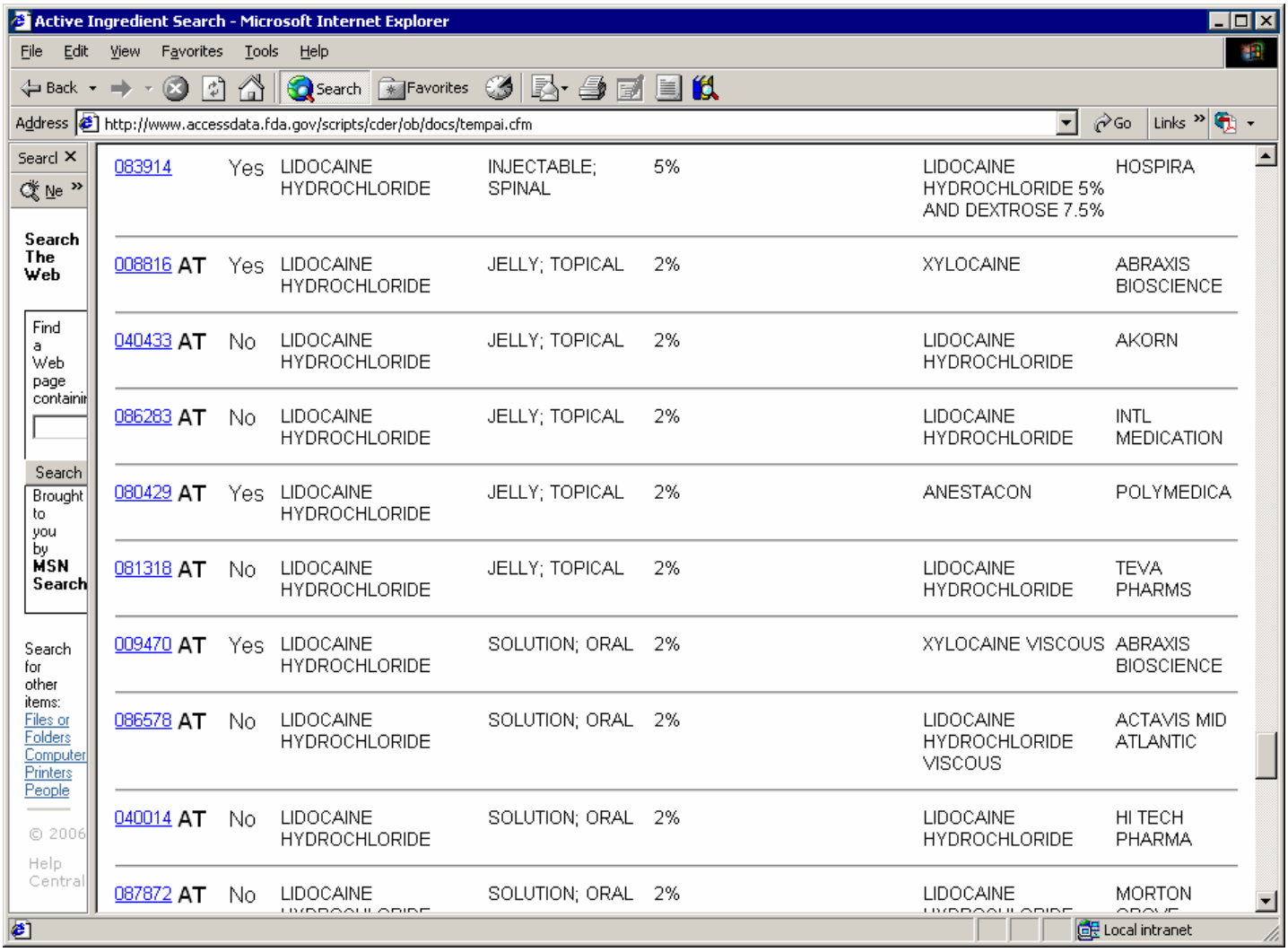
Sec. VIII	**Raw Materials Controls** 1. **Active Ingredients** a. Addresses of bulk manufacturers **YES:** (b) (4) b. Type II DMF authorization letters or synthesis **YES:** (b) (4) c. COA(s) specifications and test results from drug substance mfgr(s) **YES** d. Applicant certificate of analysis **YES** e. Testing specifications and data from drug product manufacturer(s) **YES** f. Spectra and chromatograms for reference standards and test samples **YES** g. CFN numbers 2. **Inactive Ingredients** a. Source of inactive ingredients identified **YES** b. Testing specifications (including identification and characterization) **YES** c. Suppliers' COA (specifications and test results) **YES** d. Applicant certificate of analysis **YES**	☒
Sec.IX	**Description of Manufacturing Facility** 1. Full Address(es)of the Facility(ies) **YES: Hi-Tech** 2. CGMP Certification: **YES** 3. CFN numbers	☒
Sec. X	**Outside Firms Including Contract Testing Laboratories** 1. Full Address **YES** 2. Functions **YES** 3. CGMP Certification/GLP **YES** 4. CFN numbers	☒
Sec. XI	**Manufacturing and Processing Instructions** 1. Description of the Manufacturing Process (including Microbiological Validation, if Appropriate) **YES** 2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified **YES** **Exhibit:** (b) (4) **Production:** (b) (4) 3.If sterile product: (b) (4) 4.Filter validation (if aseptic fill) (b) (4) 5. Reprocessing Statement **Y**	☒
Sec. XII	**In-Process Controls** 1. Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures), Batch Reconciliation and Label Reconciliation **YES** 2. In-process Controls - Specifications and data **YES**	☒

Batch #	Th. Amt.	Act. Amt. Filled	Act. Amt. Packaged in 30 ml Tube
601781	(b) (4)		

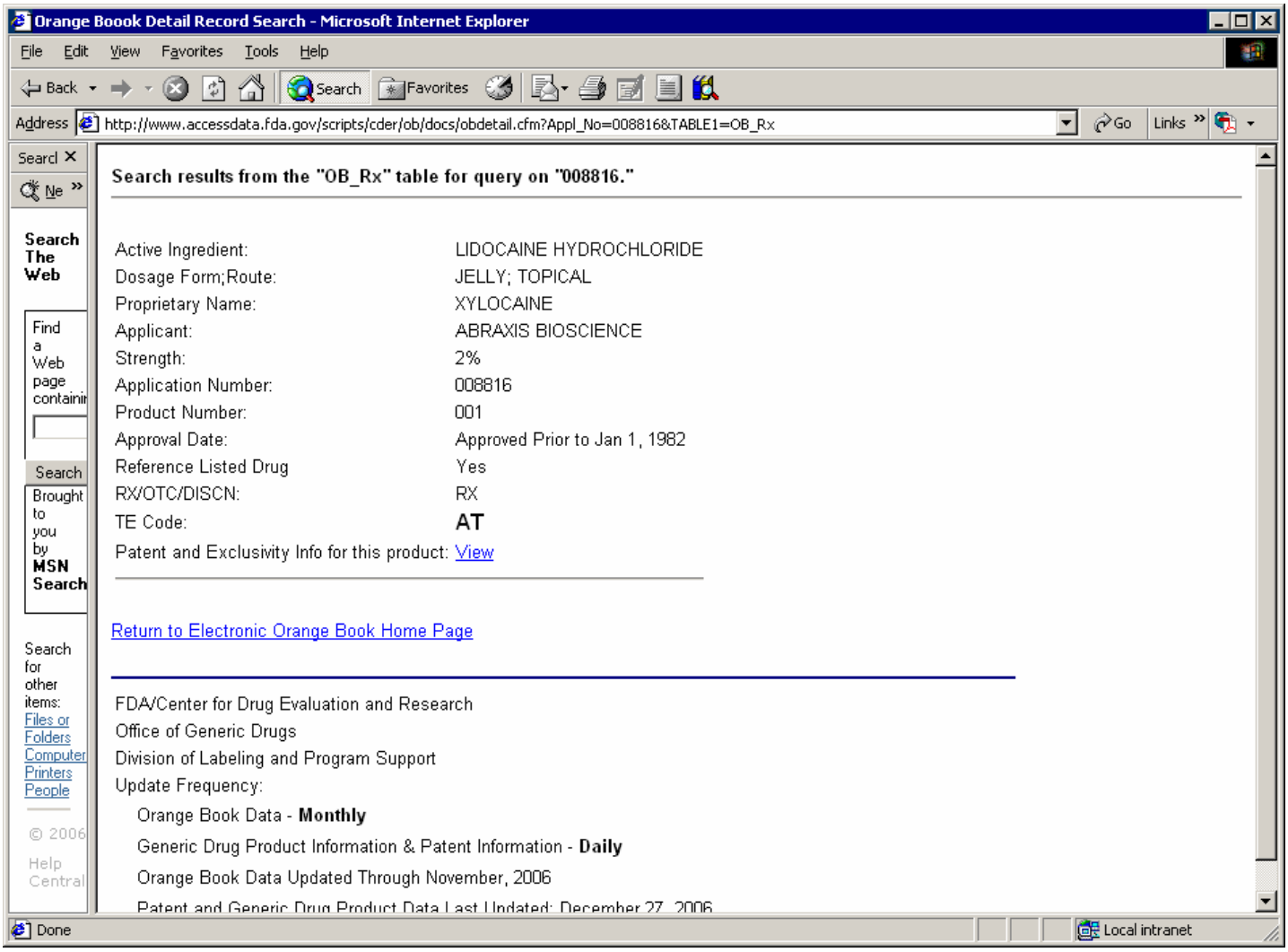
Sec. XIII	**Container** 1. Summary of Container/Closure System (if new resin, provide data) **YES** 2. Components Specification and Test Data (Type III DMF References) **YES** 3. Packaging Configuration and Sizes **YES** 4. Container/Closure Testing **YES** 5. Source of supply and suppliers address **YES**	☒
Sec. XIV	**Controls for the Finished Dosage Form** 1. Testing Specifications and Data **YES** 2. Certificate of Analysis for Finished Dosage Form **YES**	☒
Sec. XV	**Stability of Finished Dosage Form** 1. Protocol submitted **YES** 2. Post Approval Commitments **YES** 3. Expiration Dating Period **YES** 4. Stability Data Submitted **YES** a. 3 month accelerated stability data **YES** b. Batch numbers on stability records the same as the test batch **YES**	☒
Sec. XVI	**Samples** - Statement of Availability and Identification of: 1. Drug Substance **YES** 2. Finished Dosage Form **YES** 3. Same lot numbers **YES**	☒
Sec. XVII	**Environmental Impact Analysis Statement YES**	☒
Sec. XVIII	**GDEA (Generic Drug Enforcement Act)/Other**: 1. Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) N/A 2. Debarment Certification (original signature): **YES** 3. List of Convictions statement (original signature) **YES**	☒

OGD Template Revised 04/01/2004 /T.Hinchliffe

1 Page has been Withheld in Full as b4 (CCI/TS) immediately following this page



083914		Yes	LIDOCAINE HYDROCHLORIDE	INJECTABLE; SPINAL	5%	LIDOCAINE HYDROCHLORIDE 5% AND DEXTROSE 7.5%	HOSPIRA
008816	AT	Yes	LIDOCAINE HYDROCHLORIDE	JELLY; TOPICAL	2%	XYLOCAINE	ABRAXIS BIOSCIENCE
040433	AT	No	LIDOCAINE HYDROCHLORIDE	JELLY; TOPICAL	2%	LIDOCAINE HYDROCHLORIDE	AKORN
086283	AT	No	LIDOCAINE HYDROCHLORIDE	JELLY; TOPICAL	2%	LIDOCAINE HYDROCHLORIDE	INTL MEDICATION
080429	AT	Yes	LIDOCAINE HYDROCHLORIDE	JELLY; TOPICAL	2%	ANESTACON	POLYMEDICA
081318	AT	No	LIDOCAINE HYDROCHLORIDE	JELLY; TOPICAL	2%	LIDOCAINE HYDROCHLORIDE	TEVA PHARMS
009470	AT	Yes	LIDOCAINE HYDROCHLORIDE	SOLUTION; ORAL	2%	XYLOCAINE VISCOUS	ABRAXIS BIOSCIENCE
086578	AT	No	LIDOCAINE HYDROCHLORIDE	SOLUTION; ORAL	2%	LIDOCAINE HYDROCHLORIDE VISCOUS	ACTAVIS MID ATLANTIC
040014	AT	No	LIDOCAINE HYDROCHLORIDE	SOLUTION; ORAL	2%	LIDOCAINE HYDROCHLORIDE	HI TECH PHARMA
087872	AT	No	LIDOCAINE	SOLUTION; ORAL	2%	LIDOCAINE	MORTON


Orange Boook Detail Record Search - Microsoft Internet Explorer
File Edit View Favorites Tools Help
Back Search Favorites
Address http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=008816&TABLE1=OB_Rx
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Search The Web
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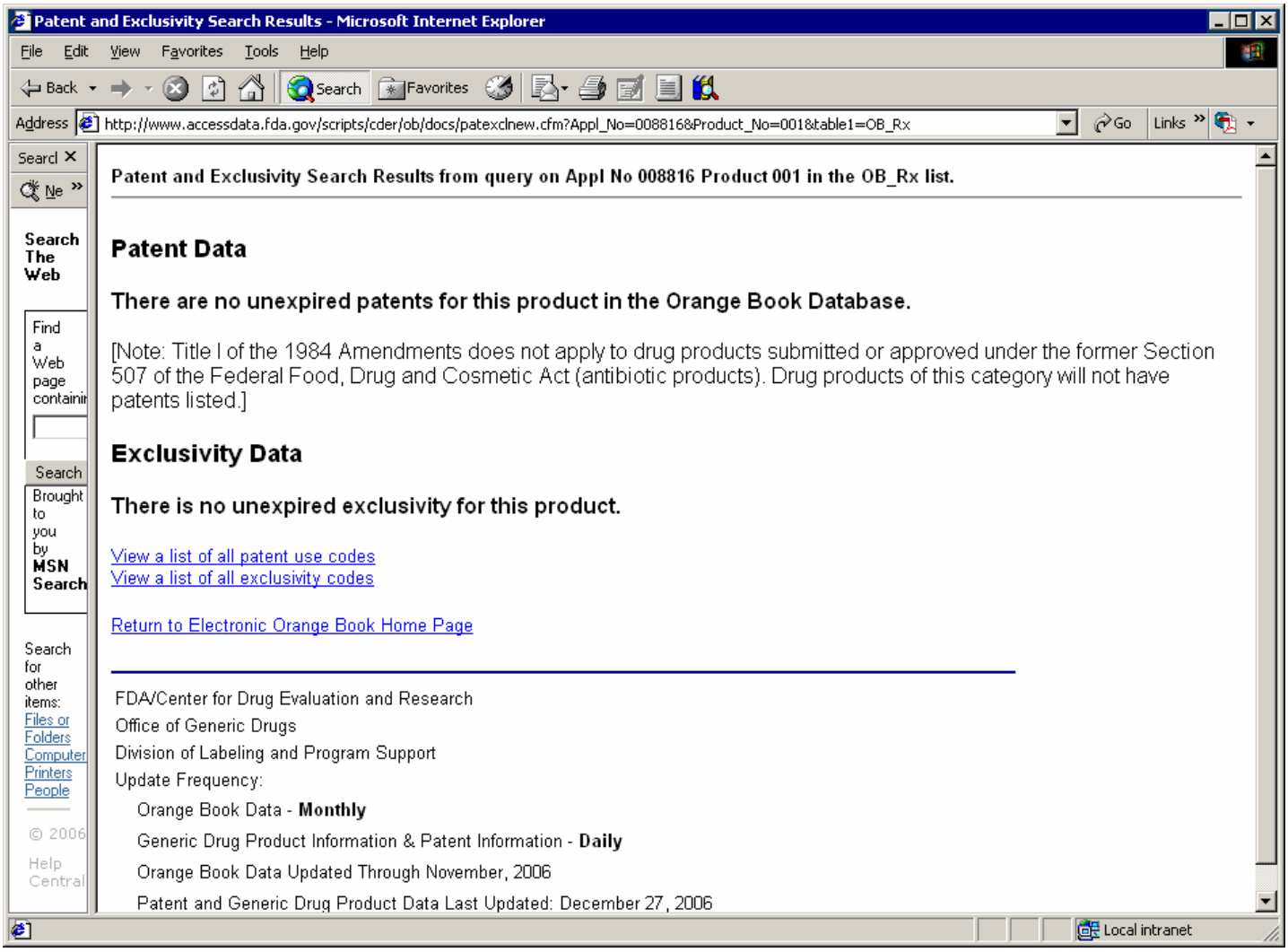
Search
Brought to you by MSN Search
Search for other items: Files or Folders Computer Printers People
© 2006
Help Central
Search results from the "OB_Rx" table for query on "008816."
Active Ingredient: LIDOCAINE HYDROCHLORIDE
Dosage Form;Route: JELLY; TOPICAL
Proprietary Name: XYLOCAINE
Applicant: ABRAXIS BIOSCIENCE
Strength: 2%
Application Number: 008816
Product Number: 001
Approval Date: Approved Prior to Jan 1, 1982
Reference Listed Drug Yes
RX/OTC/DISCN: RX
TE Code: AT
Patent and Exclusivity Info for this product: View
Return to Electronic Orange Book Home Page
FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - Monthly
Generic Drug Product Information & Patent Information - Daily
Orange Book Data Updated Through November, 2006
Patent and Generic Drug Product Data Last Updated: December 27, 2006
Done
Local intranet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Back Search Favorites
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Brought to you by MSN Search
Search for other items: Files or Folders Computer Printers People
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Help Central
Patent and Exclusivity Search Results from query on Appl No 008816 Product 001 in the OB_Rx list.
Patent Data
There are no unexpired patents for this product in the Orange Book Database.
[Note: Title I of the 1984 Amendments does not apply to drug products submitted or approved under the former Section 507 of the Federal Food, Drug and Cosmetic Act (antibiotic products). Drug products of this category will not have patents listed.]
Exclusivity Data
There is no unexpired exclusivity for this product.
View a list of all patent use codes
View a list of all exclusivity codes
Return to Electronic Orange Book Home Page
FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - Monthly
Generic Drug Product Information & Patent Information - Daily
Orange Book Data Updated Through November, 2006
Patent and Generic Drug Product Data Last Updated: December 27, 2006
Local intranet

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

/s/

Saundra Middleton
2/26/2007 12:00:57 PM
Signing for Martin Shimer

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 40-837

Hi-Tech Pharmacal Co., Inc.
Attention: Joanne Curri
369 Bayview Avenue
Amityville, NY 11701

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Lidocaine Hydrochloride Jelly USP, 2%

DATE OF APPLICATION: November 20, 2006

DATE (RECEIVED) ACCEPTABLE FOR FILING: November 21, 2006

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Jeanne Skanchy
Project Manager
301-827-5719

Sincerely yours,

{See appended electronic signature page}

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
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/

Saundra Middleton
2/26/2007 12:02:09 PM
Signing for Wm Peter Rickman

Telephone Fax

ANDA 40-837

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park
North I
7520 Standish Place
Rockville, MD 20855-2773
301-827-7342

TO: Hi Tech Pharmacal Co., Inc. TEL: 631-789-8228 ext. 4127

ATTN: Joanne Curri FAX: 631-841-4166

FROM: Ann Vu

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lidocaine Hydrochloride Jelly USP, 2%

Pages (including cover): 13

SPECIAL INSTRUCTIONS:

Labeling Comments and Attached RLD labeling

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-837 Date of Submission: November 20, 2006

Applicant's Name: Hi-Tech Pharmacal Co., Inc.

Established Name: Lidocaine Hydrochloride Jelly USP, 2%

Labeling Deficiencies:

1. CONTAINER –30 mL

   a. Please revise the title to "Lidocaine Hydrochloride Jelly USP, 2%"

   b. "hydroxypropyl methylcellulose" rather than "hydroxypropylmethylcellulose" [add a space]

   c. Include "sodium hydroxide" and "hydrochloric acid" in the listing of inactive ingredients as appearing in the DESCRIPTION section of the package insert labeling and/or comment.

   d. Revise the statement "Consult package…information." to read "USUAL DOSAGE: See package insert."

   e. Revise the storage temperature statement to read "Store at controlled room temperature, (b) (4) [see USP]".

   f. Include the route of administration "For topical use only".

   g. We encourage the inclusion of the text "Discard unused portion." We refer you to the statement "The unused portion should be discarded after initial use." found in your DESCRIPTION section of the package insert labeling.

   h. Revise to read "methylparaben" rather than "methyl-paraben".

   i. Please ensure that the lot number and expiration date are on the label. Refer to 21 CFR 201.17 and 201.18.

2. CARTON – 1s (30 mL)

   Refer to CONTAINER comments.

3. INSERT

   a. GENERAL

      i. Use the term "mcg" rather than "μg".

      ii. Use the term "to" rather than a hyphen when expressing a range.

iii. Delete the terminal zeros when referencing an amount. [e.g., “6 mcg” rather than “6.0 μg”]

iv. Please note that USAN names are common nouns and should be treated as such in the text of labeling (i.e., lower case). Upper case may be used when the USAN name stands alone on labels or in the title of the package insert

b. TITLE

i. Please add the phrase “Rx only” directly below the established name.

ii. Refer to CONTAINER comment a.

c. DESCRIPTION

i. First paragraph:

…” (See INDICATIONS AND USAGE for…)”

ii. We encourage the inclusion of the molecular formula and weight.

iii. Refer to CONTAINER comment b.

d. WARNINGS

Last paragraph, third sentence, revise “...the jelly may be dry...” to “...the jelly may dry...”

e. PRECAUTIONS

i. General

Third paragraph, second sentence, revise to read “Since it is not...”

ii. Carcinogenesis, Mutagenesis, Impairment of Fertility

Refer to enclosed RLD labeling. Please follow the RLD labeling’s format.

iii. Use in Pregnancy

Refer to enclosed RLD labeling.

iv. Nursing Mothers

Refer to enclosed RLD labeling.

v. Pediatric Use

Refer to enclosed RLD labeling.

f. OVERDOSAGE – Management of Local Anesthetic Emergencies:

i. Second paragraph, third sentence, correct the spelling of “thiamylal”.

ii. Let the penultimate sentence of the second paragraph “If not treated…” begin a new third paragraph.

iii. Last paragraph, revise “...lidocaine HCL...” to “...lidocaine hydrochloride...”

g. DOSAGE AND ADMINISTRATION

i. For Surface Anesthesia of the Male Adult Urethra

A) First paragraph, third sentence, revise "...lidocaine HCL..." to "...lidocaine hydrochloride..."

B) Let the last sentence "Prior to catherization…" be the new last paragraph. In the same sentence, revise to read "smaller volumes [plural].

ii. Lubrication for Endotracheal Intubation:

First sentence, revise "on" to "of".

h. MAXIMUM DOSAGE

Revise "...lidocaine HCL..." to "...lidocaine hydrochloride..."

i. HOW SUPPLIED

i. We note that a detachable applicator cone and a key for expressing the contents are listed in this section for your 30 mL tube package size. However, you did not submit data to support this statement in the container/closure section. Please submit the data/or explain. Also include data that the cone could be boiled for 5 minutes, may be gas sterilized or cold sterilized.

ii. See comment (e) under CONTAINER.

Submit labels and labeling electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – ANDA.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission please provide a side-by-side comparison of your proposed labeling with your last labeling submission with all differences annotated and explained.

{See appended electronic signature page}

_____

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Hi•Tech PHARMACAL Co. Inc.

June 28, 2007

Mr. Gary J. Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II
7500 Standish Place
Room 150
Rockville, MD 20855

ORIG AMENDMENT
N/AF

RE: Labeling Amendment to Pending ANDA 40-837
Product: Lidocaine Hydrochloride Jelly USP, 2%

Dear Mr. Buehler,

Reference is made to the above cited abbreviated new drug application dated November 20, 2006 and the agency's labeling deficiencies dated April 16, 2007.

Submitted herewith please find final printed labeling (container label, individual folding carton, and package insert) as well as a side-by-side comparison of Hi-Tech's newly revised labeling with the labeling submitted on November 20, 2006. Additionally, please find enclosed a disk that contains the electronic labeling and SPL.

Should you have any questions concerning the submitted information, please contact Joanne Curri at 631-789-8228, extension 4127.

Sincerely,

HI-TECH PHARMACAL CO., INC.

Joanne Curri

Joanne Curri
Director of Regulatory Affairs

RECEIVED
JUN 29 2007
OGD

369 BAYVIEW AVENUE, AMITYVILLE, N.Y. 11701 • PHONE: (631) 789-8228 • FAX: (631) 789-8429 • www.hitechpharm.com

Telephone Fax

ANDA 40-837

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park
North I
7520 Standish Place
Rockville, MD 20855-2773
301-827-7342

TO: Hi Tech Pharmacal Co., Inc. TEL: 631-789-8228 ext. 4127

ATTN: Joanne Curri FAX: 631-841-4166

FROM: Ann Vu

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lidocaine Hydrochloride Jelly USP, 2%

Pages (including cover): 4_

SPECIAL INSTRUCTIONS:

Labeling Comments

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-837 Date of Submission: June 28, 2007

Applicant's Name: Hi-Tech Pharmacal Co., Inc.

Established Name: Lidocaine Hydrochloride Jelly USP, 2%

Labeling Deficiencies:

1. CONTAINER –30 mL

   Acceptable in final print.

2. CARTON – 1s (30 mL)

   Acceptable in final print.

3. INSERT

   A. HOW SUPPLIED

      You may not delete the cone since it is used for administration of the drug product. Please submit the cone specification data to both labeling and chemistry. Also include data that the cone could be boiled for 5 minutes, may be gas sterilized or cold sterilized.

   B. Please provide a sample of the drug product and cone in order for us to evaluate the directions in the DOSAGE AND ADMINISTRATION section. Forward the sample to:

      ATTN: Thuyanh Vu
      OGD/CDER/FDA
      Document Control Room
      Metro Park, North II
      7500 Standish Place, Room 150
      Rockville, MD 20855-2733

Submit labeling electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – ANDA.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission please provide a side-by-side comparison of your proposed labeling with your last labeling submission with all differences annotated and explained.

{See appended electronic signature page}

_____

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
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/

Charles Hoppes

7/25/2007 10:27:50 AM

MAJOR AMENDMENT

ANDA 40-837

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

APPLICANT: Hi-Tech Pharmacal Co., Inc. TEL: 631-789-8228

ATTN: Joanne Curri FAX: 631-841-4166

FROM: Jeanne Skanchy PROJECT MANAGER: (301) 827-5719

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated November 20, 2006, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lidocaine Hydrochloride 2% Jelly.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (5 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If this represents a second or greater occasion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance.

SPECIAL INSTRUCTIONS:

In an effort to improve document flow and availability to review staff, please submit your response in electronic PDF format, with a signed cover letter and 356h form.

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-837 APPLICANT: Hi-Tech Pharmacal Co., Inc.

DRUG PRODUCT: Lidocaine Hydrochloride Jelly USP, 2%

The deficiencies presented below represent MAJOR deficiencies.

A. Deficiencies:

1. Please ensure that the amount of Hydroxypropyl methylcellulose ((b) (4)) proposed in the formulation will not impact the suspendability of the drug as compared with the RLD.

2. Throughout your application, you refer to Lidocaine Hydrochloride. However, LOA for drug substance you provided is for Lidocaine only. Please clarify and provide the correct LOA including drug master file number to evaluate any updated information.

3. Regarding drug substance, we have the following comments:

a. (b) (4)

b.

c.

d.

e.

f.

Please provide the revised drug substance specifications and results for the test batch.

4. For drug substance identification, the background check IR spectra on page 71 appears to show peaks at about the same wave numbers as those found in the test sample and the reference standard spectra. Please explain. Please provide UV spectra of active ingredient, Lidocaine hydrochloride to justify the identity and detection wavelength of the molecule.

5. Please provide your in-house as well as the manufacturer's detailed certificate of analysis for hydrochloric acid, because it is listed as one of the ingredients in the composition table to be used for pH adjustment.

6. A comparison of the ANDA manufacturing process versus the proposed commercial process is not included. Please provide a process and equipment comparison with justifications for any changes.

7. Please describe the maximum holding time for the bulk finished drug product prior to packaging in the market containers. Please also clarify that any bulk holding times are included in the calculation of the drug product expiry.

8. Regarding container/closure system, we have the following comments:

   a. The DMF holder (b) (4) letter on page 284 indicates that the Aluminum tubes are collapsible. However, your component description does not address this. Please clarify.

   b. Please provide composition information on the (b) (4).

   c. Please clarify (b) (4)

   d. Please clarify (b) (4)

   e. We notice that a detachable applicator cone and a key for expressing the contents are included in the 30 mL tube labeling section. However, there is no supporting composition, test data, COA and manufacturer/DMF information provided in the ANDA under Container/Closure section. Please explain.

9. Please establish specification for (b) (4)

10. Regarding finished drug product, we have the following comments:

    a. Please add specification for container appearance to the finished drug product testing protocol.

    b. Please be advised that drug product impurities specifications, based upon ICH Q3B and maximum daily dose, would normally be acceptable. However, (b) (4)

[redacted] (b) (4)

c. The specification range for [redacted] (b) (4) Please revise or justify the specification.

11. Please explain how [redacted] (b) (4) .

12. Regarding stability of drug product, we have the following comments:

a. [redacted] (b) (4)

b.

c.

d.

e.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. OGD is changing its CMC review process through our question based review (QbR) initiative, which is described in more detail on the OGD website: http://www.fda.gov/cder/ogd/QbR.htm.

   OGD's QbR was designed with the expectation that ANDA applications would be organized according to the Common Technical Document (CTD), a submission format adopted by multiple regulatory bodies including the FDA. Generic firms are strongly recommended to submit their ANDAs in the CTD format (either eCTD or paper) to facilitate the implementation of the QbR and to avoid undue delays in the review of their applications.

Because of the increasing number of ANDA submissions OGD receives each year, the Quality Overall Summary (QOS) part of the CTD format is extremely important to making our new review process more efficient. Beginning in January 2007, all ANDA applicants are recommended to provide an electronic copy of a QOS that addresses OGD's QbR questions. The QbR-Quality Overall Summary Outline posted on our webpage http://www.fda.gov/cder/ogd/ contains all the questions to prepare the QOS. The QOS should be submitted in both MS Word and pdf format along with the paper or electronic submission. The QOS should be provided even if the remainder of the application is not in CTD format. OGD has prepared QOS models that can be found on the OGD web site. We ask you to use these as a guide for your submissions.

Sincerely yours,

(See appended electronic signature page)

Vilayat A. Sayeed, Ph.D.
Director
Division of Chemistry III
Office of Generic Drugs
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/

Robert Iser

10/26/2007 11:04:56 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDAs (See Attached List)

CERTIFIED MAIL-RETURN RECEIPT REQUESTED

Hi-Tech Pharmacal Co., Inc.
Attention: Joanne Curri
369 Bayview Avenue
Amityville, NY 11701

Dear Madam:

This letter is in reference to the Abbreviated New Drug Applications (ANDAs), submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for (as noted in the attached list).

We refer you to our "Not Approvable" letters (See Attached List), which detailed the deficiencies identified during our reviews of your ANDAs. The Agency may consider an ANDA applicant's failure to respond to a "Not Approvable" letter within 180 days to be a request by the applicant to withdraw the ANDA under 314.120(b). Your amendments to the applications are overdue. You must amend your applications within 10 days of receipt of this letter. Otherwise, an action to withdraw these applications will be initiated per 21 CFR 314.99.

If you do not wish to pursue approval of these applications at this time, you should request withdrawal in accord with 21 CFR 314.65. A decision to withdraw these applications would be without prejudice to refiling.

If you have further questions you may contact Saundra Middleton, Project Manager, Regulatory Support Branch, at (240) 276-8421.

Please send all correspondence to the following address:

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Sincerely yours,

{See appended electronic signature page}

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Hi-Tech Pharmacal Co., Inc.

ANDA Number	Name	Non-approvable Date
	(b) (4)	
40-837	Lidocaine Hydrochloride Jelly USP, 2%	10/26/2007
	(b) (4)	

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/s/

Saundra Middleton
7/28/2008 10:12:11 AM
Signing for Wm Peter Rickman

Hi•Tech PHARMACAL Co. Inc.

September 29, 2008

N/AC

Mr. Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II
7500 Standish Place
Room 150
Rockville, MD 20855

ORIG AMENDMENT

Re: **Major Amendment to Pending ANDA 40-837**
Lidocaine Hydrochloride Jelly USP, 2%

Dear Mr. Buehler:

Reference is made to the above cited abbreviated new drug application dated November 20, 2006 and the agency's major amendment dated October 26, 2007.

Submitted herewith is Hi-Tech's response to the agency's comments.

If you have any questions concerning the submitted information, please contact Joanne

Curri at 631-789-8228, extension 4127.

Sincerely,

HI-TECH PHARMACAL CO., INC.

Joanne Curri

Joanne Curri
Director of Regulatory Affairs

Enc.

RECEIVED
SEP 30 2008
OGD

369 BAYVIEW AVENUE, AMITYVILLE, N.Y. 11701 • PHONE: (631) 789-8228 • FAX: (631) 789-8429 • www.hitechpharm.com

FAX – Microbiology Deficiencies Enclosed

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville MD 20855-2773 (240-276-8408)

TO: Joanne Curri		**FROM:** Mark Anderson
Hi-Tech Pharmacal Co., Inc.		Microbiology Project Manager
PHONE: 631-789-8228		**PHONE:** (240) 276-8831
FAX: 631-841-4166		**FAX:** (240) 276-8725

Total number of pages, excluding this cover sheet: 3

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format. This will improve document availability to review staff.

Microbiology Deficiencies:

Enclosed are the microbiology deficiencies for ANDA 40-837 for Lidocaine Hydrochloride Jelly 2%. The submission reviewed was submitted on November 20, 2006. Please respond to this communication as quickly as possible. This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review. The response to this communication will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT-RESPONSE TO MICROBIOLOGY DEFICIENCIES should appear prominently in your cover letter.

Should you also have other outstanding deficiencies, for review purposes, please attempt to consolidate your responses into a single submission for this application.

If you have questions, feel free to call Bonnie McNeal or Mark Anderson.

H. LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS

ANDA: 40-837 APPLICANT: Hi-Tech Pharmacal Co., Inc.

DRUG PRODUCT: Lidocaine Hydrochloride 2% Jelly

Microbiology Deficiencies:

1. Regarding media fills:
   a. (b) (4)
   b.
   c.
   d.

2. Please provide validation data for the container/closure integrity testing of the packaging components used for the drug product. Please describe how your positive and negative control samples are prepared. If positive controls are prepared by breaching the container/closure system, please describe how they were breached and what was used to breach them.

3. Regarding the (b) (4) of the aluminum containers and caps used to package the drug product:
   a. (b) (4)
   b.
   c.
   d.
   e.

4. Regarding sterilization of the (b) (4)

5. Regarding the sterilization of equipment in the (b) (4)
   a. (b) (4)
   b.

c. (b) (4) [redacted]

6. Regarding the building and facility layout, please provide an indication of the flow of material and the product on the floor plan.

7. Regarding antimicrobial effectiveness testing, please provided data to validate antimicrobial effectiveness making sure testing begins with an acceptable population of compendial organism and indicate the concentration of the preservatives contained in the tested lots.

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,

{See appended electronic signature page}

Lynne A. Ensor, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
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/

Lynne Ensor

10/1/2008 04:36:54 PM

COMPLETE RESPONSE -- MAJOR

ANDA 40-837

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Hi-Tech Pharmacal Co., Inc. TEL: (631) 789-8228

ATTN: Joanne Curri FAX: (631) 789-8429

FROM: Jeanne Skanchy FDA CONTACT PHONE: (240) 276-8467

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated November 20, 2006, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lidocaine Hydrochloride Jelly USP, 2%.

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format. This will improve document availability to review staff.

We have described below our reasons for this action and, where possible, our recommendations to address these issues in the following attachments (**2** pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR AMENDMENT should appear prominently in your cover letter. Upon OGD's acceptance for filing of your ANDA, it was determined that an adequate amount of information was submitted to allow for review of your Bioequivalence and Microbiology data. You will be notified in a separate communication of any further deficiencies identified during our review of your Bioequivalence and Microbiology data. If this represents a second or greater occasion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance.

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-837 APPLICANT: Hi-Tech Pharmacal Co., Inc.

DRUG PRODUCT: Lidocaine Hydrochloride Jelly USP, 2%

The deficiencies presented below represent MAJOR deficiencies.

A. Deficiencies:

1. Based on your response to comment 12c in major amendment September 29, 2008, the agency has suspended any further review of this ANDA until an amendment containing complete information and data necessary from the new exhibit batch to support your chosen plan of action is submitted for evaluation. The new exhibit batch information should contain all in-process, drug product, and stability data necessary to support the manufacturing changes and a complete summary of process changes with scientific rationale for each change.

2. Please be informed that your drug product should be in compliance with the current USP <467> General Chapter and/or ICH Q3C. Please see the following website, http://www.fda.gov/cder/ogd/residualsolvents.pdf, for additional guidance on required data and information.

Sincerely yours,

(See appended electronic signature page)

Vilayat A. Sayeed, Ph.D.
Director
Division of Chemistry III
Office of Generic Drugs
Center for Drug Evaluation and Research

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/s/

Robert Iser
6/29/2009 09:53:31 AM
signed for V. Sayeed

Hi·Tech PHARMACAL Co. Inc.

January 15, 2010

Mr. Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II
7500 Standish Place
Room 150
Rockville, MD 20855

orig-1
SD#5

Re: **Major Amendment to Pending ANDA 40-837**
Lidocaine Hydrochloride Jelly USP, 2%

Dear Mr. Buehler:

Reference is made to the above cited abbreviated new drug application dated November 20, 2006, Hi-Tech's major amendment dated September 29, 2008 and the agency's major amendment dated June 29, 2009.

Submitted herewith is Hi-Tech's new exhibit batch information inclusive of in-process, drug product and stability data necessary to support the manufacturing changes. A complete summary of process changes with scientific rationale is provided.

Additionally, Hi-Tech is adding a 5 gm container size. Information relative to this size as well as labeling for same is included.

If you have any questions concerning the submitted information, please contact Joanne

Curri at 631-789-8228, extension 4127.

Sincerely,

HI-TECH PHARMACAL CO., INC.

Joanne Curri
Director of Regulatory Affairs

Enc.

RECEIVED
JAN 19 2010
OGD

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Hi•Tech PHARMACAL Co. Inc.

June 30, 2010

ORIG-1
SD# 6

Ms. Thuyanh Vu
Office of Generic Drugs
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II
7500 Standish Place
Room 150
Rockville, MD 20855-2733

Re: **Labeling Amendment to Pending ANDA 40-837**
Lidocaine Hydrochloride Jelly USP, 2%

Dear Ms. Vu:

Reference is made to the above cited abbreviated new drug application dated November 20, 2006 and the agency's communication dated July 25, 2007 in which it requested a sample of the cone and final packaging used to package Lidocaine Hydrochloride Jelly USP, 2%.

Submitted herewith are specifications and a drawing of the cone applicator used in the packaging. Samples of the cone and final packaging will be forwarded to the agency when it becomes available.

(b) (4) materials like this may be boiled for five minutes, gas sterilized, or cold sterilized.

If you have any questions concerning the submitted information, please contact Joanne Curri at 631-789-8228, extension 4127.

Sincerely,

Joanne Curri

Joanne Curri
Director of Regulatory Affairs

Enc.

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Hi•Tech PHARMACAL Co. Inc.

July 19, 2010

ORIG-1
SD#7

Mr. Keith Webber
Acting Director
Office of Generic Drugs
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North
7500 Standish Place
Room 150
Rockville, MD 20855

MINOR AMENDMENT - RESPONSE TO MICROBIOLOGY DEFICIENCIES

Re: **Minor Amendment – Response to Microbiology Deficiencies to Pending ANDA 40-837 Lidocaine Hydrochloride 2% Jelly**

Dear Mr. Webber:

Reference is made to the above cited abbreviated new drug application dated November 20, 2006 and the agency's minor microbiology amendment of October 1, 2008.

Submitted herewith is Hi-Tech's response to the agency's comments.

Should you have any questions or comments, please call Joanne Curri at 631-789-8228, extension 4127.

Sincerely,

Joanne Curri

Joanne Curri
Director of Regulatory Affairs

ENC.

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JUL 20 2010
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Hi•Tech PHARMACAL Co. Inc.

ORIG-1
SD-8

August 19, 2010

Mr. Keith Webber
Acting Director
Food and Drug Administration
Center for Drug Evaluation & Research
Office of Generic Drugs
Document Control Room
7620 Standish Place
Rockville, MD 20855

TELEPHONE AMENDMENT – MICROBIOLOGY DEFICIENCIES

Re: **Telephone Amendment – Response to Microbiology Deficiencies to Pending ANDA 40-837 Lidocaine Hydrochloride 2% Jelly**

Dear Mr. Webber:

Reference is made to the above cited abbreviated new drug application dated November 20, 2006, Hi-Tech's minor microbiology amendment dated July 19, 2010, and the telephone microbiology amendment of August 11, 2010.

Submitted herewith is Hi-Tech's response to the agency's comments.

Should you have any questions or comments, please call Joanne Curri at 631-789-8228, extension 4127.

Sincerely,

Joanne Curri

Joanne Curri
Director of Regulatory Affairs

ENC.

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AUG 20 2010
OGD

369 BAYVIEW AVENUE, AMITYVILLE, N.Y. 11701 • PHONE: (631) 789-8228 • FAX: (631) 789-8429 • www.hitechpharm.com

TELEPHONE MEMO

DATE: **08/11/2010**

TIME: **11:55 am**

INITIATED BY: **Eric K. Adeeku, Microbiologist**

FIRM NAME: **Hi-Tech Pharmacal Inc.**

REPRESENTATIVE: **Joanne Curri**

Telephone: **631-789-8228 Ext 4127**

SUBJECT:

1. Please provide the (b) (4)

2. Regarding actions to be taken (b) (4)

3. Regarding validation of the container/closure integrity testing please specify how many positive and negative controls were performed for each study and specify how many of the test containers passed study.

4. (b) (4)

5. Regarding building and facility layout, please provide an indication of the flow of material and the flow of product on a floor plan using color or some way to differential between the flow of material and the flow of products.

RESPONSE: Applicant's responded by providing the data requested above on 08/19/2010.

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/s/

ERIC K ADEEKU
09/22/2010

Hi•Tech PHARMACAL Co. Inc.

January 20, 2011

ORIG-1, SD#9

Keith Webber, Ph.D.
Acting Director
Office of Generic Drugs
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North VII
7620 Standish Place
Document Control Room
Rockville, MD 20855

RE: Labeling Amendment to Pending ANDA 040837
Product: Lidocaine Hydrochloride Jelly USP, 2%

Dear Dr. Webber,

Reference is made to the above cited abbreviated new drug application dated November 20, 2006. Hi-Tech has recised its labeling in accordance with the latest RLD's labeling, Xylocaine 2% Jelly (Lidocaine Hydrochloride).

Submitted herewith please find final printed labeling (container label, individual folding carton, and package insert) as well as a side-by-side comparison of Hi-Tech's newly revised labeling with the previously submitted labeling. Additionally, please find enclosed a disk that contains the electronic labeling and SPL.

Should you have any questions concerning the submitted information, please contact Joanne Curri at 631-789-8228, extension 4127.

Sincerely,

HI-TECH PHARMACAL CO., INC.

Joanne Curri

Joanne Curri
Director of Regulatory Affairs

369 BAYVIEW AVENUE, AMITYVILLE, N.Y. 11701 • PHONE: (631) 789-8228 • FAX: (631) 789-8429 • www.hitechpharm.com

Hi•Tech PHARMACAL Co. Inc.

ORIG-1
SDN-10

March 3, 2011

Mr. Keith Webber
Deputy Director
Food and Drug Administration
Center for Drug Evaluation & Research
Office of Generic Drugs
Metro Park North 7
7620 Standish Place
Rockville, MD 20855

Re: **Telephone Amendment to Pending ANDA 040837**
Lidocaine Hydrochloride 2% Jelly

Dear Mr. Webber:

Reference is made to the above cited abbreviated new drug application dated November 20, 2006 and Hi-Tech's telephone conversation of March 3, 2011 with Dr. Laxma Nagavelli.

Dr. Nagavelli requested Hi-Tech provide the agency with a commitment to add content uniformity testing from the beginning, middle and end of the 30 mL marketed tubes and from the beginning and end of the 5 mL marketed tubes.

Additionally, he requested that we revise the finished product and stability specifications to include this testing and submit the revised specifications with the commitment.

Enclosed please find Hi-Tech's commitment as well as revised finished product and stability specifications.

Should you have any questions concerning the submitted information, please feel free to call Joanne Curri at 631-789-8228, extension 4127.

Sincerely,

Joanne Curri

Joanne Curri
Director of Regulatory Affairs

ENC.

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MAR 04 2011
OGD

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ROUTING SHEET

☒ **APPROVAL** ☐ **TENTATIVE APPROVAL** ☐ **SUPPLEMENTAL APPROVAL (NEW STRENGTH)** ☐ **CGMP**

Division: III	**Team:** 12	**PM:** Leigh Ann Bradford

Electronic ANDA: Yes ☒ No ☒

ANDA #:040837
Firm Name:Hi-Tech Pharmacal Co., Inc.
ANDA Name:Lidocaine Hydrochloride Jelly USP, 2%
RLD Name:Xylocaine Jelly, 2% by APP Pharmaceuticals, LLC (008816)

Electronic AP Routing Summary Located:

V:\Chemistry Division III\Team 12\Electronic AP Summary\40837_AP-TA_Apprv_Rout_Sumry.doc

AP/TA Letter Located:

V:\Chemistry Division III\Team 12\Final Version For DFS Folder\APPROVAL LETTERS\40837_AP.doc

Project Manager Evaluation: **Date: 10/27/2010 Initials:** LB

☐ Previously reviewed and tentatively approved --- Date _____
☐ Previously reviewed and CGMP Complete Response issued -- Date _____

Original Rec'd date 11/21/2006	Date of Application 11/20/2006	Date Acceptable for Filing 11/21/2006
Patent Certification (type) PII	Date Patent/Excl. expires	Citizens' Petition/Legal Case? Yes☐ No ☐ (If YES, attach email from PM to CP coord)
First Generic Yes ☐ No ☒ **DMF#:** _____ (provide MF Jackets)	Priority Approval (Top 100, PEPFAR, etc.)? Yes ☐ No ☒ Comment: Prepared Draft Press Release sent to Cecelia Parise Yes ☐ No ☐ Date:	
☐ Suitability Petition/Pediatric Waiver	Pediatric Waiver Request: Accepted ☐ Rejected ☐ Pending ☐	

EER Status: ☐ Pending ☒ Acceptable ☐ OAI *EES Date Acceptable: 2/08/2011* ☐ Warning Letter Issued; Date:
Has there been an amendment providing for a Major change in formulation since filling? Yes ☐ No ☐ Comment:
Date of Acceptable Quality (Chemistry) 3/15/2011 Addendum Needed: Yes ☐ No ☐ Comment:
Date of Acceptable Bio 8/20/2007 Bio reviews in DARRTS: Yes ☐ No ☐ (Volume location:)
Date of Acceptable Labeling 1/31/2011 Attached labeling to Letter: Yes ☐ No ☐ Comment:
Date of Acceptable Sterility Assurance (Micro) 9/29/2010

Methods Val. Samples Pending: Yes ☐ No ☒; Commitment Rcvd. from Firm: Yes ☒ No ☐

Post Marketing Agreement (PMA): Yes ☐ No ☒ (If yes, email PM Coordinator) Comment:

Modified-release dosage form: Yes ☐ No ☒ (If yes, enter dissolution information in Letter)

Routing:

☒ Labeling Endorsement, Date emailed: 2/16/2011 REMS Required: Yes ☐ No ☒ REMS Acceptable: Yes ☐ No ☐

☒ Regulatory Support

☐ Paragraph 4 Review (Dave Read, Susan Levine), Date emailed: _____

☒ Division

☐ 1st Generic Review

☒ Bob West / Peter Rickman
☐ Keith Webber

☒Filed AP Routing Summary in DARRTs	☒Notified Firm and Faxed Copy of Approval Letter	☒ Sent Email to "CDER-OGDAPPROVALS" distribution list

Reference ID: 2922166

OGD APPROVAL ROUTING SUMMARY

1. ***Regulatory Support Branch Evaluation***

Martin Shimer **Date: 11/17/2010**

Chief, Reg. Support Branch **Initials:** MHS

Contains GDEA certification: Yes ☒ No ☐	Determ. of Involvement? Yes ☐ No ☒
(required if sub after 6/1/92)	Pediatric Exclusivity System
	RLD =Xylocaine NDA# 8-816 Date Checked N/A Nothing Submitted ☐ Written request issued ☐ Study Submitted ☐
Patent/Exclusivity Certification: Yes ☒ No ☐ If Para. IV Certification- did applicant: Notify patent holder/NDA holder Yes ☐ No ☐ Was applicant sued w/in 45 days:Yes ☐ No ☐ Has case been settled: Yes ☐ No ☐ Date settled: Is applicant eligible for 180 day	
Generic Drugs Exclusivity for each strength: Yes ☐ No ☒	
Date of latest Labeling Review/Approval Summary _____	
Any filing status changes requiring addition Labeling Review Yes ☐ No ☒	
Type of Letter: ☒ APPROVAL ☐ TENTATIVE APPROVAL ☐ SUPPLEMENTAL APPROVAL (NEW STRENGTH) ☐CGMP ☐ OTHER:	
Comments:It is noted that the archival 1.1 jacket for this ANDA remains missing after an e-mail request was sent out to all of OGD to look for this jacket. Therefore, my assessment will be based upon information that was captured during the filing review on the checklist. ANDA submitted on 11/21/2006, BOS=Xylocaine NDA 08-816, PII cert provided. ANDA ack for filing on 11/21/2006 (LO dated 2/26/2007). There are no remaining unexpired patents or exclusivities which protect the RLD. This ANDA is eligible for immediate Full Approval.	

2. ***Labeling Endorsement***

Reviewer, T.Vu:
Date2/16/2011
InitialsLS for TV

Labeling Team Leader, J.Grace:
Date2/16/2011
InitialsLS for JG

REMS required?
☐Yes ☒No

REMS acceptable?
☐Yes ☐No ☒n/a

Comments:
From: Grace, John F
Sent: Wednesday, February 16, 2011 3:31 PM
To: Vu, Thuyanh (Ann); Sears, Leigh Ann
Subject: RE: Labeling sign-off for ANDA 040837 (Lidocaine HCL Jelly, 2%)
concur.

John F. Grace
Team Leader, Labeling Review Team 1 (HFD-613)
FDA/CDER/OPS/OGD/DLPS/LRB/LRT1
7520 Standish Place, MPN1
Rockville, MD 20855
(240)276-8985
john.grace@fda.hhs.gov

From: Vu, Thuyanh (Ann)
Sent: Wednesday, February 16, 2011 3:17 PM
To: Sears, Leigh Ann; Grace, John F
Subject: RE: Labeling sign-off for ANDA 040837 (Lidocaine HCL Jelly, 2%)
Please sign off for me. I reviewed OB, Drugs@FDA and DAARTS.

Thanks
Ann

From: Sears, Leigh Ann
Sent: Wednesday, February 16, 2011 2:22 PM
To: Grace, John F; Vu, Thuyanh (Ann)
Subject: Labeling sign-off for ANDA 040837 (Lidocaine HCL Jelly, 2%)
Hello John and Ann,

Please perform labeling sign-off. This ANDA is ready for full approval.

Thanks,
Leigh Ann

3. ***Paragraph IV Evaluation*** **PIV's Only**
David Read **Date 3/23/11**
OGD Regulatory Counsel **Initials rlw/for**
Pre-MMA Language included ☐
Post-MMA Language Included ☐
Comments: N/A. There are no paragraph IV certifications associated with this ANDA.

4. ***Quality Division Director /Deputy Director Evaluation*** **Date 3/2/2011**
Chemistry Div. **III (Sayeed)** **InitialsDSG**
Comments:cmc acceptable.

5. ***First Generic Evaluation*** **First Generics Only**
Frank Holcombe **Date 3/23/11**
Assoc. Dir. For Chemistry **Initials rlw/for**
Comments: (First generic drug review)
N/A. Multiple ANDAs have been approved for this drug product.

OGD Office Management Evaluation

6. Peter Rickman **Date 3/23/11**
Director, DLPS **Initials rlw/for**
Para.IV Patent Cert: Yes☐ No☐
Pending Legal Action: Yes ☐ No ☐
Petition: Yes☐ No☐
Comments: Bioequivalence waiver granted under 21 CFR 320.24(b)(6). Office-level bio endorsed 8/20/07.

Final-printed labeling (FPL) found acceptable for approval (Approval Summary #2) 1/31/11, as endorsed 2/16/11. No REMS is required.

CMC found acceptable for approval (Chemistry Review #4) 3/15/11.

Microbiology/Sterility Assurance found acceptable for approval (Microbiology Revierw #2) 9/29/10.

7. Robert L. West
Deputy Director, OGD
Date 3/23/11
Initials RLWest

Para.IV Patent Cert: Yes☐ No☒
Pending Legal Action: Yes☐ No☒
Petition: Yes☐ No☒
Press Release Acceptable ☐
Date PETS checked for first generic drug _____

Comments: Acceptable EES dated 2/8/11 (Verified 3/23/11). No "OAI" Alerts noted.

There are no patents or exclusivity currently listed in the "Orange Book" for this drug product.

This ANDA is recommended for approval.

8. ***OGD Director Evaluation***
Keith Webber
Deputy Director, OPS

Comments: RLWest for Keith Webber, Ph.D. 3/23/11.
First Generic Approval ☐
PD or Clinical for BE ☐
Special Scientific or Reg.Issue ☐
Press Release Acceptable ☐

Comments:

9. Project Manager
Date 3/23/2011
Initials LS

Check Communication and Routing Summary into DARRTS

Orange Book Report:

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Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Reference ID: 2922166

Patent and Exclusivity Search Results from query on Appl No 008816 Product 001 in the OB_Rx list.

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There are no unexpired patents for this product in the Orange Book Database.

<>

There is no unexpired exclusivity for this product.

View a list of all patent use codes
View a list of all exclusivity codes

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FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through February, 2011
Patent and Generic Drug Product Data Last Updated: March 21, 2011

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Reference ID: 2922166

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/s/

LEIGH A SEARS
03/23/2011