CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

201094Orig1s000

Trade Name:	Glydo
Generic or Established:	Lidocaine Hydrochloride Jelly USP, 2%
Sponsor:	Sagent Pharmaceuticals, Inc.
Approval Date:	April 28, 2014

CENTER FOR DRUG EVALUATION AND RESEARCH

201094Orig1s000

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CENTER FOR DRUG EVALUATION AND RESEARCH

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APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 201094

Sagent Pharmaceuticals, Inc.
Attention: Kalpesh Shroff
Associate Director, Regulatory Affairs
1901 N. Roselle Road Suite 700
Schaumburg, IL 60195-3176

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated December 23, 2009, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Glydo (Lidocaine Hydrochloride Jelly, USP), 2% Topical Jelly.

Reference is made to the complete response letter issued from the Agency dated December 12, 2012. Reference also is made to your amendments dated April 23, May 1, July 3, 10, and 30, and September 23, 2013; and March 7, 2014.

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 Glydo (Lidocaine Hydrochloride Jelly, USP), 2% Topical Jelly, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug product (RLD), Xylocaine (Lidocaine Hydrochloride Jelly, USP) 2% Topical Jelly, of Oak Pharmaceuticals, Inc.

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 section 505-1(i) of the Act.

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(s) directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
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 Office of Prescription Drug Promotion with a completed Form FDA 2253 at the time of their initial use.

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

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/UCM072392.pdf. The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

{See appended electronic signature page}

Kathleen Uhl, M.D.
Acting Director
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/

KATHLEEN UHL
04/28/2014

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201094Orig1s000

OTHER ACTION LETTERS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

ANDA201094

COMPLETE RESPONSE

Sagent Pharmaceuticals, Inc.
Attention: Kalpesh Shroff R.A.C.
Associate Director, Regulatory Affairs
1901 N. Roselle Road, Suite 700
Schaumburg, IL 60195

Dear Sir:

Please refer to your Abbreviated New Drug Application (ANDA) dated December 23, 2009, received on December 23, 2009, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lidocaine Hydrochloride Jelly USP, 2%

We acknowledge receipt of your amendments dated May 7, June 24, July 14, and August 6, 2010; May 27, July 29, September 30, November 18, and December 8, 2011; and March 23, July 25, September 19, and September 21, 2012.

We have completed our review of this ANDA, and have determined that we cannot approve this ANDA in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

PRODUCT QUALITY

Division of Chemistry has no further questions at this time.

MICROBIOLOGY

The Division of Microbiology has no further questions at this time.

BIOEQUIVALENCE

The Division of Bioequivalence I (DBI) has completed its review of your amendment submission dated March 23, 2012, 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.

LABELING

LABELING DEFICIENCIES:

1. GENERAL COMMENTS:
   a. Revise [redacted] (b) (4) to read "hypromellose". "Hypromellose" is the official USP name.

   b. Your proposed proprietary name [redacted] (b) (4) is under review. FDA will inform you of any comments when they become available.

2. BLISTERS AND CARTON:
   Revise the expression of strength to include a primary and secondary expression of strength:

   a. For the 6 mL strength: Revise to read "120 mg per 6 mL (20 mg per mL)".

   b. For the 11 mL strength: Revise to read "220 mg per 11 mL (20 mg per mL)".

   c. Revise the "Each mL contains:" statement to read "Each mL contains: 20 mg Lidocaine hydrochloride, hypromellose..."

2. SYRINGE: 6 mL and 11 mL
   a. Refer to container comments (a,b).

   b. Please provide a picture of the container label on the syringe. The pictures should clearly display the calibration on the label and the syringe.

   c. Please revise your labels so that there is no intervening text between the units on the calibration and the syringe.

   d. Please ensure the font size for the text is at least 4 point type.

3. INSERT:
   Please refer to GENERAL COMMENTS.

Submit labeling electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format. Please provide the labeling in the Structured Product Labeling (SPL) format.

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://service.govdelivery.com/service/subscribe.html?code=USFDA_17

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with the reference listed drug labeling with all differences annotated and explained.

A partial response to this letter will not be processed as a resubmission and will not start a new review cycle. The resubmission to this will be considered to represent a MINOR AMENDMENT. The designation as a **RESUBMISSION/AFTER ACTION – MINOR COMPLETE RESPONSE AMENDMENT** should appear prominently in your cover letter.

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the ANDA under 21 CFR 314.65. You may also request an extension of time in which to resubmit the ANDA. A resubmission response must fully address all the deficiencies listed.

The drug product may not be legally marketed until you have been notified in writing that this ANDA is approved.

If you have any questions, call Esther Chuh, Pharm. D., Regulatory Project Manager, at (240) 276-8530.

Sincerely yours,

{See appended electronic signature page}

Gregory P. Geba, M.D., M.P.H.
Director
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/

GREGORY P GEBA
12/12/2012

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201094Orig1s000

LABELING

GLYDO™ (lidocaine HCl jelly USP, 2%)

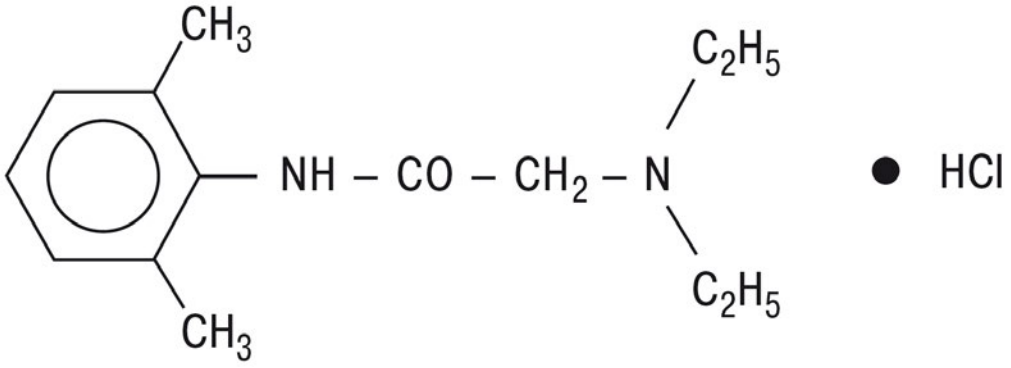
SAGENT™

℞ only

DESCRIPTION

GLYDO (lidocaine HCl jelly USP, 2%) is a sterile aqueous product that contains a local anesthetic agent and is administered topically. (See **INDICATIONS** for specific uses.)

GLYDO (lidocaine HCl jelly USP, 2%) contains lidocaine HCl which is chemically designated as acetamide, 2-(diethyl-amino)-N-(2,6-dimethylphenyl)-, monohydrochloride and has the following structural formula:



GLYDO (lidocaine HCl jelly USP, 2%) also contains hypromellose, and the resulting mixture maximizes contact with mucosa and provides lubrication for instrumentation. The unused portion should be discarded after initial use.

GLYDO (lidocaine HCl jelly USP, 2%) is available in 6 mL and 11 mL single-use prefilled syringes. Each mL contains 20 mg of lidocaine HCl. The formulation also contains hypromellose, and sodium hydroxide to adjust pH to 6.0 to 7.0.

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-l-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 2.0 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 6.0 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

GLYDO (lidocaine HCl 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 GLYDO.

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.

GLYDO 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.

GLYDO 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 GLYDO 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 GLYDO 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
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 HCl 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 GLYDO 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 GLYDO 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

The outer orifice is washed and disinfected. The plastic tip is introduced into the orifice, where it is firmly held in position. The jelly is instilled by an easy syringe-like action, until the patient has a feeling of tension or until about 15 mL (i.e., 300 mg of lidocaine hydrochloride) is instilled. A penile clamp is then applied for several minutes at the corona and then additional jelly (about 15 mL) 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 (i.e., 600 mg) is usually required to fill and dilate the male urethra. Prior to catheterization, smaller volumes of 5 to 10 mL (100-200 mg) are usually adequate for lubrication.

For Surface Anesthesia of the Female Adult Urethra

Slowly instill 3 to 5 mL (60 to 100 mg of lidocaine HCl) 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 HCl 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 GLYDO administered should not exceed 4.5 mg/kg (2 mg/lb) of body weight.

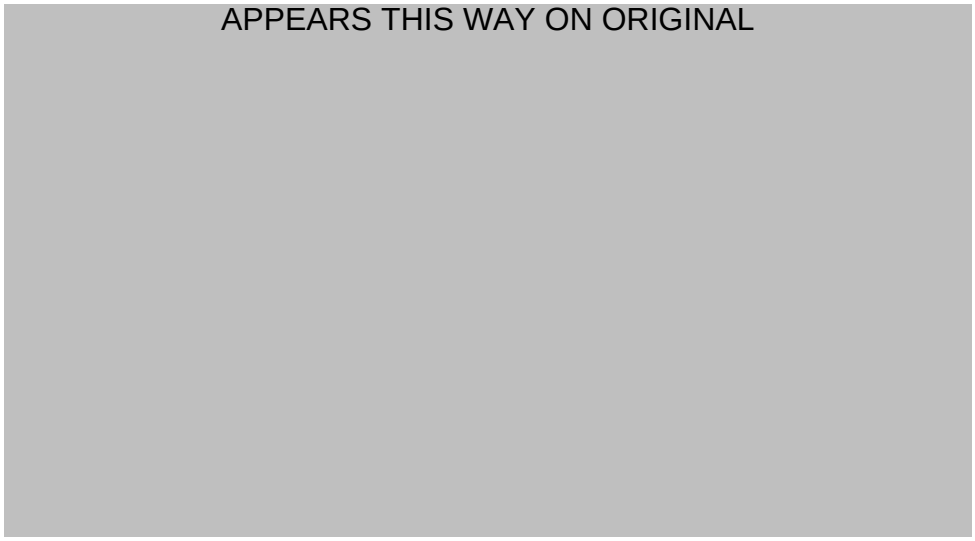
HOW SUPPLIED
GLYDO™ (lidocaine HCl jelly USP, 2%) is supplied as follows:

	GLYDO™ (lidocaine HCl jelly USP, 2%)	
NDC	**(20 mg per mL)**	**Package Factor**
25021-673-76	120 mg per 6 mL Single-Use Prefilled Syringe	10 syringes per carton
25021-673-77	220 mg per 11 mL Single-Use Prefilled Syringe	10 syringes per carton

Storage Conditions
Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

Sterile, Preservative-free, PVC-free.
The container closure is not made with natural rubber latex.

Mfd. for SAGENT Pharmaceuticals
Schaumburg, IL 60195 (USA)
Mfd. by Klosterfrau Berlin GmbH
Made in Germany

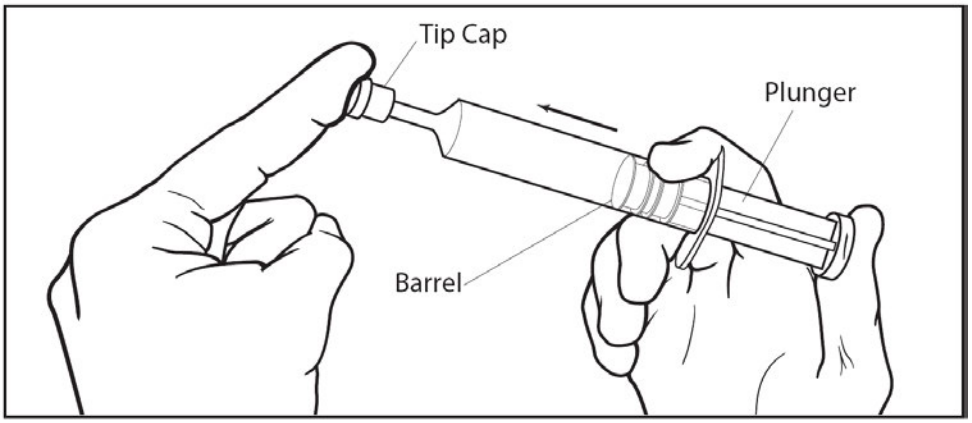

APPEARS THIS WAY ON ORIGINAL

INSTRUCTIONS FOR USE

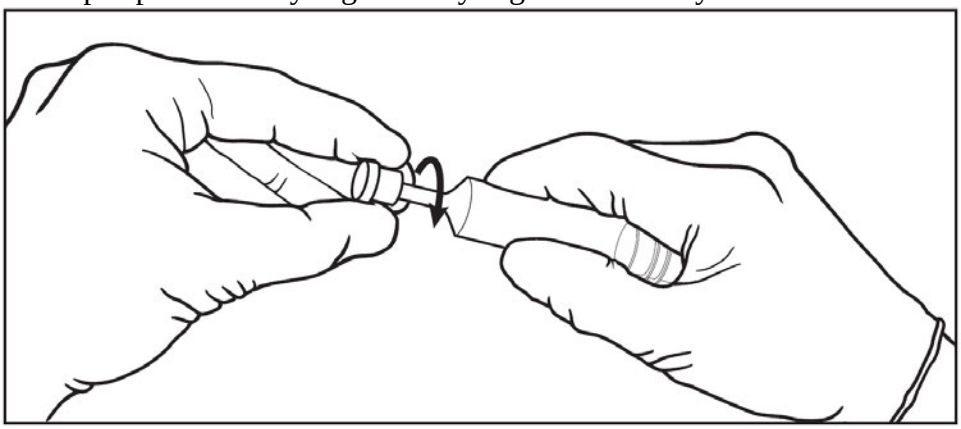
Please note: The blister package contains a sterile syringe.
Do not open the blister until ready to use.

1. When ready to use, open the blister and drop the syringe onto a sterile field.

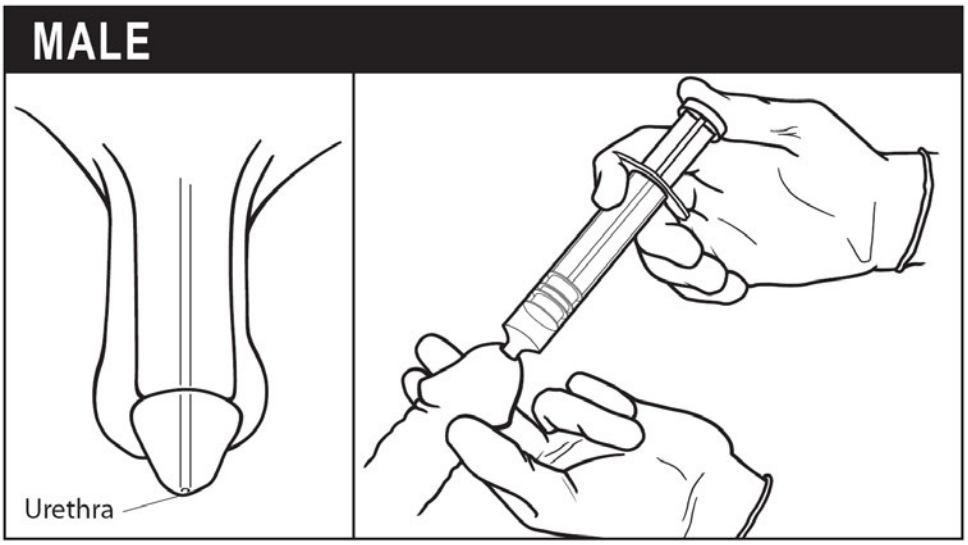
2. Before removing the tip cap, press in the plunger to remove any resistance that may be present. This helps ensure that the syringe will empty easily and uniformly.

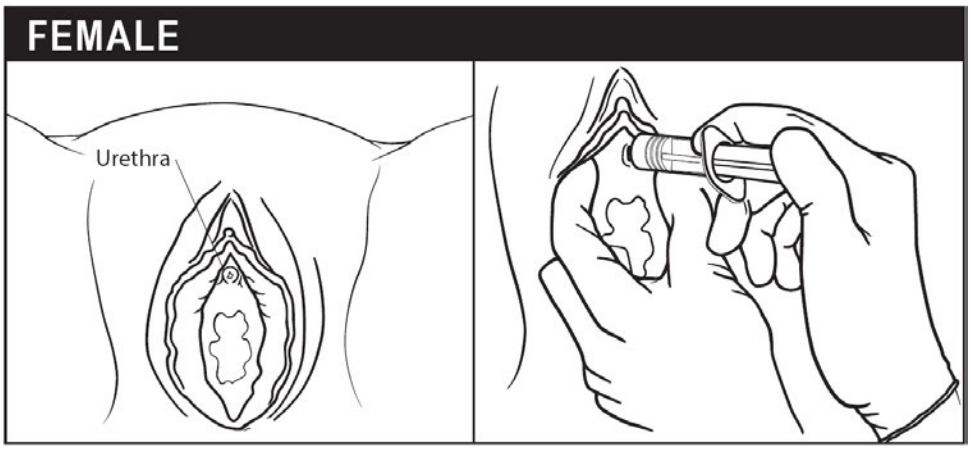


3. Remove the tip cap from the syringe. The syringe is now ready for use.



4. GLYDO (lidocaine HCl jelly USP, 2%) should be instilled slowly and evenly into the urethra. See the **DOSAGE AND ADMINISTRATION** section for additional details.





5. Wait for a few minutes after instillation of GLYDO (lidocaine HCl jelly USP, 2%) for the anesthetic to take full effect. Full anesthetic effect will occur in 5 to 10 minutes after complete instillation.

6. Any gel not used in a single application must be discarded.

Lot: Exp.:

NDC 25021-673-76

glydo™

(lidocaine HCl jelly USP, 2%)
120 mg per 6 mL (20 mg per mL)

Sterile **TOPICAL** Anesthetic

6 mL

10 x 6 mL Single-Use
Prefilled Syringes

℞ only
Preservative-free
SAGENT™

Sterile, Preservative-free, PVC-free.
The container closure is not made with natural rubber latex.
Each mL contains: 20 mg Lidocaine hydrochloride, hypromellose, sodium hydroxide to adjust pH to meet USP limits of 6 to 7, purified water.
Any gel not used in a single application must be discarded.
Usual Dosage: See package insert for dosage information.
Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

(01)20325021673762

SAGENT™
Mfd. for SAGENT Pharmaceuticals
Schaumburg, IL 60195 (USA)
Mfd. by Kosteritzan Berlin GmbH
Made in Germany
©2014 Sagent Pharmaceuticals, Inc. xxxxxxx

EXTERIOR
Glydo | Lidocaine HCl Jelly, USP 2% | 6 mL | Syringe Multiple Carton
Carton Dimensions are 156 x 192 x 50 mm

Updated on 03.03.14 - 01
By JB

INTERIOR
Glydo | Lidocaine HCl Jelly, USP 2% | 6 mL | Syringe Multiple Carton
Carton Dimensions are 156 x 192 x 50 mm

Updated on 03.03.14 - 01
By JB

(b) (4)

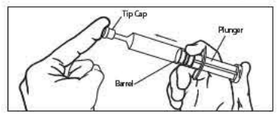
glydo™
(lidocaine HCl jelly USP, 2%)
120 mg per 6 mL (20 mg per mL)
Sterile **TOPICAL** Anesthetic

Instructions for Use
Single-Use Topical Syringe

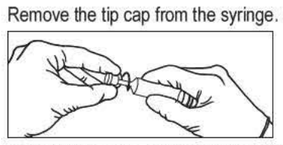
Please note: The blister package contains a sterile syringe.
Do not open the blister until ready to use.

1 When ready to use, open the blister and drop the syringe onto a sterile field.

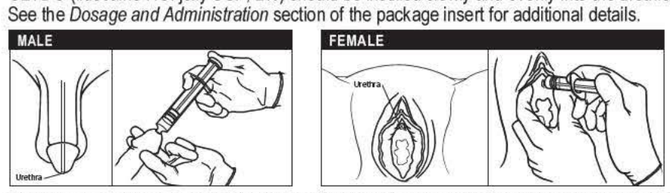
2 Before removing the tip cap, press in the plunger to remove any resistance that may be present. This helps ensure that the syringe will empty easily and uniformly.



3 Remove the tip cap from the syringe. The syringe is now ready for use.



4 GLYDO (lidocaine HCl jelly USP, 2%) should be instilled slowly and evenly into the urethra. See the *Dosage and Administration* section of the package insert for additional details.



5 Wait for a few minutes after instillation of GLYDO (lidocaine HCl jelly USP, 2%) for the anesthetic to take full effect. Full anesthetic effect will occur in 5 to 10 minutes after complete instillation.

6 Any gel not used in a single application must be discarded.

SAGENT™

xxxxxxx

Sagent trademarks and trade dress are the property of Sagent Pharmaceuticals, Inc.

Glydo | Lidocaine HCl Jelly, USP 2% | 6 mL | Syringe Blister
Blister Dimensions are 188.4 x 46.5 mm

Updated on 02.28.14-00
By JB

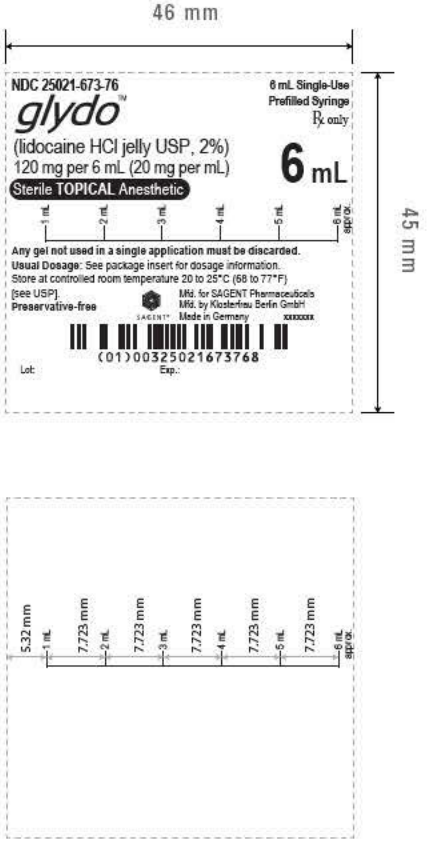
100%

(b) (4)

Glydo | Lidocaine HCl Jelly, USP 2% | 6 mL | Syringe Label
Label Dimensions are 46 x 45 mm

Updated on 02.28.14 - 00
By JB

100%



(b) (4)

EXTERIOR
Glydo | Lidocaine HCl Jelly, USP 2% | 11 mL | Syringe Multiple Carton
Carton Dimensions are 156 x 192 x 50 mm

Updated on 03.03.14 - 01
By JB

(b) (4)

(b) (4)

Sagent trademarks and trade dress are the property of Sagent Pharmaceuticals, Inc.

INTERIOR
Glydo | Lidocaine HCl Jelly, USP 2% | 11 mL | Syringe Multiple Carton
Carton Dimensions are 156 x 192 x 50 mm

Updated on 03.03.14 - 01
By JB

(b) (4)

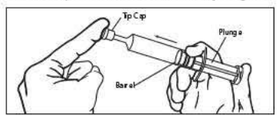
glydo™
(lidocaine HCl jelly USP, 2%)
220 mg per 11 mL (20 mg per mL)
Sterile **TOPICAL** Anesthetic

Instructions for Use
Single-Use Topical Syringe

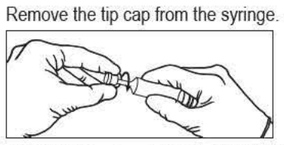
Please note: The blister package contains a sterile syringe.
Do not open the blister until ready to use.

1 When ready to use, open the blister and drop the syringe onto a sterile field.

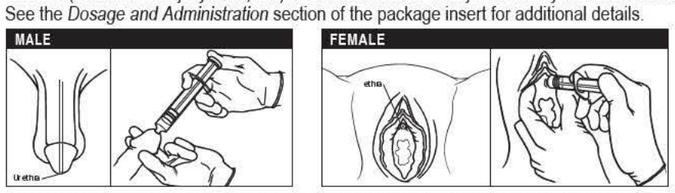
2 Before removing the tip cap, press in the plunger to remove any resistance that may be present. This helps ensure that the syringe will empty easily and uniformly.



3 Remove the tip cap from the syringe. The syringe is now ready for use.



4 GLYDO (lidocaine HCl jelly USP, 2%) should be instilled slowly and evenly into the urethra. See the *Dosage and Administration* section of the package insert for additional details.



5 Wait for a few minutes after instillation of GLYDO (lidocaine HCl jelly USP, 2%) for the anesthetic to take full effect. Full anesthetic effect will occur in 5 to 10 minutes after complete instillation.

6 Any gel not used in a single application must be discarded.

SAGENT™

xxxxxxx

Glydo | Lidocaine HCl Jelly, USP 2% | 11 mL | Syringe Blister
Blister Dimensions are 188.4 x 46.5 mm

Updated on 02.28.14 - 00
By JB

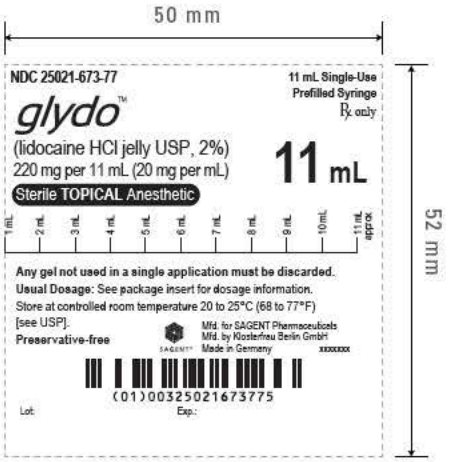
100%

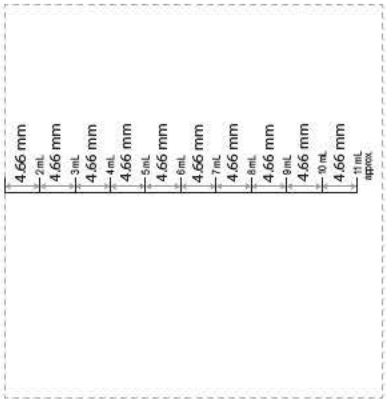
(b) (4)

Glydo | Lidocaine HCl Jelly, USP 2% | 11 mL | Syringe Label
Label Dimensions are 50 x 52 mm

Updated on 02.28.14 - 01
By JB

100%





(b) (4)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201094Orig1s000

LABELING REVIEW(S)

APPROVAL SUMMARY #2

Office of Generic Drugs

REVIEW OF PROFESSIONAL LABELING (5th cycle)

ANDA Number:	201094
Date of Submission:	March 7, 2014
Applicant:	Sagent Pharmaceuticals, Inc.
Established Name and Strength:	Glydo (lidocaine HCl jelly, USP), 2% Jelly, 20 mg/mL
Proposed Proprietary Name:	GLYDO™ (Approved 1/9/2014)

Labeling Comments below are considered:

☐ Minor Deficiency *

* Please note that the RPM may change the status from Minor Deficiency to Easily Correctable Deficiency if other disciplines are acceptable.

☒ No Comments **(**Labeling Approval Summary)

RPM Note - Labeling comments to be sent to the firm start below:

The Labeling Review Branch has no further questions/comments at this time based on your labeling submission dated March 7, 2014.

Please continue to monitor available labeling resources such as DRUGS@FDA, the Electronic Orange Book and the NF-USP online for recent updates, and make any necessary revisions to your labels and labeling.

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://service.govdelivery.com/service/subscribe.html?code=USFDA_17.

Note RPM - Labeling comments end here

REVISIONS NEEDED POST APPROVAL? No.

After the ANDA is approved, the reviewer for the first labeling supplement may consider asking the firm for the following revisions and revised labels and labeling may be submitted in the next annual report.

1. GENERAL COMMENT: Revise the established name so that the "2%" appears outside of the parenthesis [i.e., "…(lidocaine HCl jelly, USP), 2% Jelly"].
2. (b) (4)

3. (b) (4)

NOTES/QUESTIONS TO THE CHEMIST/BIO REVIEWER/MICRO REVIEWER:

Note: The OGD Chemistry Review Division and OGD Clinical Review Division found Sagent's container closure system acceptable.

From:
Sent: Tuesday, April 17, 2012 12:47 PM
To:
Cc:
Subject: RE: lidocaine applicator

I just entered a consult in (b) (4) Thank you for finishing this so quickly.

From:
Sent: Tuesday, April 17, 2012 11:34 AM
To:
Cc:
Subject: lidocaine applicator

Hi—thanks for sending the syringes. Will probably asked that a consult be put in (b) (4) so that I can put a Memo into (b) (4) for you. That is just intended to give you the memo for documentation.

(b) (4)

So I'll do a memo in which DCR concurs that there is no apparent clinical safety risk with this applicator.

Thanks

From:
Sent: Monday, April 16, 2012 11:23 AM
To:
Cc:
Subject: RE: 201094: Sagent's lidocaine jelly

Yes, Sagent submitted the syringe. I'll bring it to Bio.

From:
Sent: Monday, April 16, 2012 7:33 AM
To:
Cc:
Subject: RE: 201094: Sagent's lidocaine jelly

(b) (4)

[redacted]

From:
Sent: Monday, April 16, 2012 7:26 AM
To:
Cc:
Subject: FW: 201094: Sagent's lidocaine jelly

our labeling reviewer is inquiring if a safety consult is warranted for the ANDA issue below.

From:
Sent: Friday, April 13, 2012 4:34 PM
To:
Cc:
Subject: 201094: Sagent's lidocaine jelly

I'm not sure if my concern warrants a clinical safety consult, could you check if I should add a consult in for Clinical Bio?

The RLD is Abraxis' Xyclocaine 2% Jelly (NDA 08816). The RLD is currently marketed in a 30 mL aluminum tube (with a detachable applicator cone and a key for expressing the contents) and a 5 mL plastic tube. In the past, the RLD was also marketed in 10 mL polypropylene and 20 mL polypropylene syringe. IMS (ANDA) currently markets single-use 5 mL, 10 mL and 20 mL lidocaine hydrochloride Jelly packaged in glass vials. IMS provides Uro-Jet vial injectors to use with the glass vials.

Sagent proposes to market the jelly in prefilled 6 mL an 11 mL (b) (4) syringes. Sagent's product is not packaged with a plastic cone. (b) (4)

[redacted]

June 23, 2011 Email to PM of OND

I'm a labeling reviewer for the Office of Generic Drugs and I have a generic drug application in house (Sagent's ANDA 201094) that is different than the RLD (Xylocaine 008816) in the packaging configuration.

The RLD's drug product comes in a 30mL aluminum tube is packaged with a plastic cone that could be attached to the tube in order to instill the product into the urethra.

The ANDA product is not packaged with a plastic cone and is meant to directly inject the gel into the urethra with the tip of the syringe.

My concerns with the syringe packaging are: lidocaine jelly "leaching" into the plastic, excess pressure upon expression by consumer.

Note that there are NO lidocaine jelly drug product that are packaged in a plastic syringe. IMS ANDA 86-283 is packaged in single use glass vial and has an accompanying URO-JET vial injector (device) to express the product. Other drug products are packaged in aluminum tubes.

Could you verify that the RLD was initially approved with the configuration of syringe of 10 mL and 20 Ml (b) (4) If the RLD initially had lidocaine syringes in the market, then there is a precedent for this ANDA syringe packaging.

Review Summary

Labeling Submitted	Date submitted	Final or Draft	Recommendation
CONTAINER 6 mL and 11 mL Syringes	3/7/2014	Final	Acceptable for approval
CARTON	3/7/2014	Final	Acceptable for approval
BLISTER	3/7/2014	Final	Acceptable for approval
INSERT	3/7/2014	Final	Acceptable for approval
SPL	3/7/2014		NONE

FOR THE RECORD: Please note that the first review cycle was completed by Thuyanh Vu, labeling reviewer.

1. **MODEL LABELING:** Xylocaine 2% Jelly (Oak Pharmaceuticals, Inc.). This is NDA 008816/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 10 mL and 20 mL polypropylene syringes are deleted as these presentations are no longer marketed.

   The DOSAGE AND ADMINISTRATION, For surface anesthesia of the male adult urethra: This section of 86283 is different than the RLD's because the packaging. IMS' 86283 lidocaine jelly is packaged in single use glass vials. The carton comes with 25 vials with 25 Uro-Jet vial injectors (verified by calling Amphastar (mother company of IMS). See number 7 for more information. IMS' drug product drug packaging is similar to Sagent's packaging. I

will use portions of this D&A section because it more accurately reflects the packaging configuration.

Approved IMS (86283) and Pending Sagents (201094) reads: (b) (4)

For Surface Anesthesia of the Male Adult Urethra

The outer orifice is washed and disinfected. The plastic tip is introduced into the orifice, where it is firmly held in position. The jelly is instilled by an easy syringe-like action, until the patient has a feeling of tension or until about 15 mL (i.e., 300 mg of lidocaine hydrochloride) is instilled. A penile…

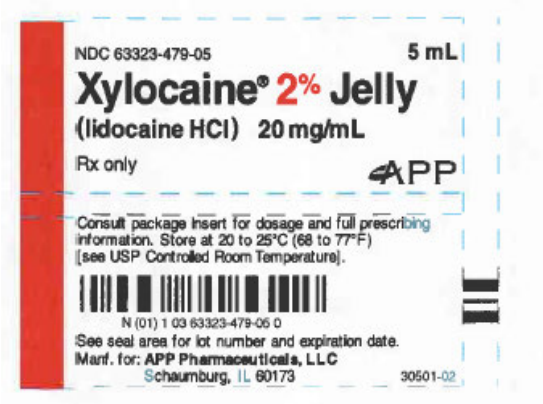
The RLD (00816) has: A Tube with cone

When using Xylocaine 2% Jelly 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

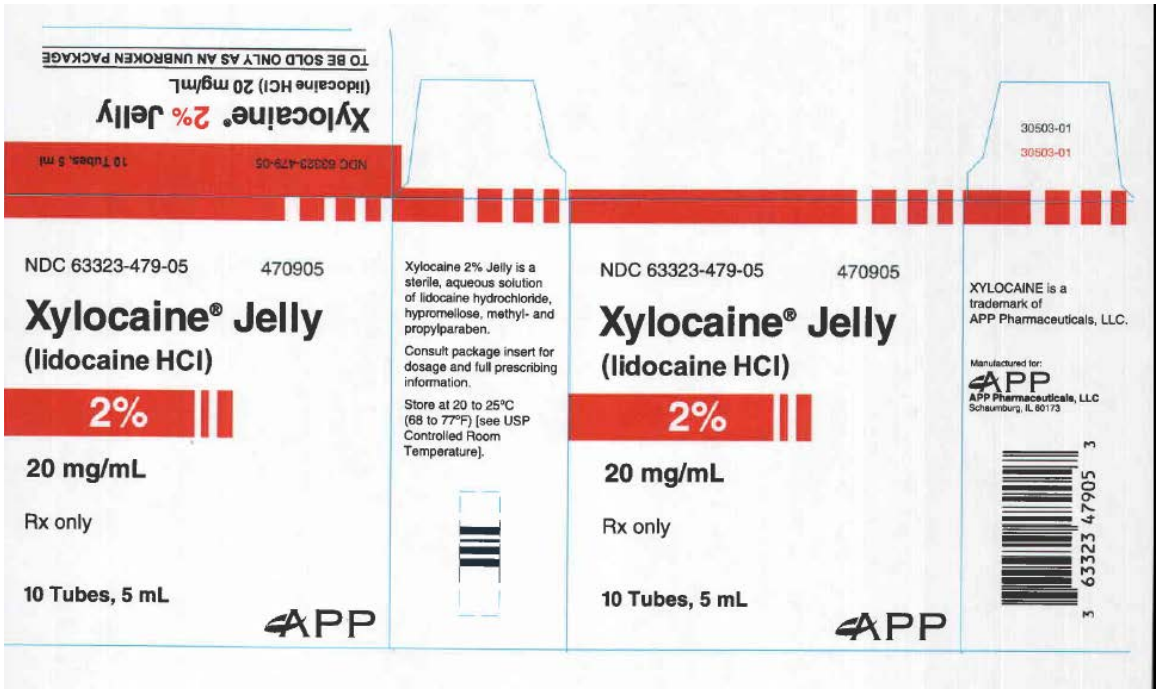
(300 mg of lidocaine HCl) into the urethra or until the patient has a feeling of tension. A penile clamp is then applied for several minutes at the corona. An additional dose of not more than 15 mL (300 mg) can be instilled for adequate anesthesia.

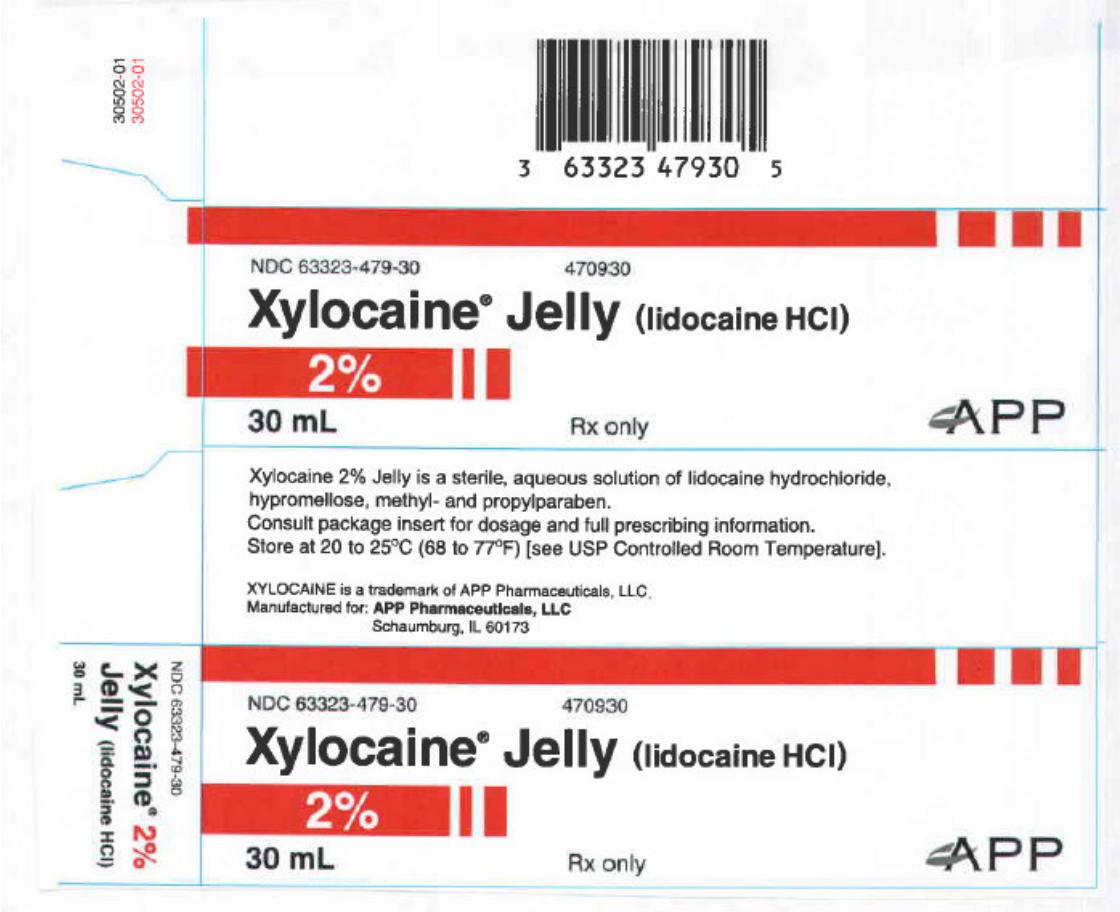
The Agency was notified on 8/2/2012 that APP Pharmaceuticals, LLC transferred the ownership of NDA 008816 to Oak Pharmaceuticals, Inc., subsidiary of Akorn, Inc.

The following container and carton labels and labeling provided below were taken from the Annual report: cover letter dated 4/26/2012.




NDC 63323-479-30
Xylocaine® 2% Jelly
(lidocaine HCl) 20 mg/mL
Rx only
30 mL
APP
Consult package insert for dosage and full prescribing information. Store at 20 to 25°C (68 to 77°F) [see USP Controlled Room Temperature].
N (01) 1 03 63323-479-30 2
See crimp closure for lot number and expiration date.
Manf. for: APP Pharmaceuticals, LLC
Schaumburg, IL 60173
30500-02


TO BE SOLD ONLY AS AN UNBROKEN PACKAGE
Xylocaine® 2% Jelly
(lidocaine HCl) 20 mg/mL
30503-01
30503-01
NDC 63323-479-05 470905
Xylocaine® Jelly
(lidocaine HCl)
2%
20 mg/mL
Rx only
10 Tubes, 5 mL
APP
Xylocaine 2% Jelly is a sterile, aqueous solution of lidocaine hydrochloride, hypromellose, methyl- and propylparaben.
Consult package insert for dosage and full prescribing information.
Store at 20 to 25°C (68 to 77°F) [see USP Controlled Room Temperature].
NDC 63323-479-05 470905
Xylocaine® Jelly
(lidocaine HCl)
2%
20 mg/mL
Rx only
10 Tubes, 5 mL
APP
XYLOCAINE is a trademark of APP Pharmaceuticals, LLC.
Manufactured for:
APP
APP Pharmaceuticals, LLC
Schaumburg, IL 60173
3 63323 47905 3



LABELS FOR ANDA 086283

MedWatch: (checked March 31, 2014)

None

2. **USP-36:** (checked March 31, 2014)

   This product is the subject of a USP-36 monograph.
   Lidocaine Hydrochloride Jelly
   Packaging and storage— Preserve in tight containers.
   pH ⟨ 791 ⟩ : between 6.0 and 7.0.

3. **PATENT AND EXCLUSIVITY (NDA 008816)**

   OB checked 4/1/2014 and there are no unexpired patents and exclusivities for this product.

   Information below is from original review.

   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.]

4. **INACTIVE INGREDIENTS [**2.3.P.1- original submission]

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.

(b) (4)

Note that the formulation does NOT have HCl for pH adjustments (b) (4) (methylparaben, propylparaben). The syringe labels state “Preservative Free”.

Information from consult requested date of 4/17/12:

The proposed test product is a preservative-free formulation (see Section III: Formulation), packaged in a ready-to-use prefilled syringe as a single-use, sterile product. In contrast, the RLD contains the (b) (4) Methylparaben and Propylparaben. There is an approved ANDA (# 086283) which also is packaged as a single use product, (b) (4) . The test product formulation does not need to be Q1/Q2 the same as the RLD with respect to (b) (4) The test product meets USP potency assay specification for lidocaine hydrochloride jelly of 95%.00 to 105.00%[2].

[1]DARRTS: ANDA 201094 REV-BIOEQ-01(General Review); Submit/Final Date 11/10/2011, Page 10-11

[2]USP 34-NF 29 Official Monograph, Page 3308-3309 (http://www.uspnf.com/uspnf/login) Last Accessed: 04.04.2012

5. **MANUFACTURING FACILITY[2.3.P.3-original submission]**

(b) (4)

6. **FINISHED PRODUCT DESCRIPTION**

(b) (4)

7. **STORAGE STATEMENT AND DISPENSING RECOMMENDATIONS**

RLD: Store at controlled room temperature 20-25C (68-77F) [see USP].

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

8. **PRODUCT LINE**

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

ANDA: 6 mL and 11 mL (b) (4) syringe

Note that this is a different packaging configuration than the aluminum tube.
The OGD Chemistry Review Division and OGD Clinical Review Division found Sagent’s container closure system acceptable.

The RLD’s 30mL aluminum tube is packaged with a plastic cone that could be attached to the tube in order to instill the product into the urethra. I examined the cone from Akorn’s

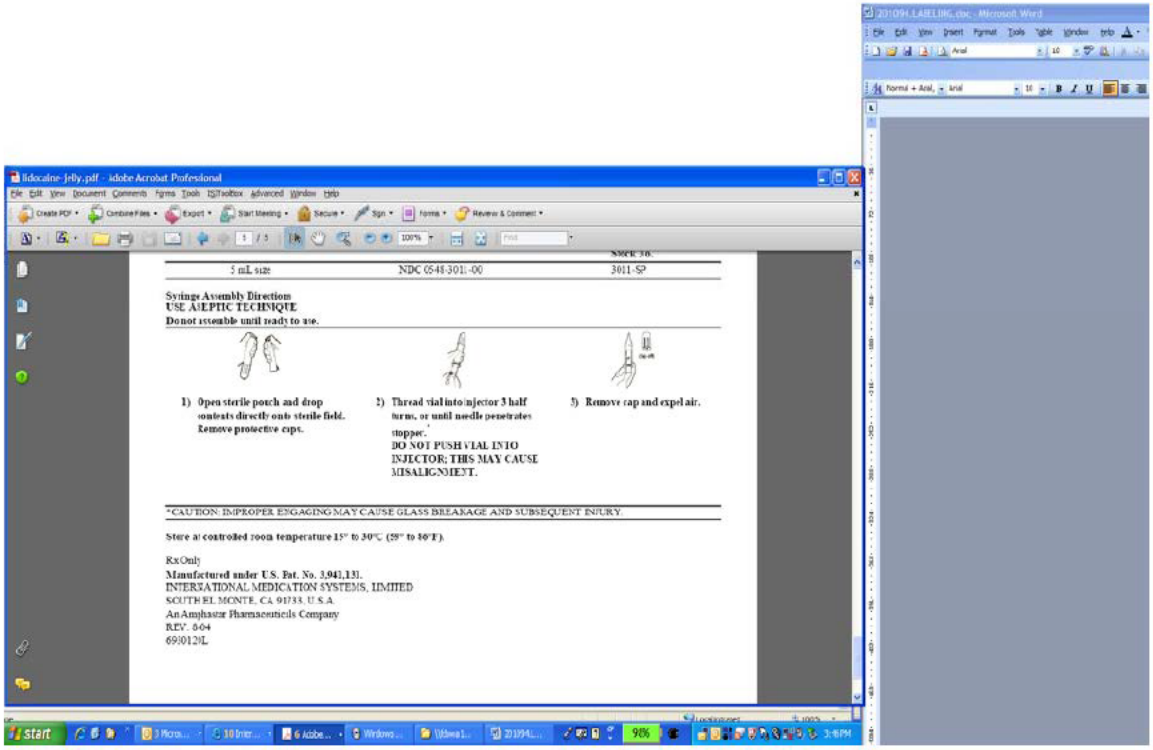
lidocaine jelly (ANDA 40433) and the diameter of the cone is slightly larger than the diameter of Sagent's syringe tip. Sagent's syringe tip is approximately (b) (4)

Sagent's product is not packaged with a plastic cone and is meant to directly inject the gel into the urethra with the tip of the syringe.

There is another product on the market (IMS's 86283) which has 5 mL, 10 mL and 20 mL lidocaine hydrochloride Jelly packaged in single use glass vial. The carton comes with 25 vials with 25 Uro-Jet vial injectors (verified by calling Amphastar (mother company of IMS). Below is the threading technique for the glass vial and Uro-Jet injector.

My concerns with this product are: lidocaine jelly "leaching" into the plastic, excess pressure upon expression by consumer. Note that there are NO lidocaine jelly drug products that are packaged in a plastic syringe. IMS ANDA 86-283 is packaged in single use glass vial and has an accompanying URO-JET vial injector (device) to express the product. Other drug products are packaged in aluminum tubes. I do not know if the lidocaine jelly will "leach" into the plastic.

According to Chan's review of 40433 noted below, the RLD was initially approved with the configuration of syringe of 10 mL and 20 mL that has a narrow tube at the end that is (b) (4) in diameter. I will ask the Division to investigate the RLD's syringes.



From Consult Review dated 4/30/12: Xylocaine 2% Jelly is supplied as 1) 30 mL aluminum tube with a detachable applicator cone and a key for expressing the contents and 2) 5 mL plastic tube (b) (4)

[1]Per OGD Medical Consultation review dated 4/19/12 for Lidocaine Hydrochloride Topical jelly, 2%.

9. Labeling reviewer's comments per old review of ANDA 40433: I spoke with 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. (b) (4) 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 & 20 mL (b) (4) .

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

10. This ANDA was transferred from Farco Pharm GmbH to Sagent Pharmaceuticals.

11. **CONTAINER/CLOSURE[2.3.P.7- original submission]**

(b) (4) The 6 mL and 11 mL syringes will be packaged in cartons of 10.

(b) (4)

From Consult Review dated 4/19/2012:

In comparison to this the Sagent syringe is a prefilled 6 mL and 11 mL (b) (4) *These two application methods (IMS and Sagent) are very similar.*

(b) (4)

The Uro-Jet applicator is similar in applicator tip to that of the proposed Sagent applicator syringe. Based on examination of the sample applicator syringes submitted by the sponsor as well as review of similar currently marketed products and the literature we do not anticipate any clinical safety issues relative to the proposed applicator syringe.

Labeling comment to firm and firm's response submitted in AF dated 4/23/2013:

b. Please provide a picture of the container label on the syringe. The pictures should clearly display the calibration on the label and the syringe.

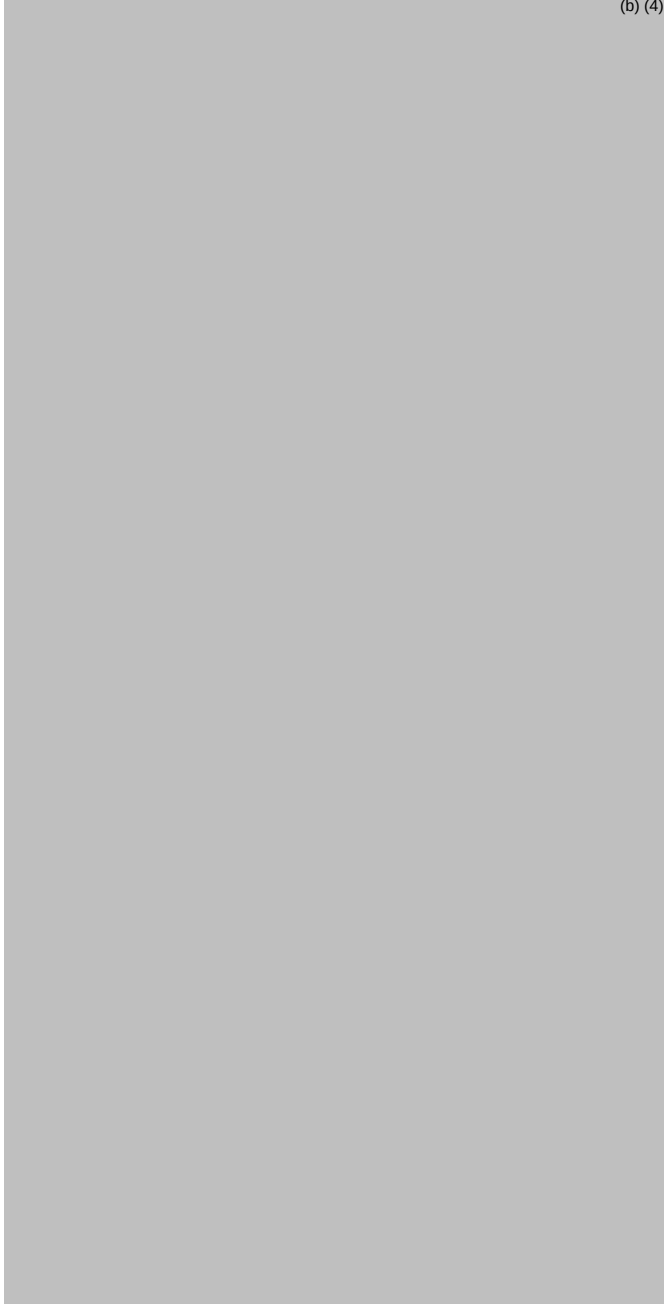
Response:

As recommended by the Agency, we have provided the pictures without plunger (6 mL strength and 11 mL strength) and with plunger (6 mL strength and 11 mL strength) of the labeling text printed on the syringes. (b) (4)

6 mL no Plunger

3 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

(b) (4)



Please note the 11 mL strength is the same as the 6 mL Syringe but not shown here.

Response:
We acknowledge the Agency's comment and confirm there is no intervening text between the units on the calibration and the syringe. We also refer you to the pictures of the syringes provided in this amendment (shown above) which provide a visual confirmation. We confirm the font size for the text is at least 4 point type.

12. **BIOAVAILABILITY/BIOEQUIVALENCE: Adequate as of 5/11/2012**
13. **RELATED APPLICATIONS: None**

14. In AF dated 8/6/2010, Vol A 4.1, the firm provided 5 samples each of 6 mL and 11 mL empty syringes for Agency's review. A consult was requested by labeling reviewer Ann Vu, and the comments can be found in the trail of emails under the section **NOTES/QUESTIONS TO THE CHEMIST** at the beginning of the review. The review of the consult is also located in DARRTS dated 4/19 and 4/30/2012.

15. **SPL DATA ELEMENTS: Submitted 3/7/2014**

16. **PROPRIETARY NAME:**

On 3/7/2014, the firm submitted a gratuitous amendment to update the labeling to include the Proprietary Name Glydo™. Prior to submission of the updated labeling amendment, the firm requested permission to use lower case letter for the proprietary name on the container, carton and blister labeling. OSE-DMEPA confirmed that the labels appear to be appropriate for submission. (refer to email correspondence below)

From:
To:
Cc:
Subject: response: ANDA 201094 Lidocaine HCL Jelly
Date: Tuesday, March 04, 2014 3:38:14 PM

ANDA 201094 package labeling (container, blister, and carton)
The attachments you sent today appears to be appropriate for submission for review.
We are stating this email is NOT a formal review of the proposed revisions.
You may request that the ANDA applicant submit these labels officially.
After the official re-submission is in:
OGD can submit an OSE consult if you would like for OSE-DMEPA to review the revised labels when they're officially submitted Alternatively, you can review the labels and labeling if there are no concerns regarding the previous OSE-DMEPA recommendations.

From:
To:
Subject: PLAN: ANDA 201094 Lidocaine HCL Jelly
Date: Friday, February 28, 2014 9:32:16 AM

ANDA 201094,
Here is our plan: We would like to avoid a teleconference, it is not necessary.
Topic: In reference to comment 2a from the 8-22-12 labeling deficiencies letter, they want to know if they can have the brand name in all lower case letters. She says that she can provide samples of other brand name drugs where the name is all in lower case letter.

Container Labels, Blister Labeling, and Carton Labeling:

Revise the presentation of the proprietary name on all labels and labeling to appear in title case lettering (b) (4) to be consistent with how proper nouns are usually scripted.

OSE: We would have to look at the labels to determine if how they presented the names is acceptable (i.e. established name is half the size of PN etc.).

If they want to get our agreement before they officially submit the labels, email the images and we can take a quick look to determine if the presentation would be OK.

We would then request the Applicant submit the labels officially, OGD can send us a consult and we can evaluate the labels and will write a review or memo to address if all our previous comments have been addressed by the applicant.

So can you request the Applicant to send you, electronically, those labels Container Labels, Blister Labeling, and Carton Labeling, (must reflect the approved PN Glydo)?

On 1/9/2014, the proposed proprietary name Glydo was found acceptable by the Office of Surveillance and Epidemiology.

On 7/3/2013, Sagent submitted a reconsideration request for the proprosed proprietary name Glydo.

In the amendment dated September 21, 2012, the firm submitted the proposed proprietary name (b) (4) for review. The name was found unacceptable

Date of Review:	March 31, 2014
Primary Reviewer:	Betty Turner
Acting Team Leader:	Angela Payne

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

/s/

BETTY B TURNER
04/10/2014

ANGELA M PAYNE
04/11/2014
ATL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201094Orig1s000

MEDICAL REVIEW(S)

Medical Consultation
Lidocaine Hydrochloride Jelly, 2%

Reference Listed Drug (RLD):	**Xylocaine® Jelly (Lidocaine Hydrochloride), 2%, NDA 00816, Oak Pharmaceuticals Inc.**
Sponsor:	**Sagent Pharmaceuticals, Inc.**
To:	Wayne DeHaven, Ph.D Reviewer Team 8 Division of Bioequivalence I (DB1) Hoainhon Nguyen Acting Deputy Director, Division of Bioequivalence I (DB1)
Thru:	John R. Peters, M.D. Director, Division of Clinical Review (DCR) Office of Generic Drugs
Reviewer:	Carol Y. Kim, Pharm. D. Clinical Reviewer, Division of Clinical Review (DCR) Office of Generic Drugs
Drug Class:	Local Anesthetics, Topical (6040400)
Chemical Name:	acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)-, monohydrochloride
Date Received: **Review Completion Date:**	April 17, 2012 April 30, 2012
Reason for Consultation:	DB1 seeks clinical opinion to determine whether the viscosity difference observed between the test and reference products would be of safety/efficacy concern.

Executive Summary:
Xylocaine® 2% Jelly is a sterile aqueous product for topical application and contains a local anesthetic agent. It 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). The onset of action is 3-5 minutes and it is ineffective when applied to intact skin.

Xylocaine 2% Jelly is supplied as 1) 30 ml aluminum tube with a detachable applicator cone and a key for expressing the contents and 2) 5 ml plastic tube with a (b) (4)

(b) (4) Based on the OGD Medical Consultation Review dated 4/19/12, Sagent's proposal to market the jelly in prefilled 6 ml and 11 ml (b) (4) syringes in sterile blister packs did not pose a clinical concern.

According to the DB1 review dated 11/10/11, Xylocaine® 2% Jelly is a Drug Efficacy Study Implementation (DESI) effective drug product (coded "AT" in the Orange Book). Thus, Sargent Pharmaceuticals Inc. (transfer of ownership from Farco-Pharma GMBH)'s Lidocaine Hydrochloride Jelly, 2%, may be eligible for a waiver of in vivo bioequivalence study requirements under the DESI status. The proposed product is a preservative-free formulation and is packaged in a ready-to-use prefilled syringe as a single-use, sterile product. For approval of this product, the DB1 has concluded that the test product does not need to be qualitatively and quantitatively the same as the reference product (b) (4) is acceptable.

However, the DB1 reviewer noted significantly different viscosity data between the test and reference products. The DB1 reviewer was concerned whether the difference in viscosity data would lead to a different surface retention or change the local drug absorption of lidocaine.

Regulatory Background:

Xylocaine 2% Jelly is the reference listed drug (RLD) approved on 3/12/1953. The summary of other ANDAs approved for Lidocaine Jelly, 2%, and their formulations are listed as follows[2]:

Appl No	TE Code	RLD	Proprietary Name	Applicant	Approval date
A040433	AT	No	LIDOCAINE HCl	AKORN	2/12/2003
A040837	AT	No	LIDOCAINE HCl	HI TECH PHARMA	3/23/2011
A086283	AT	No	LIDOCAINE HCl	INTL MEDICATION	08/07/1979
N008816	AT	Yes	XYLOCAINE	OAK PHARMS	03/12/1953
A080429	AT	No	ANESTACON	POLYMEDICA	04/11/1974
A081318	AT	No	LIDOCAINE HCl	TEVA PHARMS	4/29/1993

Formulation comparison between approved drug products and the proposed product for lidocaine 2% Jelly

[1] Per OGD Medical Consultation review dated 4/19/12 for Lidocaine Hydrochloride Topical Jelly, 2%.
[2] Tables were excerpted from the DB1 consult requested for this product.

FIRM:		RLD (Oak Pharm)	(b) (4)	Sagent (transferred from Farco-Pharma GMBH)
ANDA/NDA #:		8816		201094
Volume of Packaged Product:		5mL and 30mL		6mL and 11mL
Packaging:		tube + Applicator		Single use syringe
		mg/mL		quantity per 100 grams
Lidocaine HCl	Active	2% (20mg/mL)		2.0g (20mg/mL)[8]
Methylparaben	Inactive	(b) (4)		
Propylparaben	Inactive			
Hydroxypropylmethylcellulose	Inactive			(b) (4)
Carboxymethylcellulose Sodium	Inactive			
Purified Water	Inactive			QS[10]
Hydrochloric Acid	Inactive			
Sodium Hydroxide	Inactive			ADJUST PH[11]
Sodium Chloride	Inactive			[12]
Benzalkonium Chloride	Inactive			

(b) (4)

History of ANDA 201094 Submissions

12/23/09: Sagent Pharmaceuticals, Inc. requested a waiver of bioequivalence study.

6/9/11: The original OGD Chemistry review concluded that a systematic study needs to show the effect of variability of viscosity and swelling behavior of raw material inputs on the drug product critical quality attributes (DP COAs).

11/17/11: DB1 deficiency comments were provided to the sponsor. The DB1 noted a significant viscosity difference between products and requested justification for such difference (b) (4) In result, viscosity data from additional batches were provided to establish a more accurate viscosity range of their product.

11/18/11: In response to OGD Chemistry Deficiency letter dated 6/1/11, Sagent provided comparative analysis of viscosity of 5 batches of raw material. (b) (4) The sponsor's specification is shown below.

Specification: (b) (4)

(b) (4)

3/23/12: In response to OGD Bioequivalence Deficiency letter dated 11/17/11, Sagent provided comparative viscosity data for the approved Lidocaine Jelly Products currently available in the US market as shown below. Comparative in vitro dissolution testing data were also provided by the sponsor.

(b) (4)

Reviewer's Comment: *In this consult request, DB1 reviewer stated that Sagent's in vitro drug release testing data for semi-solid drug products have not been standardized for acceptance. Thus, dissolution data were not considered for the review.*

4/10/12: According to the OGD Chemistry review #2, Sagent's response to viscosity comment was satisfactory and the CMC reviewer recommends approval. The OGD Chemistry reviewer acknowledges that the viscosity data of the lots tested complies with the raw material (b) (4) specification which is well within the range of (b) (4) for the drug product. As

recommended by the CMC reviewer, Sagent stated that they will not make any changes in (b) (4) composition in batch formula based on variability in the raw material attributes.

LABELING

Current product labeling was approved on 7/23/04. There is no Black Box warning for this product.

Indications and Usage

Xylocaine® (lidocaine HCl) 2% Jelly is indicated for the followings:

- Prevention and control of pain in procedures involving the male and female urethra
- Topical treatment of painful urethritis
- Anesthetic lubricant for endotracheal intubation (oral and nasal)

(b) (4)

Dosage and Administration

The dosage depends on the area to be anesthetized, vascularity of the tissues, individual tolerance, and the technique of anesthesia. Dosage should be reduced for children and for elderly and debilitated patients.

Surface Anesthesia of the Male Adult Urethra: Using 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 HCl) 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.

Surface Anesthesia of the Female Adult Urethra: Using 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 3-5 ml (60-100 mg of lidocaine HCl) of the jelly into the urethra. For adequate anesthesia, several minutes should be allowed prior to performing urological procedures.

(b) (4)

Reviewer's Comment: *For the proposed test product design, the sterilization step is not required.*

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.

Reviewer's Comment: *Sagent's proposed labeling of their product includes the same treatment indications as those listed in the approved labeling of the reference product.*

(b) (4)

Maximum Dosage: No more than 600 mg of lidocaine HCl should be given in any 12 hour period.

Contraindications: Lidocaine is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type or to other components of Xylocaine 2% Jelly.

Warnings and Precautions:

- Excessive Dosage or Short Intervals Between Doses
    - Result in high plasma levels and serious adverse effects.
    - Recommend strict adherence to the recommended dosage and administration guidelines as set forth in the package insert.
    - May require the use of resuscitative equipment, oxygen, and other resuscitative drugs for management of serious adverse reactions.
    - May potentially result in rapid systemic absorption in the presence of sepsis or severely traumatized mucosa in the area of application.
- General Precautions
    - The safety and effectiveness of lidocaine depend on proper dosage, correct technique, adequate precautions, and readiness for emergencies.
    - Repeated doses of lidocaine may cause significant increases in blood levels due to slow accumulation of the drug or its metabolites.
    - Use with caution in patients with severe shock or heart block.
    - Patients allergic to para-aminobenzoic acid derivatives (e.g., procaine, tetracaine, benzocaine etc…) have not shown cross sensitivity to lidocaine.
    - Drugs used for conduct of anesthesia, like lidocaine, are considered potential triggering agents for familial malignant hyperthermia. A standard protocol for management of malignant hyperthermia should be available.

Adverse Reactions:

In general, adverse events are 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 of the part of the patient. Serious adverse events are generally systemic in nature and involve Central Nervous System or Cardiovascular System manifestations.

Pregnancy Category: Pregnancy Category B

In the rat model, there was no evidence of harm to the fetus at subcutaneous dose of up to 50 mg/kg lidocaine (300 mg/m^2 on a body surface area basis). In the rabbit model, there was no evidence of harm to the fetus at a dose of 5 mg/kg (60 mg/m^2 on a body surface area basis).

Mechanism of Action:

According to the product label, lidocaine stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses, thereby effecting local anesthetic action.

Pharmacokinetics:

Lidocaine is absorbed following topical administration to mucous membranes. Its rate and extent of absorption depends on the concentration and total dose administered, the specific site of application, and duration of exposure. The rate of absorption of local anesthetic agents following topical intratracheal application occurs more rapidly. Lidocaine is well-absorbed from the gastrointestinal tract but little intact drug may appear in the circulation due to biotransformation in the liver. Lidocaine crosses the blood-brain and placental barriers, presumably by passive diffusion. (b) (4)

Lidocaine is rapidly metabolized by the liver and both metabolites (90% of lidocaine administered) and unchanged drug (10% of lidocaine administered) are excreted by the kidneys. The pharmacological/toxicological actions of its metabolites are considered less potent than those of lidocaine.

In studies of lidocaine metabolism with intravenous bolus injection, the elimination of half-life is typically 1.5 to 2.0 hours. The half-life may be prolonged two-fold or more in patients with liver dysfunction.

(b) (4)

Product Distribution:

The following product distribution report for domestic use is taken from the most recent Annual Report-46 (5/12/11) for Xylocaine® 2% Jelly. It covers the period from 3/12/10 to 3/11/11 as shown below:

1.13.11 Distribution Data (Xylocaine® (lidocaine HCl) 2% Jelly topical solution)

Domestic				
NDC #	Product Code	Strength	Size	No. of Vials Distributed
APP 63323-479-30, AZ 0186-0330-01	470930	2%	30 mL	(b) (4)
APP 63323-479-05, AZ 0186-0330-36	470905	2%	5 mL	

[1] For reference purposes, the NDC number for APP and AstraZeneca (AZ) are provided for the corresponding domestic formulation.

Reviewer's comment: *No distribution data was provided for foreign use of* Xylocaine® 2% Jelly.

Summary of Viscosity Data Provided in the DB1 Consult

In this consult, the viscosity results of various tested products were provided by Sagent as shown below:

(b) (4)

Discussion

Lidocaine is a local anesthetic which has been extensively used by the parenteral route. Due to a short life following parenteral injection, topical or transdermal delivery of the drug was considered optimal alternate to achieve sustained analgesic effects. For local action of topical anesthetics, such as for lidocaine, (b) (4) can be used to obtain the formulation in the application site for a longer time and achieve the sustained effect of the drug. For topical use, higher localized concentration of the drug at the site of application but lower or negligible systemic drug levels may result in fewer or no adverse events. When rats were exposed to (b) (4) of variable viscosity in dietary concentrations ranging up to 20-30% for durations of 90-120 days had little evidence of adverse effects other than growth retardation at the higher doses.[5]

Based on the review of literature information and viscosity data provided by the sponsor, there is no evidence that the viscosity reported for this product would pose any clinically significant problems. It should be noted that this product is intended for application to a mucous membrane (urethra) or to facilitate lubrication of an endotracheal tube for insertion to a mucous membrane environment. The only clinically limiting factor of the viscosity would be the ease of application of the product. Given the (b) (4) (b) (4) of currently marketed lidocaine jellies for these indications, there is no evidence that the viscosity reported for this product would have any meaningful impact on the ease of administration of the proposed product for any of the approved indications.

(b) (4)

1. (b) (4)

[5] Kajal Ghosal et. al. *Der Pharmacia Sinica*, 2011, 2 (2): 152-168

(b) (4)

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/s/

CAROL Y KIM
04/30/2012

JOHN R PETERS
04/30/2012

Medical Consultation
Lidocaine Hydrochloride Topical Jelly, 2%

Re:	Labeling Review Branch Request for Consultation on Safety of Lidocaine Syringe submitted in ANDA 201094 by Sagent Pharmaceuticals, Inc.
RLD:	Xylocaine® (lidocaine HCl) 2% Jelly; NDA 008816 approved 3/12/1953; Oak Pharmaceuticals, Inc.
To:	Thuyanh Vu Labeling Reviewer Labeling Review Branch (HFD-613), Office of Generic Drugs
Reviewer:	John R Peters, M.D. Director, Division of Clinical Review (DCR), Office of Generic Drugs
Drug Class:	Local Anesthetics, Topical (6040400)
Chemical Name:	acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)-, monohydrochloride
Date Received:	April 16, 2011
Review Completion Date:	April 18, 2012

Recommendations: We do not find any significant clinical safety issue with the syringe applicator for the Lidocaine Hydrochloride Jelly, 2% proposed by Sagent Pharmaceuticals in ANDA 201094.

Sagent Proposal:

BACKGROUND

The Reference Listed Drug Product (RLD), Xylocaine® (lidocaine HCl) 2% Jelly, 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). The RLD is supplied as follows:

1) NDC 0186-0330-01 30 mL aluminum tube Box of 1, including a detachable applicator cone and a key for expressing the contents.

2) NDC 0186-0330-36 5 mL plastic [redacted] Box of 10

Per the RLD labeling approved on 7/23/04, the detachable applicator cone is used only for the specific indication of surface anesthesia of the male or female adult urethra. The currently marketed products generally utilize a detachable cone for application and a key for expressing the contents of an aluminum tube containing the jelly.

Sagent proposes to market the jelly in prefilled 6 mL and 11 mL [redacted] syringes in sterile blister packs, in boxes of 10. Sagent's product is not packaged with a plastic cone, and so the Labeling Review Branch has requested clinical input as to the safety of this proposal. The Request for Consultation from the Labeling Review Branch finalized in DARRTS on 4/17/2012 stated:

> The RLD is Abraxis' Xylocaine 2% Jelly (NDA 08816). The RLD is currently marketed in a 30 mL aluminum tube (with a detachable applicator cone and a key for expressing the contents) and a 5 mL plastic tube. In the past, the RLD was also marketed in 10 mL polypropylene and 20 mL polypropylene syringe. IMS (ANDA) currently markets single-use 5 mL, 10 mL and 20 mL lidocaine hydrochloride Jelly packaged in glass vials. IMS provides Uro-Jet vial injectors to use with the glass vials.
>
> Sagent proposes to market the jelly in prefilled 6 mL and 11 mL [redacted] syringes. Sagent's product is not packaged with a plastic cone. [redacted]

DARRTS lists the following therapeutic equivalents (AT) for Lidocaine Jelly 2%:

NDA-008816	OAK	Approved	03/12/1953
ANDA	**Sponsor**	**Status**	**Status Date**
201094	SAGENT INC	Pending	12/23/2009
040837	HI-TECH	Approved	03/23/2011
040433	AKORN I	Approved	02/12/2003
[redacted]			
086283	IMS	Approved	08/07/1979
081318	TEVA	Approved	04/29/1993
080429	POLYMEDICA	Approved	04/11/1974

[1] NDA 008816 Supplement 34 Review of Chemistry, Manufacturing and Controls by Ping Jiang-Baucom finalized in DARRTS on 4/30/10.

Reviewer's Comment: *In this group ANDA 086283 (IMS, approved 8/7/1979) is marketed in glass syringes with a syringe style injector with a cone tip that is similar to the tip of the syringe proposed by Sagent. According to the IMS website:*[2]

LIDOCAINE HCl JELLY, USP, 2% (Preservative Free)

- Preservative Free
- Complete line of prefilled syringe: 5 mL, 10 mL, 20 mL
- Conical, Rounded syringe tip
- Dual lubricant / anesthetic action
- Variety of sizes provides cost savings by reducing product waste
- Sterile packaging eliminates need for presterilization of syringe or tip

(b) (4)

[redacted]

In comparison to this the Sagent syringe is a prefilled 6 mL and 11 mL (b) (4) [redacted] *These two application methods (IMS and Sagent) are very similar.*

Label:

The most recent RLD label was approved on 7/23/2004. There is no Black Box warning.

Indications: 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) (4)

[redacted]

Mechanism of Action:

Lidocaine stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses. (b) (4) [redacted]

[2]International Medication Systems, Limited, http://www.ims-limited.com/lidocaine.htm .

(b) (4)

Warnings and Precautions:

Although there is no Black Box warning, the Warnings section of the product label does list the following (all capitals in the label): 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.

The label also notes that the product should be used with "extreme caution: in the presence of sepsis or severely traumatized mucosa in the area of application due to the risk of rapid systemic absorption.

Reviewer's Comment*: It should also be noted that the method of application to the urethra is important to the possibility of urethral damage leading to more rapid absorption. The caliber of the insertion tip and the rounded end of this tip in the proposed applicator appear to adequately address this concern.*

Pregnancy Category B

Dosage and Administration:

Surface Anesthesia of the Male Adult Urethra: 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 HCl) 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.

Surface Anesthesia of the Female Adult Urethra: 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 3–5 mL (60–100 mg of lidocaine HCl) 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.

Reviewer's Comment: *Obviously the sterilization step in these instructions would not be required for the Sagent applicator.*

[3] Catterall, WA, Mackie, K, "Local Anesthetics", Chapter 14, Goodman & Gilman's The Pharmacological Basis of Therapeutics, 11th Edition, 2006, McGraw-Hill,, Medical Publishing Division.

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.

Reviewer's Comment: *It is unclear that the Sagent product will be marketed for this use, but if so the proposed applicator should not cause a problem with application to an endotracheal tube per these instructions.*

Brief Discussion:

Urethral catheterization is a common procedure. It will be performed in the office setting prior to outpatient urethroscopy as well as very frequently in the emergency department prior to catheterization. In 2001 there were an estimated 2.2 million urethral catheterizations performed in US emergency departments alone. Urinary catheterization was found to be the fourth most painful procedure performed in the emergency department, and is significantly more painful in men than women.[4]

As early as 1884 Pease introduced the use of cocaine for anesthesia of the urethra.[5] Topical lidocaine 2% was first used in 1949 ''without untoward results and with good, rapid anesthesia.''[6] Siderias et al. performed a randomized trial of Lidocaine 2% Jelly versus Placebo (15 ml sterile water based surgical lubricant) in 2004. In this study the IMS Uro-Jet Lidocaine Jelly 2% was used. These authors do not report any complications relative to the application of the lidocaine jelly.[7]

The Uro-Jet applicator (shown above, P 2) is similar in applicator tip to that of the proposed Sagent applicator syringe. Based on examination of the sample applicator syringes submitted by the sponsor as well as review of similar currently marketed products and the literature we do not anticipate any clinical safety issues relative to the proposed applicator syringe.

Conclusions and Recommendations:

- The DCR does not find any cause for clinical concern relative to the proposed syringe applicator for Sagent's Lidocaine Hydrochloride Jelly, 2%.

(b) (4)

[redacted]

[4] Siderias, J, Guadio, F, Singer, AJ, "Comparison of Topical Anesthetics and Lubricants Prior to Urethral Catheterization in Males: A Randomized Controlled Trial", Acad Emerg Med, 2004, 11:6, Pp. 703-706.
[5] Otis FN. The hydrochlorate of cocaine in genito-urinary procedures. N Y Med J. 1884; 40:635–7.
[6] Haines JS, Grabstald H. Xylocaine: a new topical anesthetic in urology. J Urol. 1949; 62:901–2.
[7] Op Cit., "Comparison of Topical Anesthetics and Lubricants Prior to Urethral Catheterization in Males: A Randomized Controlled Trial", Acad Emerg Med, 2004, 11:6, P. 704.

References

Catterall, WA, Mackie, K, “Local Anesthetics”, Chapter 14, Goodman & Gilman’s The Pharmacological Basis of Therapeutics, 11th Edition, 2006, McGraw-Hill,, Medical Publishing Division.

Otis FN. The hydrochlorate of cocaine in genito-urinary procedures. N Y Med J. 1884; 40:635–7.

Haines JS, Grabstald H. Xylocaine: a new topical anesthetic in urology. J Urol. 1949; 62:901–2.

International Medication Systems, Limited, http://www.ims-limited.com/lidocaine.htm

Siderias, J, Guadio, F, Singer, AJ, “Comparison of Topical Anesthetics and Lubricants Prior to Urethral Catheterization in Males: A Randomized Controlled Trial”, Acad Emerg Med, 2004, 11:6, Pp. 703-706.

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/s/

BRENDA S GIERHART
04/18/2012

JOHN R PETERS
04/19/2012

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201094Orig1s000

CHEMISTRY REVIEW(S)

ANDA 201094

Lidocaine Hydrochloride Jelly USP, 2%

Sagent Pharmaceuticals, Inc.
(Formerly FARCO-PHARMA GmbH)

Mahnaz Farahani, Ph.D.

Division of Chemistry I
Review #2

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 201094

2. REVIEW #: 2

3. REVIEW DATE: March 9, 2012

4. REVIEWER: Mahnaz Farahani, Ph.D.

5. PREVIOUS DOCUMENTS:

Original submission	December 23, 2009
Acceptable for filing	December 23, 2009

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Minor amendment	11/18/2011

7. NAME & ADDRESS OF APPLICANT:

Name:	Sagent Pharmaceuticals Inc. (formerly FARCO-PHARMA GmbH)
Address:	**1901 N. Roselle Road, Suite 700** **Schaumburg, IL 60195**
Representative:	Kalpesh Shroff
Telephone:	(b) (6)
Fax	847-908-1601

8. DRUG PRODUCT NAME/CODE/TYPE:

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

9. LEGAL BASIS FOR SUBMISSION:

The basis for this submission is Xylocaine® 2% Jelly (Lidocaine Hydrochloride):

NDA number: 008816
Reference Listed Drug (RLD): Xylocaine® Jelly 2% (Lidocaine Hydrochloride)
Firm: APP Pharms
ANDA Suitability Petition Required: NO (No change in dosage form, route or active ingredient)

This submission contains information regarding a proposed Lidocaine Hydrochloride Jelly USP 2% product which has been modelled after the RLD Xylocaine® 2% Jelly by APP Pharms. The proposed product contains an active ingredient in the same concentration and dosage form as the RLD. The proposed product contains no inactive ingredients or other change in formulation from the RLD that may significantly affect absorption of the active ingredient in accordance with the provisions established in 21 CFR 314.94(a)(9)(v). The proposed product differs from the RLD only in that it [redacted] (b) (4) is packaged in a single-use syringe. The proposed labelling is identical to the RLD labelling with respect to the indications and usage as well as the dosage and administration instructions.

10. PHARMACOL. CATEGORY:

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).

11. DOSAGE FORM: Jelly

12. STRENGTH/POTENCY: 2% w/w

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: __x_Rx ___OTC

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

_____SPOTS product – Form Completed

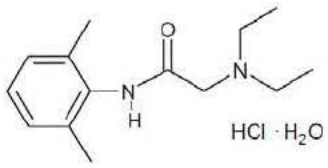
___x__Not a SPOTS product

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

Chemical Name: 2-(diethylamino)-N-(2,6-dimethylphenyl) acetamide monohydrochloride, monohydrate

2-(diethylamino)- 2',6'-acetoxylidide,
monohydrochloride, monohydrate

Molecular formula: $C_{14}H_{22}N_2O \cdot HCl \cdot H_2O$
Molecular weight: 288.8



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	Type	Holder	Item Referenced	Code[1]/ Status[2]	Date Review Completed	Comments
(b) (4)	II		(b) (4)	Adequate	4/9/12	Mahnaz Farahani, Ph.D.
	III			4		
	III			4		

[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	RECOMMENDATION	DATE	REVIEWER

Chemistry Review Data Sheet

REVIEWS			
Microbiology	Acceptable	11/18/11	Steven Donald
EES	Pending		
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Pending		
EA	Satisfactory (exclusion requested)	December 10, 2009	
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: Minor amendment

The Chemistry Review for ANDA 201094

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The ANDA is non-approvable. CMC is acceptable

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

Lidocaine hydrochloride jelly USP, 2% is available in sterile blister packs of 6 mL or 11 mL syringes, in cartons of 10.

The selection of the drug substance and excipients was based on the composition of the RLD.

The generic drug product has been prepared to match the RLD with the same matrix, hydroxypropylmethylcellulose (HPMC) but does not contain the [redacted] (b) (4) methyl- and propylparaben in order to provide physicians with a single-use preservative free option. The Lidocaine Hydrochloride Jelly 2% has been formulated to have a [redacted] (b) (4) which is in the range of the viscosity measured for the RLD and for similar products (IMS product) –

Drug substance:

The drug substance (API) is lidocaine hydrochloride USP.

CAS No.: 6108-05-0, empirical formula: $C_{14}H_{23}ClN_2O \cdot H_2O$

The concentration of the proposed product is 2% (w/w), which is equivalent to the concentration of lidocaine hydrochloride in the Reference Listed Drug Xylocaine® 2% Jelly.

Lidocaine hydrochloride does not have an optically active isomer (there is no chiral center).

It is a White crystalline powder, very soluble in water, freely soluble in alcohol, soluble in chloroform and insoluble in ether

pH of 0.5% solution: 4.0-5.5

Melting point: 74ºC to 79ºC

B. Description of How the Drug Product is Intended to be Used

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).

Maximum daily dose (MDD): 1200 mg/day (from labeling insert)

DS: (b) (4)
DP:

C. Basis for Approvability or Not-Approval Recommendation

The ANDA is non-approvable. **CMC is approvable.**

Chemistry Assessment

I. Review of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body of Data

S Drug Substance

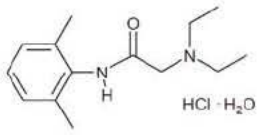
S.1 General Information: Satisfactory

S.1.1 Nomenclature: Satisfactory

Chemical Name:
2-(diethylamino)-N-(2,6-dimethylphenyl) acetamide monohydrochloride, monohydrate
2-(diethylamino)- 2',6'-acetoxylidide, monohydrochloride, monohydrate

CAS Registry No.: [6108-05-0]

S.1.2 Structure



Molecular Formula: $C_{14}H_{22}N_2O \cdot HCl \cdot H_2O$;

Molecular Weight: 288.8

S 1.3 General Properties: Satisfactory

White crystalline powder
Very soluble in water, freely soluble in alcohol, soluble in chloroform and insoluble in ether
pH of 0.5% solution: 4.0-5.5
Melting point: 74°C to 79°C
Lidocaine hydrochloride does not have an optically active isomer (there is no chiral center).

S.2 Manufacture

cc: ANDA 201094
ANDA DUP
Division File
Field Copy

Endorsements:

HFD-645 M. Farahani/3/9/12
HFD-627/J.Fan/4/2/12
HFD-617/T. Tran/4/9/12

V:\Chemistry Division I\Team 13\FIRMSAM\SAGENT\201094.R02.Lidocaine HCl.doc

TYPE OF LETTER: : ANDA is not acceptable. CMC is acceptable

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

/s/

MAHNAZ FARAHANI
04/10/2012

TRANG Q TRAN
04/10/2012

JAMES M FAN
04/10/2012

ANDA 201094

Lidocaine Hydrochloride Jelly USP, 2%

Sagent Pharmaceuticals, Inc.
(Formerly FARCO-PHARMA GmbH)

Mahnaz Farahani, Ph.D.

Division of Chemistry I
Review #1

(b) (4)

Table of Contents

(b) (4)

Chemistry Review Data Sheet

1. ANDA: 201094

2. REVIEW #: 1

3. REVIEW DATE: March 12, 2011, June 6, 2011

4. REVIEWER: Mahnaz Farahani, Ph.D.

5. PREVIOUS DOCUMENTS:
   N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original submission	December 23, 2009
Acceptable for filing	December 23, 2009

7. NAME & ADDRESS OF APPLICANT:

Name:	Sagent Pharmaceuticals Inc. (formerly FARCO-PHARMA GmbH)
Address:	**1901 N. Roselle Road, Suite 700** **Schaumburg, IL 60195**
Representative:	Thomas Moutvic
Telephone:	(b) (6)
Fax	847-908-1601

8. DRUG PRODUCT NAME/CODE/TYPE:

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

(b) (4)

9. LEGAL BASIS FOR SUBMISSION:

The basis for this submission is Xylocaine® 2% Jelly (Lidocaine Hydrochloride):

NDA number: 008816
Reference Listed Drug (RLD): Xylocaine® Jelly 2% (Lidocaine Hydrochloride)
Firm: APP Pharms
ANDA Suitability Petition Required: NO (No change in dosage form, route or active ingredient)

This submission contains information regarding a proposed Lidocaine Hydrochloride Jelly USP 2% product which has been modelled after the RLD Xylocaine® 2% Jelly by APP Pharms. The proposed product contains an active ingredient in the same concentration and dosage form as the RLD. The proposed product contains no inactive ingredients or other change in formulation from the RLD that may significantly affect absorption of the active ingredient in accordance with the provisions established in 21 CFR 314.94(a)(9)(v). The proposed product differs from the RLD only in that it (b) (4) is packaged in a single-use syringe. The proposed labelling is identical to the RLD labelling with respect to the indications and usage as well as the dosage and administration instructions.

10. PHARMACOL. CATEGORY:

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).

11. DOSAGE FORM: Jelly

12. STRENGTH/POTENCY: 2% w/w

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

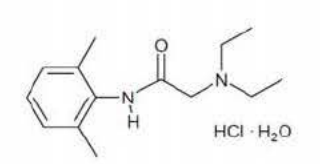
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: 2-(diethylamino)-N-(2,6-dimethylphenyl) acetamide monohydrochloride, monohydrate

Chemistry Review Data Sheet

2-(diethylamino)- 2',6'-acetoxylidide,
monohydrochloride, monohydrate

Molecular formula: $C_{14}H_{22}N_2O \cdot HCl \cdot H_2O$
Molecular weight: 288.8



(b) (4)

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	Type	Holder	Item Referenced	Code[1]/ Status[2]	Date Review Completed	Comments
(b) (4)	II		(b) (4)	Adequate	3/17/11	Mahnaz Farahani, Ph.D.
	III			4		
	III			4		

[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	RECOMMENDATION	DATE	REVIEWER

Chemistry Review Data Sheet

REVIEWS			
Microbiology	Deficient	3/7/11	Shen, Kun
EES	Pending		
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Pending		
EA	Satisfactory (exclusion requested)	December 10, 2009	
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

(b) (4)

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:

(b) (4)

The Chemistry Review for ANDA 201094

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The ANDA is non-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

Lidocaine hydrochloride jelly USP, 2% is available in sterile blister packs of 6 mL or 11 mL syringes, in cartons of 10.

The selection of the drug substance and excipients was based on the composition of the RLD.

The generic drug product has been prepared to match the RLD with the same matrix, (b) (4) methyl- and propylparaben in order to provide physicians with a single-use preservative free option. The Lidocaine Hydrochloride Jelly 2% has been formulated to have a (b) (4) (b) (4) which is in the range of the viscosity measured for the RLD and for similar products (IMS product) –

Drug substance:

The drug substance (API) is lidocaine hydrochloride USP.

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It is a White crystalline powder, very soluble in water, freely soluble in alcohol, soluble in chloroform and insoluble in ether

pH of 0.5% solution: 4.0-5.5

Melting point: 74°C to 79°C

B. Description of How the Drug Product is Intended to be Used

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).

Maximum daily dose (MDD): 1200 mg/day (from labeling insert)

DS: (b) (4)
DP:

C. Basis for Approvability or Not-Approval Recommendation

The ANDA is non-approvable.

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

/s/

MAHNAZ FARAHANI
06/09/2011

TRANG Q TRAN
06/09/2011

JAMES M FAN
06/09/2011

QUALITY DEFICIENCY - MINOR

ANDA 201094

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North VII
7620 Standish Place
Rockville, Maryland 20855

APPLICANT: Sagent Pharmaceuticals, Inc. TEL: (847) 908-1655

ATTN: Kalpesh Shroff FAX: (847) 908-1601

FROM: Trang Q. Tran FDA CONTACT PHONE: (240) 276-8518

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated December 23, 2009, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lidocaine Hydrochloride Jelly USP, 2%.

The Division of Chemistry has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached ____pages. 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**, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. Your cover letter should clearly indicate that the response is a ***QUALITY MINOR AMENDMENT / RESPONSE TO INFORMATION REQUEST*** and should appear prominently in your cover letter.

We also request that you include a copy of this communication with your response. Please direct any questions concerning this communication to the project manager identified above.

SPECIAL INSTRUCTIONS:

Effective 01-Aug-2010, the new mailing address for Abbreviated New Drug Application (ANDA) Regulatory Documents will be:

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North VII
7620 Standish Place
Rockville, Maryland 20855

All ANDA documents will only be accepted at the new mailing address listed above. For further information, please refer to the following websites prior to submitting your ANDA Regulatory documents: Office of Generic Drugs (OGD): http://www.fda.gov/cder/ogd or Federal Register: http://www.gpoaccess.gov/fr/

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 201094 APPLICANT: Sagent Pharmaceuticals, Inc.

DRUG PRODUCT: Lidocaine Hydrochloride Jelly USP, 2%

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

(b) (4)

1.

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/s/

JAMES M FAN
06/09/2011
for Paul Schwartz

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201094Orig1s000

BIOEQUIVALENCE REVIEW(S)

DIVISION OF BIOEQUIVALENCE AMENDMENT REVIEW

ANDA No.	201094
Drug Product Name	Lidocaine Hydrochloride Jelly
Strength(s)	2%
Applicant Name	Sagent Pharmaceuticals Inc (transfer of ownership from the original submitter, Farco-Pharma GMBH)
Address	1901 N. Roselle Road, Suite 700 Schaumburg, IL 60195 – 3176, U.S.A Main: 847-908-1600, Fax: 847-908-1601
Applicant's Point of Contact (Authorized US Agent)	Kalpesh Shroff Associate Director, Regulatory Affairs
Contact's Telephone Number	(847) 908-1655
Contact's Fax Number	(847) 908-1601
Original Submission Date(s)	12/23/2009
Submission Date(s) of Amendment(s) Under Review	03/23/2012 (supporting document # 13 & 14)
Reviewer	Wayne DeHaven, Ph.D.
Overall Review Result	**COMPLETE (ADEQUATE)**

REVIEW OF A STUDY AMENDMENT

1 EXECUTIVE SUMMARY

This is the review of an amendment to a waiver request for a topical jelly product.

Sagent Pharmaceuticals Inc (transfer of ownership from Farco-Pharma GMBH) has requested a waiver of *in vivo* bioequivalence (BE) study requirements under 21 CFR 320.24 (b)(6) for its test product, Lidocaine Hydrochloride Jelly, 2%. The reference listed drug (RLD) product is Xylocaine®, 2% (Lidocaine Hydrochloride) Jelly (NDA #008816) manufactured by Oak Pharmaceuticals Inc (transfer of ownership from APP Pharmaceuticals) and is a Drug Efficacy Study Implementation (DESI) effective drug product [coded "AT" in the Orange Book (OB)].[1]

The viscosity of the test product is not the same as the viscosity of the reference product. The DBI questioned whether such viscosity difference between the test and RLD could lead to different surface retention of the lidocaine, and thus potentially different local drug absorption (and safety/efficacy profile). Therefore, Sagent was asked to justify for

[1] Electronic Orange Book (Last Accessed 03.28.2012)
http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=008816&TABLE1=OB_Rx

such difference, [redacted] (b) (4) (b) (4). This deficiency comment was sent to the firm via fax on November 17, 2011.

The firm responded in the amendment dated March 23, 2012[3], and in its response, included additional comparative viscosity analysis of the approved Lidocaine Jelly drug products currently available in US market (not just the RLD). They stated that they have produced only two stability batches of this drug product and do not have any additional viscosity data for submission to the Office of Generic Drugs (OGD) from additional batches to establish a more accurate viscosity range of our product.

In addition, Sagent submitted *in vitro* drug release (dissolution) testing data comparing the test product to the RLD product, as well as other US marketed products, using the European Pharmacopoeia (EP) method [at 32°C (skin temperature) and 37°C (core body temperature)].

After review of the entire amendment, the DBI still had reservations regarding the acceptability of Sagent's proposed Lidocaine Jelly, 2%, based on the viscosity difference compared to the RLD. The DBI requested the clinical opinion of the OGD's Division of Clinical Review (DCR) to determine whether the viscosity difference would be of safety/efficacy concern.

The DCR concluded that the test product *"is within the reference product's measured viscosity range is not likely to result in different absorption or surface retention of the active lidocaine."* Based on DCR's findings and recommendation, and in addition to the firm's responses to the deficiencies, the DBI considers the viscosity difference as acceptable.

The DBI deems the test product Lidocaine Hydrochloride Jelly 2%, manufactured by Sagent Pharmaceuticals to be bioequivalent to the reference listed drug product (RLD), Xylocaine®, 2% (Lidocaine Hydrochloride Jelly) manufactured by Oak Pharmaceuticals Inc.

The application is **acceptable** with no deficiencies.

[2] DARRTS ANDA #201094 RAMSON, TERESA V 11/17/2011
[3] DARRTS ANDA #201094 Supporting Document #14 03/26/2012

2 TABLE OF CONTENTS

3 BACKGROUND

There is a single Division of Bioequivalence I (DBI) review regarding this application located in DARRTS. This review is as follows:

ANDA #201094: DEHAVEN, WAYNE I 11/10/2011 REV-BIOEQ-01(General Review): As stated in the Executive Summary, the application was considered incomplete due to concerns regarding viscosity.

4 SUBMISSION SUMMARY

4.1 Drug Product Information, PK/PD Information, and Relevant DB History

Please see ANDA #201094: DEHAVEN, WAYNE I 11/10/2011 N/A 11/10/2011 REV-BIOEQ-01(General Review) Original-1 (Not Applicable) Archive. The PK/PD information and relevant Division of Bioequivalence (DB) History has not changed since the referenced review above. Per Drugs@FDA, the label has not been updated since July 23, 2004.[4]

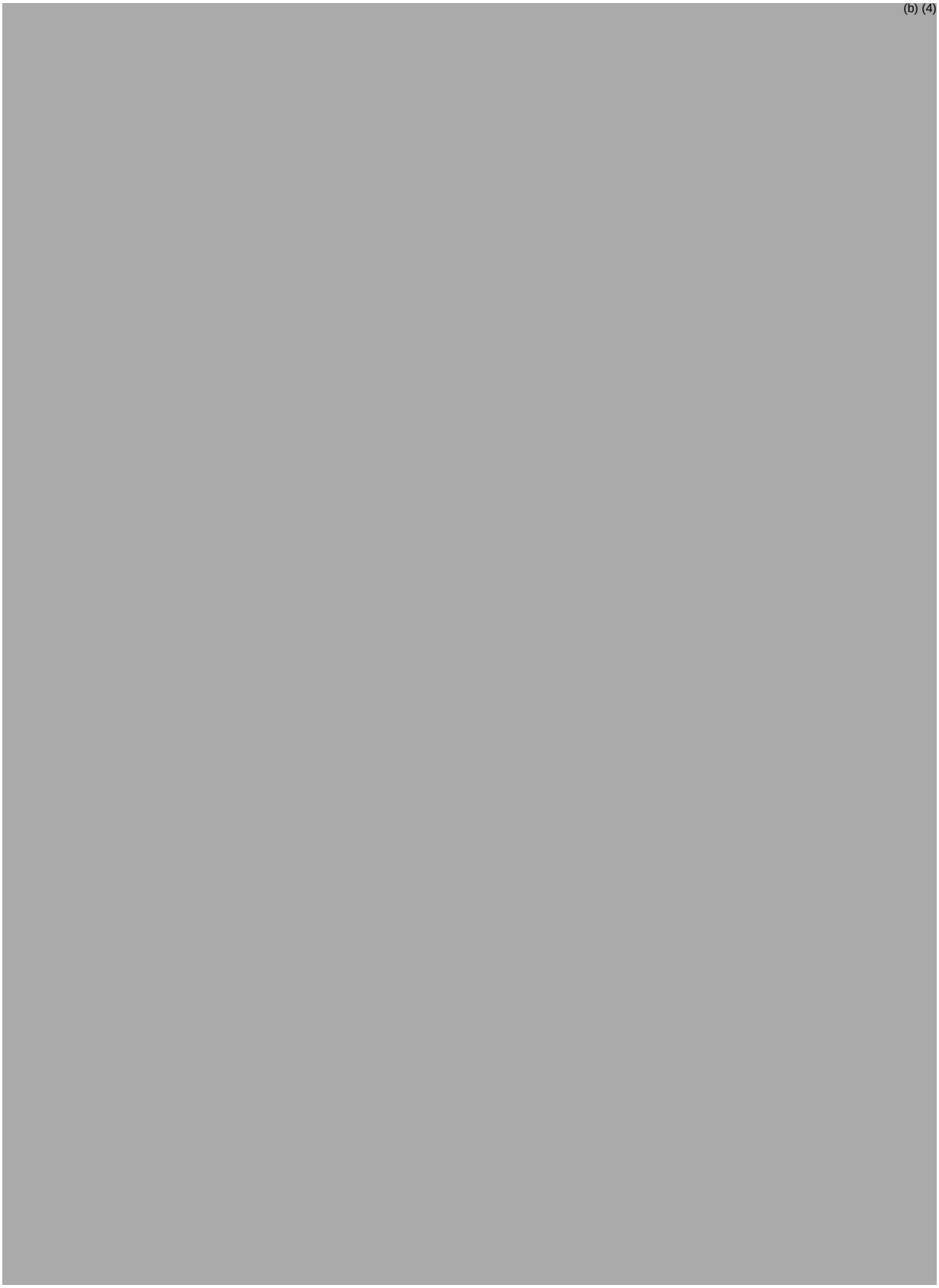
4.2 Contents of Submission

Study Types	Yes/No?	How many?
Amendment	Yes	1

[4] http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm [Keyword = Xylocaine; Last Accessed 05/02/2012]

4.3 Review of Submission

(b) (4)



This data confirms that the approved Lidocaine Jelly drug products (b) (4) (b) (4) *These approved drug products have the same indication as that listed below:*

> *"Xylocaine (lidocaine HCl) 2% Jelly 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)."*

Additionally, the package insert, under Pharmacokinetics and Metabolism, also states

> *"Lidocaine may be absorbed following topical administration to mucous membranes, its rate and extent of absorption varies depending upon concentration and total dose administered, the specific site of application and duration of exposure."*

This information suggests that the viscosity may not have a significant impact or may not lead to different surface retention of the active pharmaceutical ingredient (API), and thus different local drug absorption.

In order to demonstrate the equivalence of the subject drug product with the RLD (Rate of drug release through a membrane), we have performed in vitro dissolution testing with the approved Lidocaine Jelly drug products currently available in US market.

In vitro testing is a well accepted method used to characterize performance characteristics of a finished topical dosage form. In general, in-vitro testing can be used as an indicator of in-vivo bioavailability. Important changes in the characteristics of a drug product formula or the thermodynamic properties of the drug(s) it contains should show up as a difference in drug release.

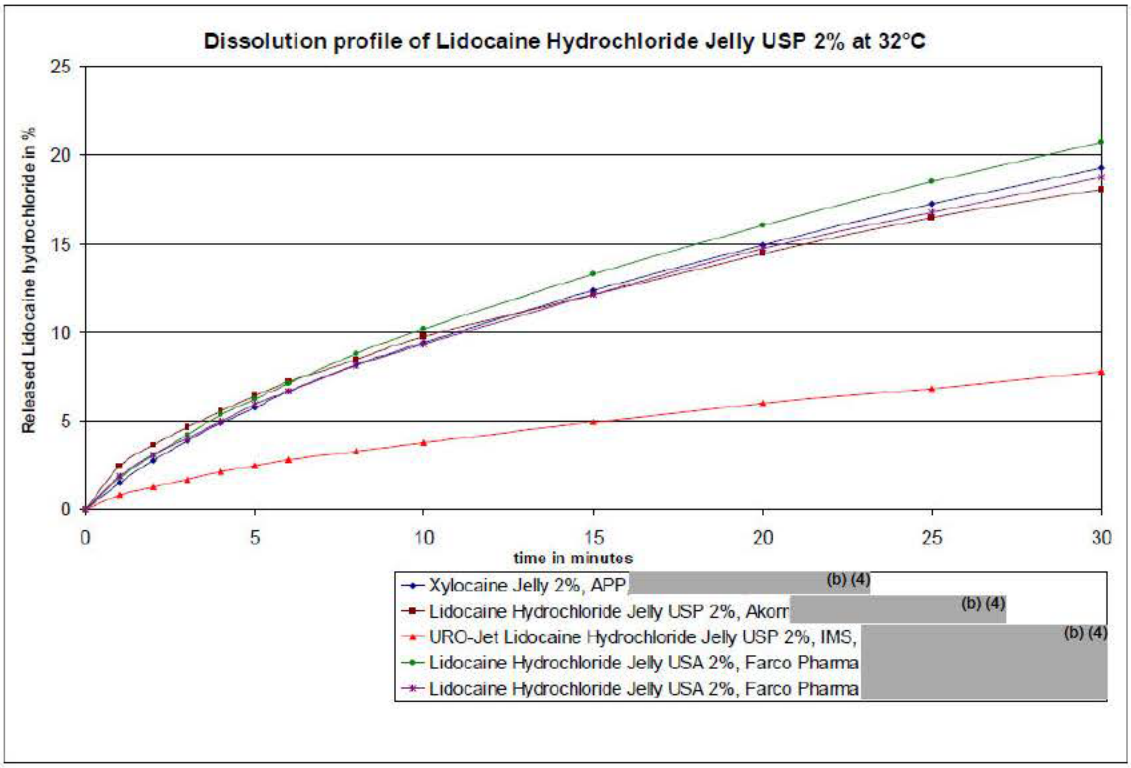
The test method used is based on the European Pharmacopoeia (EP) method 2.9.4 (DISSOLUTION TEST FOR TRANSDERMAL PATCHES). The in vitro dissolution test method is provided in section 3.2.P.3.2. This test was performed on two different temperatures as listed below covering average temperature range from tip to core of urethra.

1. *at 32°C (skin temperature)*
2. *at 37°C (Core body temperature)*

The comparative in vitro dissolution data is presented in the following table.

Dissolution profile of Lidocaine Hydrochloride Jelly USP 2%, at 32°C (skin temperature),

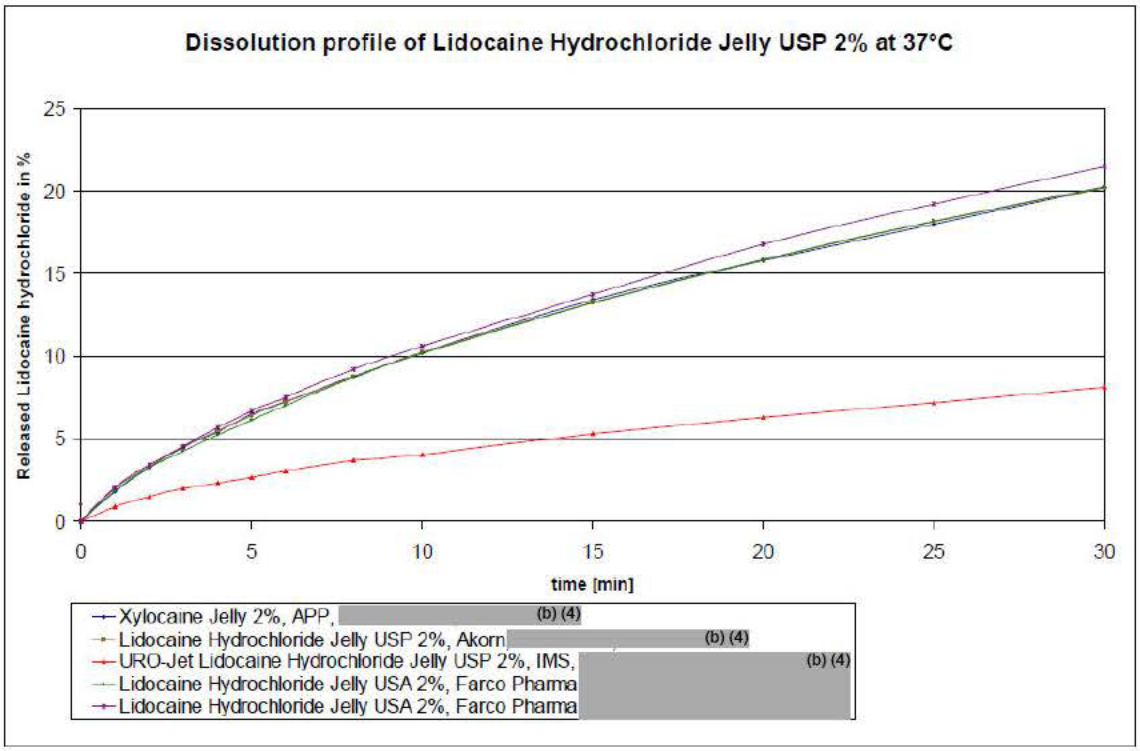
Time [min]	Lidocaine Hydrochloride concentration in the acceptor medium in %				
	Xylocaine Jelly 2%, APP, [redacted] (b) (4)	Lidocaine HCl Jelly USP2%, Akorn, [redacted] (b) (4)	URO-Jet Lidocaine HCl Jelly USP2% [redacted] (b) (4)	Lidocaine HCl Jelly USA 2%, Farco-Pharma, [redacted] (b) (4)	Lidocaine HCl Jelly USA 2%, Farco-Pharma, [redacted] (b) (4)
0	0.00	0.00	0.00	0.00	0.00
1	1.51	2.48	0.82	1.81	1.88
2	2.76	3.63	1.25	3.06	3.08
3	3.89	4.65	1.69	4.19	4.02
4	4.90	5.54	2.14	5.35	4.98
5	5.77	6.45	2.47	6.23	5.97
6	6.66	7.22	2.80	7.13	6.69
8	8.18	8.47	3.27	8.80	8.14
10	9.43	9.75	3.76	10.21	9.34
15	12.37	12.15	4.93	13.31	12.15
20	14.93	14.44	6.00	16.03	14.73
25	17.24	16.47	6.82	18.51	16.80
30	19.29	18.08	7.80	20.73	18.77
F1=		8	55	8	4
F2=		92	58	93	98



Dissolution profile of Lidocaine Hydrochloride Jelly USP 2%, at 37°C (Core body temperature)

Time [min]	*Lidocaine Hydrochloride concentration in the acceptor medium in %*				
	Xylocaine Jelly 2%, APP, (b) (4)	Lidocaine HCl Jelly USP 2%, Akorn,	URO-Jet Lidocaine HCl Jelly USP 2% (b) (4)	Lidocaine HCl Jelly USA 2%, Farco-Pharma,	Lidocaine HCl Jelly USA 2%, Farco-Pharma, (b) (4)
0	0.0	0.0	0.00	0.00	0.00
1	1.8	1.9	0.88	1.82	2.04
2	3.2	3.3	1.49	3.24	3.45
3	4.4	4.5	1.97	4.23	4.55
4	5.4	5.4	2.31	5.25	5.68
5	6.5	6.4	2.66	6.13	6.66
6	7.2	7.2	3.01	7.04	7.50
8	8.7	8.7	3.67	8.7	9.20
10	10.24	10.2	4.05	10.14	10.60

15	13.40	13.2	5.31	13.26	13.73
20	15.80	15.82	6.32	15.84	16.76
25	17.97	18.14	7.19	18.1	19.18
30	20.1	20.1	8.09	20.2	21.48
F1 =		3	55	6	2
F2=		9	58	96	100



The above in vitro dissolution test data demonstrates that viscosity does not have an impact on release of drug substance through the membrane for the drug product with similar formulation.

As it is demonstrated from the in vitro dissolution test data that viscosity does not have an impact on availability of the drug, for the drug product with similar formulation, we are of the opinion that the wide viscosity specification range given (b) (4) *for the test product, should not affect the availability of the drug product.*

(b) (4)

We would like to inform Agency that we have produced only two stability batches of this drug product and do not have any additional viscosity data for submission to the Agency from additional batches to establish a more accurate viscosity range of our product.

Reviewer's Comments:

- The proposed test product is a preservative-free formulation (see DARRTS DEHAVEN, WAYNE I 11/10/2011 REV-BIOEQ-01(General Review), packaged in a ready-to-use prefilled syringe as a single-use, sterile product. In contrast, the RLD contains (b) (4) methylparaben and propylparaben. There is an approved ANDA (#086283) which also is packaged as a single-use product (b) (4) (b) (4) The test product formulation does not need to be Q1/Q2 the same as the RLD with respect to (b) (4) The test product meets USP potency assay specification for lidocaine hydrochloride jelly of 95%.00 to 105.00%[6].

- The viscosity of the current test product is not comparable to that of the RLD product. The DBI questioned whether the viscosity difference between the test and RLD could lead to different surface retention of the lidocaine, and thus possibly different local drug absorption. Therefore, the DBI recommended Sagent justify for such difference, (b) (4) (b) (4) The DBI also recommended Sagent submit additional viscosity data from additional batches to establish a more accurate viscosity range for the test product[7].

- Sagent submitted additional comparative viscosity analysis of the approved Lidocaine Jelly drug products currently available in the US market (not just the RLD). (b) (4) (b) (4) for the RLD Xylocaine®, Sagent's test product, Akorn's generic product, and IMS' URO-JET product, respectively. Xylocaine®, Sagent's test product, and Akorn's product (b) (4) (b) (4)

- Sagent also stated that the label comment *"Lidocaine may be absorbed following topical administration to mucous membranes, its rate and extent of absorption varies depending upon concentration and total dose administered, the specific site of application and duration of exposure"* suggests *"that the viscosity may not have a significant impact or may not lead to different surface retention of the*

[5] DARRTS: ANDA 201094 REV-BIOEQ-01(General Review); Submit/Final Date 11/10/2011, Pg. 10-11
[6] USP 34-NF 29 Official Monograph, Page 3308 – 3309 (http://www.uspnf.com/uspnf/login) Last Accessed: 04/04./2012
[7] DARRTS: ANDA 201094 REV-BIOEQ-01(General Review); Submit/Final Date 11/10/2011

active pharmaceutical ingredient (API), and thus different local drug absorption."

- Lastly, Sagent submitted *in vitro* dissolution testing with the approved Lidocaine Jelly products currently available in the US market. Sagent stated that *"In vitro testing is a well accepted method used to characterize performance characteristics of a finished topical dosage form. In general, in-vitro testing can be used as an indicator of in-vivo bioavailability. Important changes in the characteristics of a drug product formula or the thermodynamic properties of the drug(s) it contains should show up as a difference in drug release."*

- The test was carried out using the European Pharmacopoeia (EP) method for transdermal patches [at 32°C (skin temperature) and 37°C (core body temperature)]. The temperature ranges were meant to mirror the average temperature range from the tip to the core of the urethra.

- Currently the DBI does not have a recommended dissolution testing method for this product and such testing has not been adequately standardized. Nonetheless, these data show that, under these testing conditions, the three products which released lidocaine similarly [Xylocaine® (RLD), Sagent's test product, and Akorn's product] (b) (4) (b) (4) (b) (4) Therefore, under these conditions, viscosity is not the rate limiting step in the lidocaine release.

Clinical Consult:

- Despite Sagent's aforementioned arguments, the DBI still had reservations accepting this viscosity difference between the test product and Xylocaine®. The DBI requested a clinical consult to determine whether the viscosity difference observed between the test and RLD products (Lidocaine Hydrochloride Jelly, 2%) should be of a safety and/or efficacy concern[8].

- The clinical review was completed April 30, 2012[9]. The Division of Clinical Review (DCR) concluded that the test product *"is within the reference product's measured viscosity range is not likely to result in different absorption or surface retention of the active lidocaine."* Further, the clinical reviewer stated *"The only clinically limiting factor of the viscosity would be the ease of application of the product. Given* (b) (4) *currently marketed lidocaine jellies for these indications, there is no evidence that the viscosity reported for*

[8] DARRTS ANDA 201094 DEHAVEN, WAYNE I 04/17/2012 FRM-CONSULT-01(General Consult Request)
[9] DARRTS ANDA 201094 KIM, CAROL Y 04/30/2012 CONSULT REV-CLINICAL-01(General Consult Review)

this product would have any meaningful impact on the ease of administration of the proposed product for any of the approved indications."

(b) (4)

(b) (4)

(b) (4)

Reviewer's Overall Comments:

- Based on the firm's arguments, as well as the meaningful insight from DCR, the DBI agrees that the difference in viscosities between Sagent's Lidocaine Jelly, 2% and the RLD, Xylocaine® is not likely to result in different absorption or surface retention of the active lidocaine.

- The firm's response is acceptable. Sagent Pharmaceuticals' waiver request of *in vivo* bioequivalence study requirements for its Lidocaine Hydrochloride Jelly, 2% [under regulations 21 CFR 320.24 (b)(6)] is **acceptable (adequate).**

(b) (4)

4.4 Deficiency Comments

None

4.5 Recommendations

Sagent Pharmaceuticals' waiver request of *in vivo* bioequivalence study requirements for its Lidocaine Hydrochloride Jelly, 2% (under regulations 21 CFR 320.24 (b)(6)) is **acceptable (adequate).**

The Division of Bioequivalence I (DBI) deems the test product Lidocaine Hydrochloride Jelly 2%, manufactured by Sagent Pharmaceuticals to be bioequivalent to the reference listed drug product (RLD), Xylocaine®, 2% (Lidocaine Hydrochloride) Jelly manufactured by Oak Pharmaceuticals Inc.

The firm should be informed of these recommendations.

4.6 Comments for Other OGD Disciplines

Discipline	Comment
N/A	--

BIOEQUIVALENCE COMMENTS TO BE COMMUNICATED TO THE FIRM

ANDA: 201094

APPLICANT: Sagent Pharmaceuticals Inc

DRUG PRODUCT: Lidocaine Hydrochloride Jelly, 2%

The Division of Bioequivalence I (DBI) has completed its review of your amendment submission dated March 23, 2012, 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 I
Office of Generic Drugs
Center for Drug Evaluation and Research

5 OUTCOME PAGE

ANDA: 201094

COMPLETED ASSIGNMENT FOR 201094 ID: 16794

Reviewer: DeHaven, Wayne **Date Completed:**

Verifier: **Date Verified:**

Division: Division of Bioequivalence

Description: Lidocaine Hydrochloride Jelly, 2% (Sagent Pharmaceuticals)

Productivity:

ID	***Letter Date***	***Productivity Category***	***Sub Category***	***Productivity***	***Subtotal***
16794	3/23/2012	Other	Study Amendment	1	1
16794	3 23/2012	Other	Study Amendment (Clinical Consult)	1	1
				Total:	2

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

/s/

WAYNE I DEHAVEN
05/10/2012

APRIL C BRADDY
05/11/2012

HOAINHON N CARAMENICO on behalf of DALE P CONNER
05/11/2012

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	201094
Drug Product Name	Lidocaine Hydrochloride Jelly
Strength(s)	2%
Applicant Name	Sagent Pharmaceuticals Inc (transfer of ownership from the original submitter, Farco-Pharma GMBH)
Address	1901 N. Roselle Road, Suite 700 Schaumburg, IL 60195 – 3176, U.S.A Main: 847-908-1600, Fax: 847-908-1601
Applicant's Point of Contact (Authorized US Agent)	Kalpesh Shroff Associate Director, Regulatory Affairs
Contact's Telephone Number	(847) 908-1655
Contact's Fax Number	(847) 908-1601
Original Submission Date(s)	12/23/2009
Submission Date(s) of Amendment(s) Under Review	N/A
Reviewer	Wayne DeHaven, Ph.D.
OVERALL REVIEW RESULT	**INCOMPLETE (INADEQUATE)**

1 EXECUTIVE SUMMARY

This is a review of a waiver request for a topical jelly product. The application is **incomplete (inadequate)** at this time.

Sagent Pharmaceuticals Inc (transfer of ownership from Farco-Pharma GMBH) has requested a waiver of *in vivo* bioequivalence (BE) study requirements under 21 CFR 320.24 (b)(6) for its test product, Lidocaine Hydrochloride Jelly, 2%. The reference listed drug (RLD) is Xylocaine®, 2% (NDA #008816) manufactured by Oak Pharmaceuticals Inc (transfer of ownership from APP Pharmaceuticals) and is a Drug Efficacy Study Implementation (DESI) effective drug product (coded "AT" in the Orange Book (OB)).

The proposed test product is a preservative-free formulation, packaged in a ready-to-use prefilled syringe as a single-use, sterile product. In contrast, the RLD contains (b) (4) methylparaben and propylparaben. There is an approved ANDA (#086283) which also is packaged as a single-use product, (b) (4) The test product formulation does not need to be Q1/Q2 the same as the RLD, (b) (4) is acceptable. The test product meets USP specification for lidocaine hydrochloride jelly of 95%.00 to 105.00%.

However, the viscosity of the test product is not similar to the viscosity of the reference product. The significant viscosity difference between the test and RLD could lead to different surface retention of the lidocaine, and thus different local drug absorption. Therefore, Sagent should justify for such difference, (b) (4) (b) (4). Sagent should submit additional viscosity data from additional batches to establish a more accurate viscosity range of the test product. Until Sagent's submits this additional information, the application is considered **incomplete (inadequate)**.

The firm should be informed of the DBE's recommendation.

Brief DBE History:

The DBE has previously accepted two ANDAs for this drug product under section 21 CFR 320.24 (b)(6). Those are **i) Hi Tech's** ANDA 040837 [see DARRTS for ANDA 040837 in SEO, SHIRLEY K 08/20/2007 N/A 08/20/2007 REV-BIOEQ-01(General Review) Original-1 Archive] and **ii) Akorn's** ANDA 040433 (see v:\firmsam\akorn\ltrs&rev\40433sta.801).

2 TABLE OF CONTENTS

3 SUBMISSION SUMMARY

3.1 Drug Product Information[1]

Test Product	Lidocaine Hydrochloride Jelly, 2%
Reference Product	Xylocaine® Jelly (Lidocaine Hydrochloride), 2%
RLD Manufacturer	Oak Pharmaceuticals Inc (transfer of ownership from APP Pharmaceuticals)
NDA No.	008816
RLD Approval Date	03/12/1953
TE Code	AT
Indication[2]	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).

3.2 PK/PD Information[2,3]

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.
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 cm2 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
Tmax	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

[1] http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=008816&TABLE1=OB_Rx
[2] http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=33063#nlm34067-9
[3] http://www.clinicalpharmacology-ip.com/Forms/search.aspx?s=xylocaine

3.3 OGD Recommendations for Drug Product

Number of studies recommended: N/A – Waiver Request

Bioequivalence based on:

See additional attachments (section 4.3) for meeting minutes in which it was determined that BE studies can be waived for this product based on 21 CFR 320.24 (b) (6). For more details, also see the following reviews:

1. v:\firmsam\akorn\ltrs&rev\40433sta.801
2. v:\firmsam\akorn\ltrs&rev\40433w.401
3. DARRTS ANDA #040837 SEO, SHIRLEY K 08/20/2007 N/A 08/20/2007 REV-BIOEQ-01(General Review) Original-1 Archive

Note: The regulation **21 CFR 320.24(b)(6)** should be cited for the determination of bioequivalence when reviewing pre-62 topical jelly, since topical products that are not solutions cannot be "waived" under the current regulations through 21 CFR 320.22(b)(3).

Source of most recent recommendations: See Additional Attachments Section of this review

Summary of OGD or DBE History:

According to the Orange Book (OB), the following are approved for Lidocaine Jelly, 2%:

Appl No	TE Code	RLD	Proprietary Name	Applicant	Approval date
A040433	**AT**	No	LIDOCAINE HCl	AKORN	2/12/2003
A040837	**AT**	No	LIDOCAINE HCl	HI TECH PHARMA	3/23/2011
A086283	**AT**	No	LIDOCAINE HCl	INTL MEDICATION	Prior to 01/01/1982
N008816	**AT**	Yes	XYLOCAINE	OAK PHARMS	Prior to 01/01/1982
A080429	**AT**	No	ANESTACON	POLYMEDICA	Prior to 01/01/1982
A081318	**AT**	No	LIDOCAINE HCl	TEVA PHARMS	4/29/1993

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…"

The following ANDAs are listed in DARRTS:

ANDA #	Submitter	Current Status	Status Date
040433	AKORN INC	Approved	2/12/2003
086283	INTERNATIONAL MED SYST	Approved	8/7/1979
081318	TEVA	Approved	4/29/1993
201094	SAGENT	Pending	12/23/2009
040837	HI TECH	Approved	3/23/2011
080429	POLYMEDICA	Approved	4/11/1974
[redacted]	[redacted]	[redacted]	[redacted] (b) (4)

Highlighted yellow is the current product under review

3.4 Contents of Submission

Study Types	Yes/No?	How many?
Waiver requests	Yes	1

3.5 Formulation

Location in appendix	See Section 4.1
If a tablet, is the RLD scored?	N/A
If a tablet, is the test product biobatch scored	N/A
Is the formulation acceptable?	**FORMULATION ACCEPTABLE**
If not acceptable, why?	N/A

3.6 Waiver Request(s)

Strengths for which waiver is requested	2%
Proportional to strength tested in vivo?	N/A
Is dissolution acceptable?	N/A
Waivers granted?	**NOT GRANTED**
If not then why?	pending justification that the viscosity difference between the test product and RLD do not affect safety or efficacy of the product

3.7 Deficiency Comment

The significant viscosity difference between the test and RLD could lead to different surface retention of the lidocaine, and thus different local drug absorption. Therefore, Sagent should justify for such difference, (b) (4) (b) (4). Sagent should submit additional viscosity data from additional batches to establish a more accurate viscosity range of the test product.

3.8 Recommendations

Sagent Pharmaceuticals' waiver request of *in vivo* bioequivalence study requirements for its Lidocaine Hydrochloride Jelly, 2% (under regulations 21 CFR 320.24 (b)(6)) is **incomplete (inadequate)** at this time pending the submission of justification for the viscosity difference between the test product and the RLD.

3.9 Comments for Other OGD Disciplines

Discipline	Comment
N/A	--

4 APPENDIX

4.1 Formulation Data

FIRM:		RLD (Oak Pharm)	(b) (4)	Sagent (transferred from Farco-Pharma GMBH)
ANDA/NDA #:		8816		201094
Volume of Packaged Product:		5mL and 30mL		6mL and 11mL
Packaging:		tube + Applicator		Single use syringe
		mg/mL		quantity per 100 grams
Lidocaine HCl	Active	2% (20mg/mL)		2.0g (20mg/mL)[4]
Methylparaben	Inactive	(b) (4)		
Propylparaben	Inactive			
Hydroxypropylmethylcellulose	Inactive			(b) (4)
Carboxymethylcellulose Sodium	Inactive			
Purified Water	Inactive			QS[6]
Hydrochloric Acid	Inactive			
Sodium Hydroxide	Inactive			ADJUST PH[7]
Sodium Chloride	Inactive			[8]
Benzalkonium Chloride	Inactive			

(b) (4)

[redacted] (b) (4)

According to the firm, *the pivotal ANDA batches (lot #s 526049 and 722069) [redacted] were manufactured* [redacted] (b) (4) The USP monograph for lidocaine hydrochloride jelly states that the product *contains not less than 95.0% and not more than 105.0% of the labeled amount of lidocaine hydrochloride.* [redacted] (b) (4)).

Re

1. [redacted] (b) (4)
2. [redacted]
3. [redacted]
4. The test product formulation does not need to be Q1/Q2 the same as the RLD, and [redacted] (b) (4) is acceptable.

4.2 Comparative Physicochemical Data

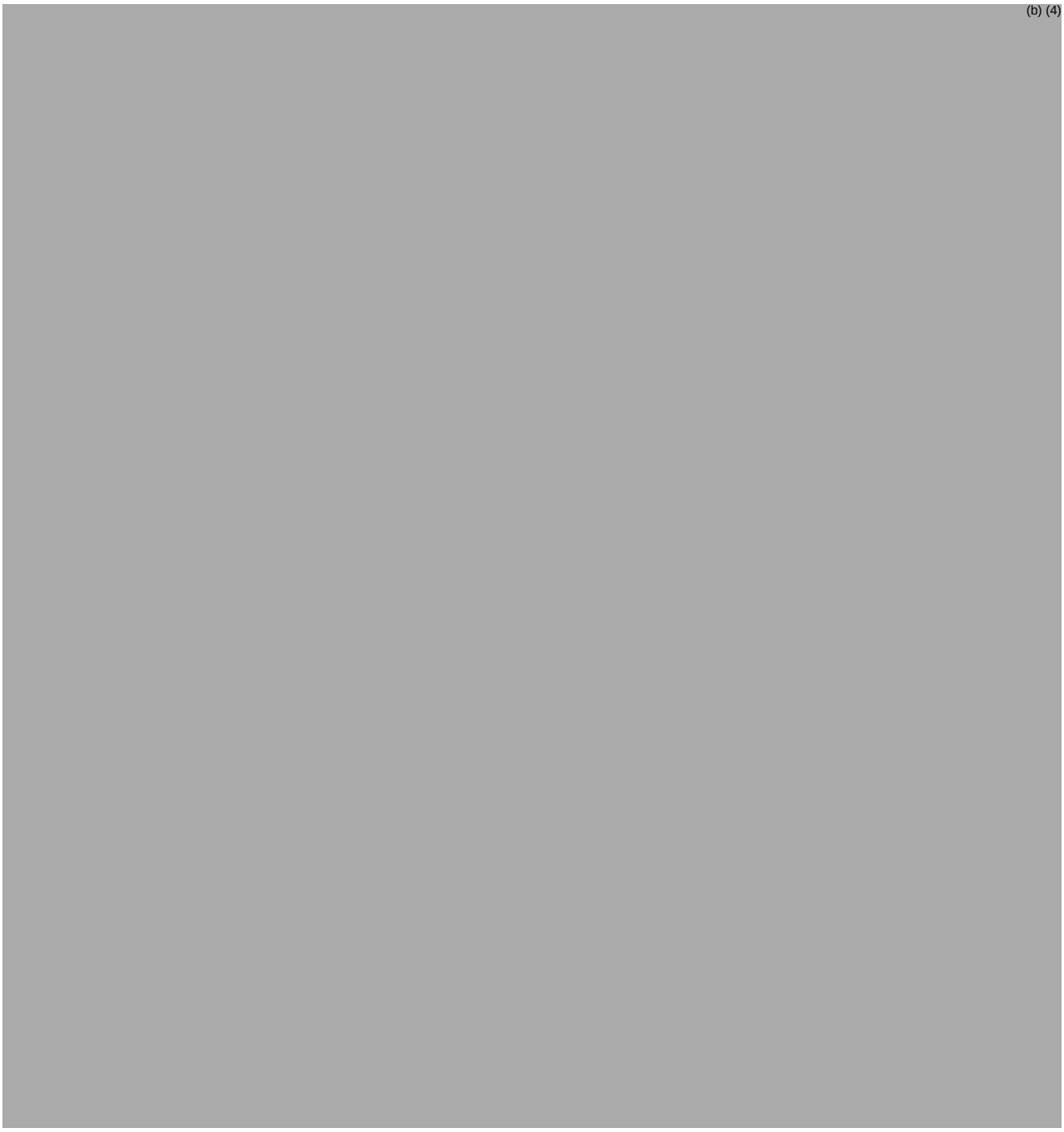
1. According to the submission, Sagent's objective was to develop a generic Lidocaine Hydrochloride Jelly 2% drug product based on the Xylocaine® 2% Jelly manufactured by Oak Pharmaceuticals. Sagent considered the following items:

- The proposed product should receive an AT rating upon FDA approval to Xylocaine® 2% Jelly approved by FDA in 1953
- The proposed product should be a preservative free formulation, packaged in a ready-to-use prefilled syringe as a single-use, sterile product that is easy to open and convenient to use
- The proposed product should comply with the requirements of USP monograph for "LIDOCAINE HYDROCHLORIDE JELLY 2%"

2. Based on these considerations, the following product quality characteristics were defined for the test product:

- lidocaine hydrochloride assay: 1.90 – 2.10 % (per USP monograph)
- (b) (4)
- pH: 6 – 7 (per USP monograph)
- sterile (per USP)

(b) (4)


(b) (4)

4.3 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. Omeprazole – pH at the end of the dosing interval. The data in the published literature does not support that the pH returns to baseline at the end of the dosing interval. The measured GI pH range is all over the board and is not consistent. The problem that the pH will be within a certain range to degrade the coating and lead to the product being ineffective is theroretical and not supported by data. Would it be useful to have dissolution data at an intermediate pH 3.5? It is unlikely that this would provide the Agency with useful data, since the GI pH of individual patients is so variable.

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 nonsolution 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 methylparaben. 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 DEFICIENCY TO BE PROVIDED TO THE APPLICANT

ANDA: 201094

APPLICANT: Sagent Pharmaceuticals Inc

DRUG PRODUCT: Lidocaine Hydrochloride Jelly, 2%

The Division of Bioequivalence (DBE) has completed its review and the following deficiency has been identified:

You have provided the following physicochemical property data for the test and reference products:

(b) (4)

[redacted]

Based on the above data, the DBE is concerned that the significant viscosity difference between the test and RLD as shown here could lead to different surface retention of the active pharmaceutical ingredient (API), and thus different local drug absorption. Therefore, please justify for such difference, as well as the wide viscosity specification range given [redacted] (b) (4) for the test product. Please submit additional viscosity data from additional batches to establish a more accurate viscosity range of your product.

Sincerely yours,

{See appended electronic signature page}

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

4.4 Outcome Page

ANDA: 201094

COMPLETED ASSIGNMENT FOR 201094 ID: 15079

Reviewer: DeHaven, Wayne **Date Completed:**

Verifier: **Date Verified:**

Division: Division of Bioequivalence

Description: Lidocaine Hydrochloride Jelly, 2% (Sagent Pharmaceuticals)

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
15079	12/23/2009	Other	Waiver Topical	1	1
				Bean Total:	1

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

/s/

WAYNE I DEHAVEN
11/09/2011

SHRINIWAS G NERURKAR
11/09/2011

HOAINHON N CARAMENICO on behalf of DALE P CONNER
11/10/2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201094Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

October 11, 2011

ANDA: 201094

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

Review Number: 3

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
09/30/2011	09/30/2011	N/A	10/06/2011

Submission History : N/A

Submit Date(s)	Microbiology Review #	Review Date(s)
12/23/2009	1	12/10/2011
05/27/2011	2	06/09/2011

Applicant/Sponsor
Name: Sagent Pharmaceuticals, Inc.
Address: 1901 N. Roselle Rd, Suite 100, Schaumburg, IL 60195
Representative: Dr. Tom Moutvic
Telephone: (b) (6)

Name of Reviewer: Steven P. Donald, M.S.

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

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: ANDA Amendment

2. SUBMISSION PROVIDES FOR: Response to Agency's deficiency letter dated August 17, 2011.

3. MANUFACTURING SITE: Klosterfrau Berlin GmbH, (b) (4) (b) (4) Germany

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Lidocaine HCl is a jelly packaged in 6 ml and 11 ml syringes at a concentration of 2% and applied topically. Single use container.

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

6. PHARMACOLOGICAL CATEGORY: anesthetic 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. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: Electronic submission. This topical drug product is labeled as sterile and will be Micro/OGD reviewed.

filename: 201094a2.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -
The 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) [redacted].

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/Steven P. Donald, M.S.
Microbiology Team Leader/CDR Paul Dexter, M.S.

C. CC Block
cc: Field Copy

Product Quality Microbiology Assessment

The subject amendment provides responses to the microbiology deficiencies conveyed to the applicant in the agency's letter of August 17, 2011. The original deficiencies are italicized.

1. *We acknowledge the BI data provided for the validation and requalification studies for* (b) (4) *of the product filled syringes. However, population confirmation study results are not provided. Please indicate the confirmed population of the BIs used in these studies.*

Response:

The applicant notes that they have made changes to their procedure to include BI population confirmation, as well as D-value as these were not part of the procedure, previously. Data are presented for the determination of D-value and population of (b) (4) The confirmed population of this sample is (b) (4) the confirmed D-value is reported to be 1.7 minutes. The original validation studies used 5 different BI lots, two of which were manufactured by (b) (4) and one of which matches the lot for the information provided in this deficiency. Data for the other lots have not been provided.

Note to Reviewer:

The drug product is a sterile, topical anesthetic. The applicant has committed to determining the population of all BIs used in validation studies in the future. All other aspects of the sterilization validation were acceptable. Due to the nature and application of this drug product, this reviewer believes the insufficient BI information represents little if any risk and will not request the population confirmation population information for the other BIs.

Acceptable

2. *Regarding production and validation* (b) (4) *parameters, while the acceptance criteria appear to indicate identical parameters in the sterilization cycles for both production and validation, it is implied that* (b) (4) *Please clarify and identify any differences between validation and production conditions for sterilization of the subject drug product. Please provide the rationale for any difference, as necessary.*

Response:

The applicant confirms that the manufacture of the drug product uses the identical program cycle (b) (4) for routine production and the validation study. A table is presented comparing all parameters of the cycle and each parameter is identical for both production and validation. The applicant explains the apparent discrepancy which

led to the deficiency and explains the use of the (b) (4) to this reviewers satisfaction.

Acceptable

B Comment:

Please consider revising the Jelly Bioburden acceptance limit (10^4 cfu/g) to more closely reflect the actual bioburden determined from screen batches (b) (4)

Response:

The applicant acknowledges the Agency's suggestion and confirms that they will take this recommendation into consideration based on data generated from the commercial lots and will revise the Jelly Bioburden acceptance limit, as necessary.

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

/s/

STEVEN P DONALD
11/07/2011

KUN SHEN
11/07/2011

PAUL L DEXTER
11/18/2011

Product Quality Microbiology Review

June 09, 2011

ANDA: 201094

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

Review Number: 2

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
05/27/2011	05/27/2011	N/A	06/06/2011

Submission History : N/A

Submit Date(s)	Microbiology Review #	Review Date(s)
12/23/2009	1	12/10/2011

Applicant/Sponsor
Name: Sagent Pharmaceuticals, Inc.
Address: 1901 N. Roselle Rd, Suite 100, Schaumburg, IL 60195
Representative: Dr. Tom Moutvic
Telephone: (b) (6)

Name of Reviewer: Steven P. Donald, M.S.

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

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: ANDA Amendment

2. SUBMISSION PROVIDES FOR: Response to Agency's deficiency letter dated March 7, 2011.

3. MANUFACTURING SITE: Klosterfrau Berlin GmbH, (b) (4) Berlin, Germany

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Lidocaine HCl is a jelly packaged in 6 ml and 11 ml syringes at a concentration of 2% and applied topically. Single use container.

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

6. PHARMACOLOGICAL CATEGORY: anesthetic 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. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: Electronic submission. This topical drug product is labeled as sterile and will be Micro/OGD reviewed.

filename: 201094a1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -

The submission is **not recommended** for approval on the basis of sterility assurance. Specific comments and deficiencies are provided in the "Product Quality Microbiology Assessment" and "List of Microbiology Deficiencies and Comments" sections.

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)

[redacted]

B. Brief Description of Microbiology Deficiencies –incomplete validation information for terminally sterilized loads.

C. Assessment of Risk Due to Microbiology Deficiencies -

The safety risk associated with the microbiology deficiencies is considered low.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block

Microbiologist/Steven P. Donald, M.S.
Microbiology Team Leader/CDR Paul Dexter, M.S.

C. CC Block

cc: Field Copy

Product Quality Microbiology Assessment

The subject amendment provides responses to the microbiology deficiencies conveyed to the applicant in the agency's letter of March 7, 2011. The original deficiencies are italicized.

1. *Regarding container/closure integrity: the data provided for the container/closure integrity test does not adequately assess the integrity of the subject container/closure. The description of the bacterial challenge* (b) (4) *Please provide test results to adequately validate container closure integrity, including the method of detection and the sensitivity of the testing method.* (b) (4) (b) (4) (b) (4) *Please confirm the container closure system used during validation is the same or equivalent as that used for the commercial batch of the drug. If any component is different from the subject drug product container/closure, please provide justification or rationale for its use.*

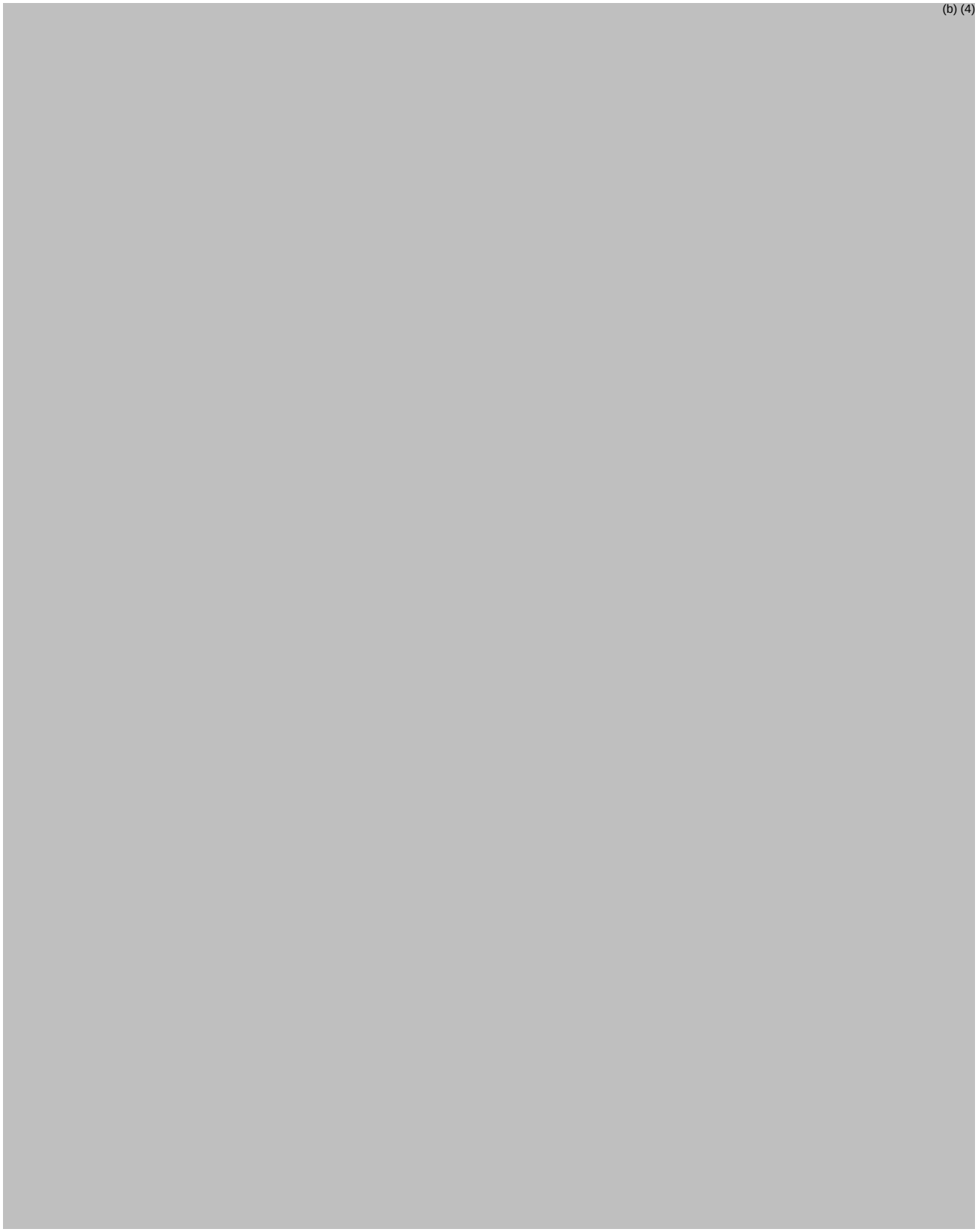
Response:

A test protocol is provided: Testing Protocol Container Closure Integrity Studies with Medium –Filled 6 ml and 11 ml Plastic Syringes. The protocol is dated 11 May 2010. Testing is performed by (b) (4) subcontractor.

The testing protocol describes the use of two syringe types, the 6 ml and 11 ml, which are both used as the container/closure of the subject drug product. (b) (4) (b) (4)

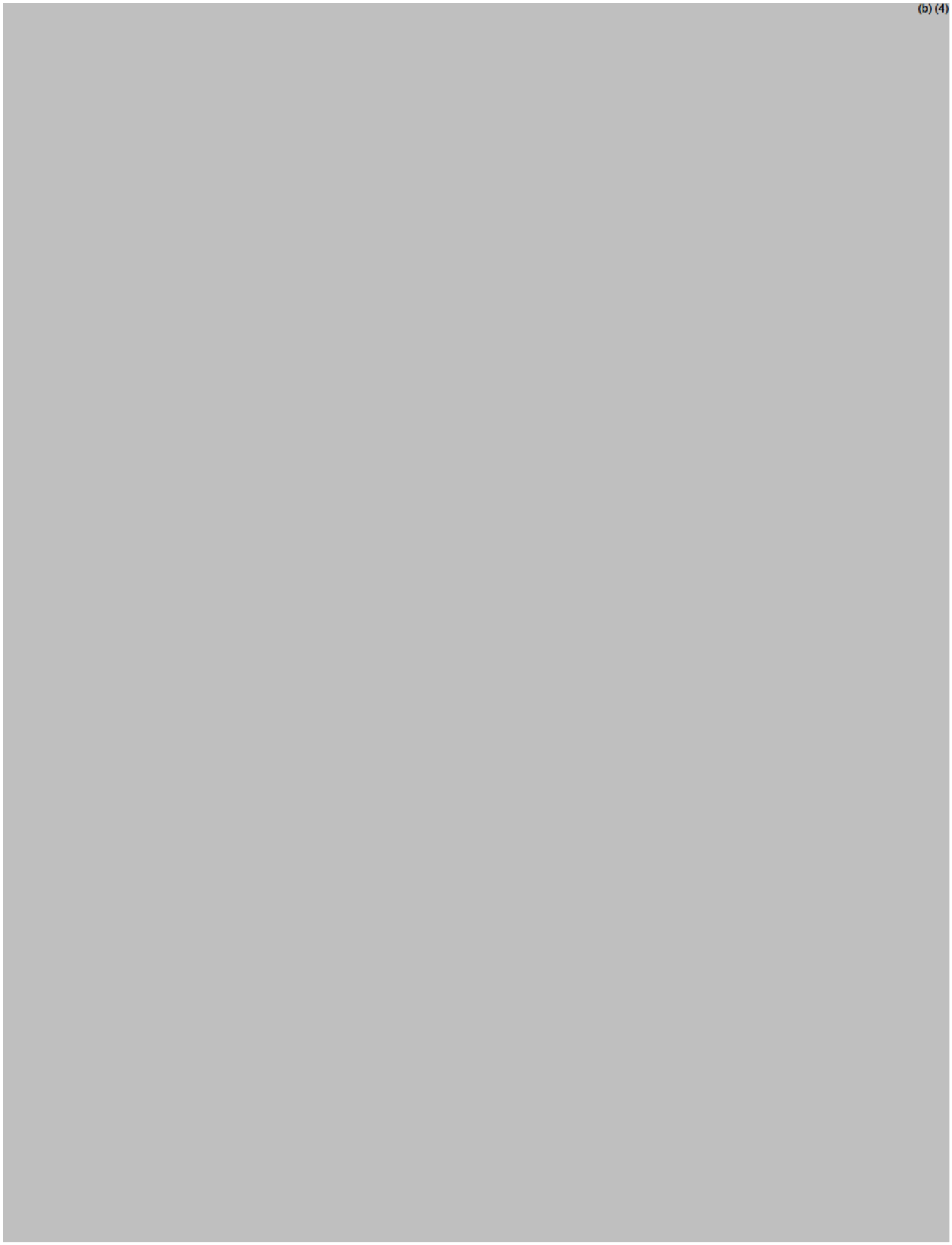
Acceptance Criteria:

(b) (4)



Acceptable

(b) (4)



Acceptable

4. *Please provide bioburden alert and action levels for purified water.*

Response:

There are no formal alert and action levels in place for purified water, but the acceptance level of 10 cfu/mL for the release of the purified water is 10 fold lower than the requirement for purified water in the USP or EP (100 cfu/mL). Additionally, the purified water (b) (4)

Acceptable

5. *Regarding validation of the* (b) (4) *in the* (b) (4)

   a. (b) (4)

(b) (4)

Response:

(b) (4)

Original Validation Runs of 6 ml Syringe: 2008
A total of 32 (b) (4) are used in the runs, just as in the RQ data that was previously reported. A total of 25 (b) (4) are used at identified

locations. None of the (b) (4) exhibited growth. (b) (4)

Run #1:
Run # 433078S2

Maximum F_0 value attained: 30.9 min
Minimum F_0 value attained: 23.5 min

Run #2:
Run # 433078S4

Maximum F_0 value attained: 30.2 min
Minimum F_0 value attained: 22.9 min

Run #3:
Run # 434078S2

Maximum F_0 value attained: 29.3 min
Minimum F_0 value attained: 23.7 min

Original Validation Runs of 11 ml Syringe: 2008
A total of 25 (b) (4) are used in the runs. A total of 25 (b) (4) are used at identified locations. None of the (b) (4) exhibited growth. (b) (4)

Run #1:
Run # 838067S2

Maximum F_0 value attained: 28.7 min
Minimum F_0 value attained: 21.0 min

Run #2:
Run # 839067S1

Maximum F_0 value attained: 27.1 min
Minimum F_0 value attained: 21.6 min

Run #3:
Run # 839067S2

Maximum F_0 value attained: 28.0 min
Minimum F_0 value attained: 21.6 min

Note to Reviewer:
The applicant states that the treated BIs did not exhibit growth, however no other information is provided. Since the applicant has provided BI information for the RQ runs in the 05/27/2011 submission as well as in the response to deficiencies for the 05/27/2011 submission, this reviewer will not provide comment.

Note to Reviewer:
The applicant does not state that the acceptance criteria were met, however the graphical data submitted with this response to deficiencies (b) (4)

Acceptable

b. *For the biological indicator studies previously provided, as well as for future studies, please additionally include both positive and negative growth control results as well as a confirmation of the BI population and expiry.*

Response:
The applicant states that positive controls, (b) (4) and negative controls, media only, were a part of each validation run. All growth control results are provided for the 6 ml and 11 ml validation runs. Dates correspond to the RQ studies presented in original submission.

Data provided for two runs (6 ml syringe RQ studies):
Sterilization date: 09/06/2009
Test date: 26/06/2009
No growth (0/30) in tested positions
Positive controls = positive
Negative controls = negative

Data provided for one run (11ml syringe RQ studies):
Sterilization date: 09/04/2009
Test date: 29/04/2009
No growth (0/30) in tested positions
Positive controls = positive

Negative controls = negative

BI manufacture data provided for all BIs (Original validation and RQ data) are presented [redacted (b) (4)]

Population confirmation data are not presented for any of the BIs used in the PQ or RQ studies. The applicant states that they commit to determining the D-value of BIs used and compare to the manufacturer's D-values.

Comment:
We acknowledge the BI data provided for the validation and requalification studies for [redacted (b) (4)] of the product filled syringes. However, population confirmation study results are not provided. Please indicate the confirmed population of the BIs used in these studies.

Not Acceptable

c. *Please indicate the approach to validation, whether it is based on fixed, minimum and maximum loads or worst-case* [redacted (b) (4)]

Response:
The approach of the validation is based on fixed maximum loads. A maximum sterilization load contains [redacted (b) (4)] packages of 10 syringes for each presentation. Only fixed maximum loads (= fixed loads) are used in the production.

Note to Reviewer: The number of packages in the 6 ml or 11 ml syringe loads is the same [redacted (b) (4)]

Acceptable

d. Please confirm both production and validation sterilization parameters and also state acceptance criteria for both.

Response:
The applicant provides the following Table (copied from submission) listing the acceptance criteria:

(b) (4)

Note to Reviewer:
The applicant states that (b) (4) They also state this does not apply to production. It is not clear to this reviewer if the cycles are identical or not.

Comment:
While the acceptance criteria appear to indicate identical parameters in the sterilization cycles for both production and validation, it is implied that (b) (4)

Please clarify and identify any differences between validation and production conditions for sterilization of the subject drug product. Please provide the rationale for any difference, as necessary.

Not Acceptable

e. (b) (4)

Response:

(b) (4)

Acceptable

f. (b) (4)

is demonstrated with the BI in this arrangement within the load. Alternatively, (b) (4)

Please compare the D-value of the BI in the bulk drug solution with the manufacturer's D-value for the same BI in the surrogate solution, as necessary, and how its use presents a worst-case situation under the chosen validation conditions. Please provide additional studies as necessary.

Response:

(b) (4)

(b) (4) The applicant commits to perform D-value determinations in the future. (b) (4) No growth is noted in test samples. Positive growth controls are performed and are acceptable.

Acceptable

3. LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS:

ANDA: 201094 APPLICANT: Sagent Pharmaceuticals, Inc

DRUG PRODUCT: Lidocaine Hydrochloride Jelly 2%

A. Microbiology Deficiencies:

1. We acknowledge the BI data provided for the validation and requalification studies for [redacted] (b) (4) of the product filled syringes. However, population confirmation study results are not provided. Please indicate the confirmed population of the BIs used in these studies.

2. Regarding production and validation [redacted] (b) (4) parameters, while the acceptance criteria appear to indicate identical parameters in the sterilization cycles for both production and validation, it is implied that [redacted] (b) (4) Please clarify and identify any differences between validation and production conditions for sterilization of the subject drug product. Please provide the rationale for any difference, as necessary.

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

Please consider revising the Jelly Bioburden acceptance limit (10^4 cfu/g) to more closely reflect the actual bioburden determined from screen batches [redacted] (b) (4)

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}

CDR Paul Dexter, M.S.
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/

STEVEN P DONALD
07/15/2011

KUN SHEN
07/29/2011

PAUL L DEXTER
08/15/2011

Product Quality Microbiology Review

December 10, 2010

ANDA: 201094

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

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
12/23/2009	12/23/2009	N/A	12/09/2010

Submission History : N/A

Applicant/Sponsor
Name: Sagent Pharmaceuticals, Inc.
Address: 1901 N. Roselle Rd, Suite 100, Schaumburg, IL 60195
Representative: Dr. Tom Moutvic
Telephone: (b) (6)

Name of Reviewer: Steven P. Donald, M.S.

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 a sterile drug product

3. MANUFACTURING SITE: Klosterfrau Berlin GmbH, (b) (4) (b) (4) Germany

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Lidocaine HCl is a jelly packaged in 6 ml and 11 ml syringes at a concentration of 2% and applied topically. Single use container.

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

6. PHARMACOLOGICAL CATEGORY: anesthetic 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. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: Electronic submission. This topical drug product is labeled as sterile and will be Micro/OGD reviewed.

filename: 201094.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -

The submission is **not recommended** for approval on the basis of sterility assurance. Specific comments and deficiencies are provided in the "Product Quality Microbiology Assessment" and "List of Microbiology Deficiencies and Comments" sections.

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 –

Incomplete container/closure integrity testing; specifications for environmental monitoring of purified water or bulk drug solution not provided; incomplete validation information for (b) (4)

C. Assessment of Risk Due to Microbiology Deficiencies -

The safety risk associated with the microbiology deficiencies is considered moderate.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block

Microbiologist/Steven P. Donald, M.S.
Microbiology Team Leader/CDR Paul Dexter, M.S.

C. CC Block

cc: Field Copy

Product Quality Microbiology Assessment

1. REVIEW OF COMMON TECHNICAL DOCUMENT-QUALITY (CTD-Q) MODULE 3.2: BODY OF DATA

P DRUG PRODUCT

P.1 Description of the Composition of the Drug Product

- Description of drug product –

LIDOCAINE HYDROCHLORIDE JELLY (lidocaine HCl) 2% is a sterile aqueous product that contains a local anesthetic agent and is administered topically. Lidocaine hydrochloride jelly USP, 2% is available in sterile blister packs of 6 mL or 11 mL syringes, in cartons of 10.

Acceptable

- Drug product composition – (manuf-process-and-cntrols.pdf, pg.15)

(b) (4)

The commercial batch size is approximately two times the pilot batch size which is approximately (b) (4)

Acceptable

- Description of container closure system –
  - (b) (4)

- (b) (4)

(b) (4)

Acceptable

P.2 Pharmaceutical Development

P.2.5 Microbiological Attributes

(b) (4)

(b) (4)

(b) (4)

Not Acceptable

- Preservative Effectiveness – Unlike the RLD which is provided in a multidose container, preservatives are not used for this single use product.

P.3 Manufacture

P.3.1 Manufacturers

Klosterfrau Berlin **GmbH**

(b) (4)

(b) (4) Germany

P.3.3 (b) (4)

(b) (4)

Acceptable

R REGIONAL INFORMATION

(b) (4)

Acceptable

R.2 Comparability Protocol: None

2. REVIEW OF COMMON TECHNICAL DOCUMENT-QUALITY (CTD-Q) MODULE 1

A. PACKAGE INSERT

LIDOCAINE HYDROCHLORIDE JELLY (lidocaine HCl) 2% is a sterile aqueous product that contains a local anesthetic agent and is administered topically. Storage Conditions: Store at controlled room temperature 15-30°C (59-86°F).

Acceptable

3. LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS:

ANDA: 201094 APPLICANT: Sagent Pharmaceuticals, Inc

DRUG PRODUCT: Lidocaine Hydrochloride Jelly 2%

Microbiology Deficiencies:

1. Regarding container/closure integrity: the data provided for the container/closure integrity test does not adequately assess the integrity of the subject container/closure. (b) (4) Please provide test results to adequately validate container closure integrity, including the method of detection and the sensitivity of the testing method. If employing a bacterial immersion assay, please utilize a bacterial challenge with a cfu/ml suspension greater than previously provided. Please describe test conditions such as the utilization of vacuum or pressure during the challenge phase of the assay. Please also describe the method of detection for bacterial ingress. Also, please include positive and negative growth controls as well as a breach positive control to demonstrate test sensitivity and describe how it was prepared. Please confirm the container closure system used during validation is the same or equivalent as that used for the commercial batch of the drug. If any component is different from the subject drug product container/closure, please provide justification or rationale for its use.
2. (b) (4)
3. Please describe the requalification program for the production (b) (4) used for (b) (4) of the subject drug product.
4. Please provide bioburden alert and action levels for purified water.

5. Regarding validation of the [redacted] loads in the [redacted]:

   a. Please provide data and summaries from the initial qualification of the autoclave that demonstrate the uniformity, reproducibility and conformance to specifications of the production sterilization cycle. Please include results from a minimum of three consecutive successful cycles for each type of [redacted] load. Please include in these studies, [redacted] as well as bioindicator all studies. Please provide the dates of all studies as well as the location of all BIs and [redacted] for all validation runs.

   b. For the biological indicator studies previously provided, as well as for future studies, please additionally include both positive and negative growth control results as well as a confirmation of the BI population and expiry.

   c. Please indicate the approach to validation, whether it is based on fixed, minimum and maximum loads or worst-case [redacted]

   d. Please confirm both production and validation sterilization parameters and also state acceptance criteria for both.

   e. [redacted]

   f. [redacted]

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}

CDR Paul Dexter, M.S.
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/

STEVEN P DONALD
02/14/2011

KUN SHEN
02/15/2011

NEAL J SWEENEY
03/03/2011

PAUL L DEXTER
03/04/2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201094Orig1s000

PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name Reconsideration Review

Date:	January 06, 2014
Reviewer:	Morgan Walker, PharmD, MBA Division of Medication Error Prevention and Analysis
Team Leader:	Lubna Merchant, PharmD, M.S Division of Medication Error Prevention and Analysis
Acting Director:	Kellie Taylor, PharmD, MPH Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Glydo (Lidocaine HCl) Jelly, USP 2%
Application Type/Number:	ANDA 201094
Applicant/sponsor:	Sagent Pharmaceuticals Inc.
OSE RCM #:	2013-1608

*** This document contains proprietary and confidential information that should not be released to the public.***

1 INTRODUCTION

This review responds to a July 3, 2013 request from Sagent Pharmaceuticals to reconsider the proprietary name Glydo for ANDA 201094. DMEPA found the proposed proprietary name unacceptable in OSE review #2010-1607 dated April 13, 2011. DMEPA objected to the proposed name Glydo based on similarities of the name to the currently marketed product, Glyco (Glycolic Acid) Gel pursuant to 21 CFR 201.10(5) which states "The labeling of a drug may be misleading by reason of designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient."

2 METHODS AND MATERIALS REVIEWED

DMEPA used Failure Mode and Effects Analysis (FMEA) in our review of the request for reconsideration from Sagent. We also considered our initial review of the proposed proprietary name, Glydo (OSE review #2010-1607 dated April 13, 2011), in which we expressed concerns regarding possible confusion with the currently marketed product, Glyco.

3 RESULT AND DISCUSSION

In the request for reconsideration of the proprietary name, Glydo, the Applicant submitted their research for Glyco-the product identified as having a potential for confusion with Glydo. This Section summarizes our assessment of the information provided by the Applicant in support of a reconsideration of the proposed proprietary name.

3.1 LOOK-ALIKE AND SOUND-ALIKE SIMILARITY OF GLYDO AND GLYCO

In our initial review of the proposed name, Glydo, we objected to the proposed name Glydo based on similarities of the name to the currently marketed product, Glyco (Glycolic Acid) Gel pursuant to 21 CFR 201.10(5) which states "The labeling of a drug may be misleading by reason of designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient."

In the request for reconsideration, Sagent Pharmaceuticals noted that the IMS Health sales data for the period of 2008 to present for any branded product named Glyco found no sales for this product. They also stated that further research into the product Glyco revealed that it is manufactured by Topix pharmaceuticals and is available as following products:
Fluoro/Gly Pads™ - 30 Pads (textured)
Glyco Treatment Pads™- 30 Pads (textured)
Fluoro/Gly Gel Peel™ – 4 FL. OZ.

They state that the single product name "Glyco" is not a registered trademark and is no longer in use by Topix; and both Glyco and Gly are currently being used as a shortened descriptive abbreviation for Glycolic Acid in their lengthened new branded product names. A prescription filling error for Glydo confused for Glyco could not be filled, since Glyco does not exist as a stand-alone branded product. They also note that Glydo has a different product profile (e.g., different dosage form, different strength, different concentration, different dosing, different indication etc). Additionally Glyco products could only be sold to a licensed physician (dermatologist) via their sales representatives due to the high concentration of glycolic acid, for use in chemical peels within their office settings.

We acknowledge that the listing in databases use descriptors ("Treatment Pads") along with the root name Glyco, but post-marketing experience with other products that use a multi-segment proprietary name shows that prescribers write and order products with only the first name of the product and omit the rest of the product name[1]. In this case, it is conceivable that clinicians prescribe and order Glyco Treatment Pads™- 30 Pads as "Glyco", thus creating potential for confusion with Glydo. We also disagree with their rationale that the differences in product characteristics would mitigate confusion. Our root cause analysis of postmarketing errors involving highly similar name pairs shows that the differences in product characteristics are not sufficient to mitigate confusion.

However, we agree with the Applicant that the different settings of use of these two products and the limited availability of Glyco may minimize confusion. Glydo will be a prescription only product applied via the trans-urethral route of administration intended to be used for procedures versus Glyco products will be used by a licensed dermatologist for use in chemical peels within their office settings. Additionally, as stated by the Applicant, Glyco products could only be acquired by a licensed dermatologist via a sales representative from Topix. A pharmacy or pharmacist will not be able to acquire these products as they are sold only to physicians directly from Topix.

At the time of our previous review of the name Glydo, it was unknown to us that Glyco could only be acquired directly from the manufacturer by a licensed dermatologist via a sales representative thereby limiting its availability. Therefore, this information was not considered in our initial decision to find the name unacceptable.

Based on the information submitted by the Applicant stating that Glyco has a unique distribution system and limited availability, we are in agreement with the Applicant that the risk of confusion between Glydo with Glyco is minimal.

4 CONCLUSIONS

Based on our analysis of the information submitted by the Applicant in support of the name reconsideration request for Gyldo, we conclude that the name Glyco does not pose a risk for confusion with Glyco. We have reconsidered our original decision and now have no objections to the use of the proposed proprietary name, Glydo, for this product.

4.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Glydo. Based on the information you submitted stating that Glyco has a unique distribution system and limited availability, we agree that the risk of confusion between Glydo with Glyco is minimal. Therefore, we conclude Glydo is conditionally acceptable.

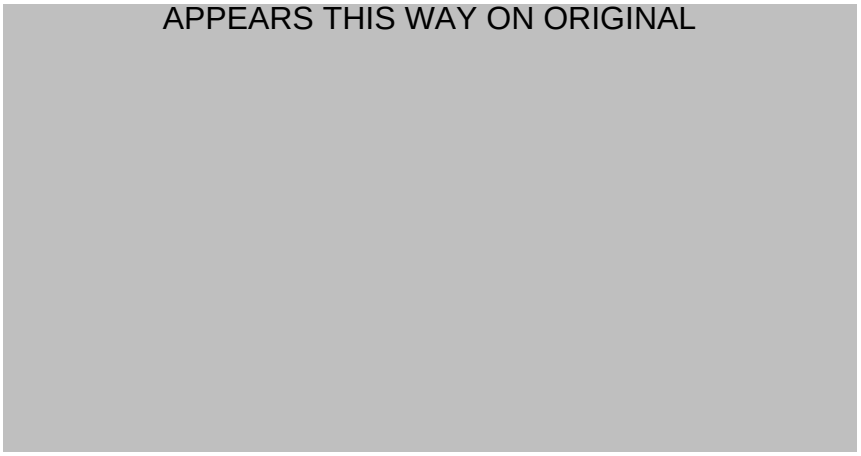
If any of the proposed product characteristics as stated in your July 3, 2013 submission are altered, the proprietary name should be resubmitted for review.

If you have further questions or need clarifications, please contact Vaishali Jarral, OSE project manager, at 301-796-4248.

[1] Lesar TS. Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8): 579-587.

5 REFERENCES

OSE Review #2010-1607, Proprietary Name Review for Glydo, Miller, Cathy A. April 13, 2011.



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/s/

LUBNA A MERCHANT
01/06/2014

KELLIE A TAYLOR
01/06/2014

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	April 26, 2013
Reviewer(s):	Vicky Borders-Hemphill, Pharm.D. Division of Medication Error Prevention and Analysis
Team Leader:	Jamie Wilkins Parker, Pharm.D. Division of Medication Error Prevention and Analysis
Deputy Director:	Kellie Taylor, Pharm.D., MPH Division of Medication Error Prevention and Analysis
Division Director:	Carol Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name(s)	(b) (4) (Lidocaine Hydrochloride) Jelly USP, 2%
Strength(s):	2% (20 mg/ mL)
Application Type/Number:	ANDA 201094
Applicant/Sponsor:	Sagent Pharmaceuticals, Inc.
OSE RCM #:	2012-2281

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/s/

BRENDA V BORDERS-HEMPHILL
04/29/2013

JAMIE C WILKINS PARKER
04/29/2013

CAROL A HOLQUIST on behalf of KELLIE A TAYLOR
05/01/2013
Signing on behalf of Kellie Taylor

CAROL A HOLQUIST
05/01/2013

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management
Division of Medication Error Prevention and Analysis

Proprietary Name Review

Date:	August 27, 2012
Reviewer:	Vicky Borders-Hemphill, Pharm.D. Division of Medication Error Prevention and Analysis
Acting Team Leader:	Jamie Wilkins Parker, Pharm.D. Division of Medication Error Prevention and Analysis
Drug Name and Strength:	(b) (4) (Lidocaine Hydrochloride) Jelly USP, 2%
Application Type/Number:	ANDA 201094
Applicant/Sponsor:	Sagent Pharmaceuticals Inc.
OSE RCM #:	2012-1739

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BRENDA V BORDERS-HEMPHILL
08/28/2012

JAMIE C WILKINS PARKER
08/28/2012

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name, Label, Labeling and Packaging Review--ANDA

Date:	June 18, 2012
Reviewer(s):	Sarah Brody, Pharm.D., Safety Evaluator Division of Medication Error Prevention and Analysis
Team Leader	Zachary Oleszczuk, Pharm.D., Team Leader Division of Medication Error Prevention and Analysis
Deputy Director	Kellie Taylor, Pharm.D., MPH, Deputy Director Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, RPh, Division Director Division of Medication Error Prevention and Analysis
Drug Name(s) and Strength(s):	(b) (4) (Lidocaine Hydrochloride) Jelly USP, 2%
Application Type/Number:	ANDA 201094
Applicant/sponsor:	Sagent Pharmaceuticals, Inc.
OSE RCM #:	2011-2657 and 2011-2659

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SARAH J BRODY
06/18/2012

ZACHARY A OLESZCZUK
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KELLIE A TAYLOR
06/19/2012

CAROL A HOLQUIST
06/19/2012

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	April 13, 2011
Application Type/Number:	ANDA 201094
Through:	Zachary Oleszczuk, PharmD Team Leader Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Cathy A. Miller, MPH, BSN, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Glydo (Lidocaine Hydrochloride) Jelly 2%
Applicant:	Sagent Pharmaceuticals, Inc.
OSE RCM #:	2010-1607

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CONTENTS

EXECUTIVE SUMMARY

This review summarizes DMEPA's evaluation of the proposed name, Glydo, for Lidocaine Hydrochloride Jelly, 2%, Sagent Pharmaceuticals, Inc.

Our proprietary name risk assessment of the proposed name, Glydo, did not identify concerns from a promotional perspective that would render the name unacceptable. However, DMEPA found the proposed name unacceptable because it is similar to the currently marketed product, Glyco (Glycolic Acid) Gel, pursuant to 21 CFR 201.10(5) which states "designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient."

1 BACKGROUND

1.1 INTRODUCTION

This review provides a response to a July 14, 2010 request from the Applicant, Sagent Pharmaceuticals, Inc., for an assessment of the proposed proprietary name, Glydo for ANDA 201094. The Division of Medication Error Prevention and Analysis (DMEPA) assesses a proposed proprietary name regarding its potential for name confusion with other proprietary or established drug names in the usual practice settings. The Division of Drug Marketing, Advertising, and Communications (DDMAC) provides an assessment on the promotional nature of the name.

1.2 REGULATORY HISTORY

The Reference Listed Drug (RLD) for this application is Xylocaine (Lidocaine Hydrochloride, USP) 2% Jelly (NDA 008816) approved on March 12, 1953. The application for Glydo (ANDA 201094) is still under review by the Office of Generic Drugs (OGD) at this time.

1.3 PRODUCT INFORMATION

Glydo (Lidocaine Hydrochloride) Jelly, USP, 2% is a sterile aqueous product that contains a local anesthetic agent and is administered topically. Glydo 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). When Glydo is used concomitantly with other products containing Lidocaine Hydrochloride, the total dose contributed by all formulations must be kept in mind.

The dosage varies of Glydo 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.

For dosage and administration for surface anesthesia of the male adult urethra, approximately 15 mL (300 mg) of Glydo should be slowly instilled 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 can be instilled for adequate anesthesia. Prior to sound or cystoscopy, a penile clamp should be applied for five to ten minutes to obtain adequate anesthesia. A total Glydo dose of 30 mL is usually required to fill and dilate the male urethra. Prior to catherization, smaller volumes of Glydo (5 mL to 10 mL) are usually adequate for lubrication.

For dosage and administration for surface anesthesia of the female adult urethra, approximately 3 mL to 5 mL (60 mg to 100 mg) of Glydo should be slowly instilled 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.

For dosage and administration for lubrication for endotracheal intubation, a moderate amount of Glydo should be applied 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. The maximum dose of Glydo is 30 mL (600 mg) in any twelve hour period.

Glydo is supplied in prefilled syringes containing 6 mL and 11 mL, in 10-count blister packs. Glydo should be stored at controlled room temperatures of 20°C to 25°C (68°F to 77°F).

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by DMEPA when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary name, Glydo.

2.1 SEARCH CRITERIA

For this review, particular consideration was given [redacted] (b) (4) with the letter, G, when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.[1,2]

To identify drug names that may look similar to Glydo, the DMEPA safety evaluators also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (five letters), upstrokes (three, capital letter G and lower case letters l and d), down strokes (one, lower case y), cross strokes (none), and dotted (none). Additionally, several letters in Glydo may be vulnerable to ambiguity when scripted. See Appendix B. As a result, the DMEPA safety evaluators also consider these alternate appearances when identifying drug names that may look similar to Glydo.

When searching to identify potential names that may sound similar to Glydo, the DMEPA safety evaluators search for names with similar number of syllables (two), stresses (GLY-do or gly-DO), and placement of vowel and consonant sounds. (See Appendix B) Additionally, the DMEPA safety evaluators consider that pronunciation of parts of the name can vary such as “Gly-” may be mispronounced as “Glee-.” Moreover, names are often mispronounced or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following inpatient medication order, outpatient and verbal prescription was communicated during the FDA prescription studies. See Appendix C for samples and results.

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[1] Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at http://www.ismp.org/Tools/confuseddrugnames.pdf

[2] Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings. After the Safety Evaluator has determined the overall risk associated with proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

3 RESULTS

The following sections describe DMEPA's findings from the database searches, CDER Expert Panel Discussion and FDA prescription studies.

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of 11 names as having some similarity to the name Glydo.

Seven of the names were thought to look like Glydo. These include: Cyclo, Glyate, Glycate, Glyceva[***], Glycine, Glyanse and Glyset. Four of the names were thought to look and sound like Glydo. These include: Gliadel, Glyco, Glyco A and Zydone.

Additionally, the DMEPA safety evaluators did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of March 4, 2011.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA (See Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to Glydo.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

The (b) (4) analysis concluded that "the proposed proprietary name, Glydo, has minimal, if any, risk of name confusion that could result in a medication error. Thus, the overall results of the (b) (4) research favorably support the use of Glydo as a proposed proprietary name for Farco-Pharma's proposed product for the 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."

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The proposed name risk assessment submitted by the Applicant, (b) (4) identified five names thought to have some potential for confusion with the name Glydo although they did not specify whether the similarity was orthographic, phonetic or both.

Three of the names (Gliadel, Glynase and Glyset) were also identified by DMEPA during the database searches. The remaining two names (Glyburide and Glycolax) were thought to have some orthographic similarities to the proposed name, Glydo, and therefore, included in the Safety Evaluator Risk Assessment.

3.4 PRESCRIPTION ANALYSIS STUDIES

A total of 30 practitioners responded to the studies however, none of the practitioner responses overlapped with existing marketed products. Twenty of the participants interpreted the name correctly as "Glydo" with correct interpretation occurring in the both the inpatient and outpatient studies. The remainder of the written responses misinterpreted the drug name. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.5 COMMENTS FROM THE DIVISION OF ANESTHESIA AND ANALGESIA PRODUCTS (DAAP)

In response to the email sent to the Division of Anesthesia and Analgesia Products (DAAP) on March 4, 2011, DAAP responded that their only concern was that the drug name, Glydo, "makes it sound like a lubricant, which is in part how it is used but it is unsure whether the ANDA will carry that indication."

On March 22, 2011, DMEPA asked DAAP for clarification on their comments at which time they deferred to OGD sine they were reviewing the ANDA.

3.6 COMMENTS FROM THE OFFICE OF GENERIC DRUGS (OGD)

In response to an email sent to OGD from DMEPA on November 4, 2010, OGD responded on November 12, 2010 that the name 'Glydo' is similar to 'Glyco' and could be mistaken for a product to treat hypoglycemia.

On March 22, 2011, DMEPA asked OGD for clarification on their comments, citing that although we found a currently marketed product named 'Glyco', the product was a topical gel and not a drug used to treat hyperglycemia. We also asked for their input on whether the indication of 'lubricant' would be approved for this ANDA. In their March 23, 2011 email response, they clarified that their comment was aimed toward the prefix being related to hyperglycemia and they did not identify a drug product by the name of Glyco used to treat hyperglycemia. They further stated that OGD would be approving the ANDA with the 'lubricant' indication.

3.7 SAFETY EVALUATOR SEARCH

Independent searches by the primary Safety Evaluator resulted in the identification of thirteen (n=13) additional names which was thought to look similar to Glydo and represent a potential source of drug name confusion. These names include: Atripla, Atryn, Cydec, Cylert, Galzin, Glytone, (b) (4) Onxol, (b) (4) Sprycel, Syeda***, Symlin and (b) (4)

Thus, we evaluated a total of 26 names: 13 names identified by the primary safety evaluator, two names identified by the external name study and 11 names identified in Section 3.1.

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4 DISCUSSION

This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this Application and considered it accordingly.

4.1 PROMOTIONAL ASSESSMENT OF THE PROPOSED NAME

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name. DMEPA, the Office of Generic Drugs and the Division Anesthesia and Analgesia Products concurred with the findings of DDMAC's promotional assessment of the proposed name.

4.2 SAFETY ASSESSMENT OF THE PROPOSED NAME

DMEPA evaluated 26 names for their potential similarity to the proposed name, Glydo. No other aspects of the name were found to pose potential confusion with the name.

Two of the 26 names did not undergo further evaluation because they were foreign products or the application was withdrawn from the Agency due to failed clinical trials. (See Appendix D).

Failure mode and effects analysis (FMEA) was applied to determine if the proposed proprietary name could potentially be confused with the 24 remaining names and lead to medication errors. This analysis determined that the name similarity between Glydo and 23 of the 24 names identified were unlikely to result in medication error for the reasons presented in Appendix E.

However, the remaining name, Glyco, was found to have orthographic and phonetic similarity with the proposed name, Glydo, pursuant to 21 CFR 201.10(5) which states "designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient."

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Glydo, is not promotional, however, it is vulnerable to name confusion with the currently marketed over-the-counter product, Glyco. Thus, the Division of Medication Error Prevention and Analysis finds the proposed name, Glydo, unacceptable. The Applicant will be notified of this conclusion via letter.

If you have further questions or need clarifications, please contact Cherye Milburn, OSE Project Manager, at 301-796-2084.

5.1 COMMENTS FOR THE PROPRIETARY NAME LETTER

We have completed our review of the proposed proprietary name, Glydo, and have concluded that the name is unacceptable for the following reason:

The proposed name, Glydo, is similar to the currently marketed product, Glydo, pursuant to 21 CFR 201.10(5) which states "designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient."

In your original submission dated June 24, 2010, you provided a secondary name, (b) (4) If you intend to have a proprietary name for this product, we recommend that you submit a new request for a proposed proprietary name review. (See the Guidance for Industry, *Contents of a Complete Submission for the Evaluation of Proprietary Names*, http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf and "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012".)

6 REFERENCES

6.1 DATABASES AND INFORMATION SOURCES

1. Micromedex Integrated Index (http://csi.micromedex.com)

Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

3. Drug Facts and Comparisons, online version, St. Louis, MO (http://factsandcomparisons.com)

Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products.

4. FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]

DARRTS is a government database used to organize Applicant and Applicant submissions as well as to store and organize assignments, reviews, and communications from the review divisions.

5. Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

6. Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

7. Electronic online version of the FDA Orange Book (http://www.fda.gov/cder/ob/default.htm)

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. U.S. Patent and Trademark Office (http://www.uspto.gov)

USPTO provides information regarding patent and trademarks.

9. Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

10. Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com)

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)

Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

12. Stat!Ref (www.statref.com)

Stat!Ref contains full-text information from approximately 30 texts; it includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology, and Dictionary of Medical Acronyms Abbreviations.

13. USAN Stems (http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

15. Lexi-Comp (www.lexi.com)

Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

16. Medical Abbreviations Book

Medical Abbreviations Book contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [3]

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [4] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and

[3] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors.html. Last accessed 10/11/2007.

[4] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

monitoring the impact of the medication.[5] DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly in spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	**Considerations when searching the databases**		
	Potential causes of drug name similarity	*Attributes examined to identify similar drug names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication

[5] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the DMEPA staff to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Analysis Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare

professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND or OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to concur/not concur with DMEPA's final decision.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[6] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

[6] Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

> ***"Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?"***

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Risk Assessment:

a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that

could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. . (See Section 4 for limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name	Scripted may appear as	Spoken may be interpreted as

Glydo		
Capital 'G'	A,C, L or S	K or L sound
lower case 'l'	e, i, r, or t	
lower case 'y'	g, p, or z	ee sound
lower case 'd'	'cl' , l or t	t sound
lower case 'o'	a, e or u	any vowel

Appendix C:

Figure 1. Glydo Study (conducted on July 29, 2010)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: Glydo #1 box to OR	Glydo One box to OR
Outpatient Prescription: Glydo #1 Box to OR	

Figure 2. FDA Prescription Study Samples and Responses.

Inpatient Written Studies	Outpatient Written Studies	Verbal Studies
Cilydo	Glydo	Glido
Clydo	Glydo	Galido
Clydo	Glydo	Glydo
Crlydo	Glydo	Glydo
Crydo	Glydo	
Elydo	Glydo	
Elydo	Glydo	
Glydo	Glydo	
Glydo	Glydo	
Glydo	Glydo	
Lydo	Glydo	
	Glydo	
	Glydo	
	Glydo	
	Glydo	

Appendix D: Names eliminated from further evaluation for reasons listed below

Proprietary Name		Similarity to Glydo	Reason
1	Cyclo	Look-Alike	Available in foreign countries only
			(b) (4)

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
1	**Atripla** (Efavirenz, Emtricitabine and Tenofovir Disoprixil Fumarate) tablets Strength: 600 mg/200 mg/300 mg Dose: One tablet once daily on an empty stomach at bedtime	Orthographic similarities: The first letter 'A' can appear like the first letter 'G' when scripted, the second upstroke letter 't' can appear like the second upstroke letter 'l', the downstroke letter 'p' can appear like the downstroke letter 'y' and the last letter 'a' can appear like the last letter 'o'. Overlapping product characteristics: Single strength availability	Varying product characteristics listed below, minimize the potential for confusion. Dosage form: Topical jelly versus oral tablet Dose: Take one versus 'X' mL Route of administration: Oral versus topical

*** This document contains proprietary and confidential information that should not be released to the public.***

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
2	**Atryn** (Antithrombin Recombinant) Powder for Injection Strength: 1750 IU/vial Dose: 100 IU baseline AT activity level X Body weight (kg)/1.3, 2.3, 5.4 or 10.2 via intravenous administration	Orthographic similarities: The first letter 'A' can appear like the first letter 'G', the second upstroke letter 't' can appear like the second upstroke letter 'l' and both names contain a downstroke letter 'y' similarly placed in the name. Overlapping product characteristics: Single strength availability	Orthographic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: There is an upstroke letter 'd' in Glydo that is not present in the name Atryn that provides orthographic distinction. Varying product characteristics: Dosage form: Powder for injection versus topical jelly Route of administration: Intravenous versus topical/urethral Dose presentation: 'X' IU based on formula versus 5 mL to 30 mL
3	**Cydec** (Carbinoxamine and Pseudoephedrine) Syrup Strength: 4 mg/60 mg per 5 mL Dose: 5 mL three to four times daily	Orthographic similarities: The first letter 'C' can appear like the first letter 'G' when scripted and both names contain a downstroke letter 'y' and an upstroke letter 'd' similarly placed in the names. Overlapping product characteristics: Single strength availability Dose overlap: 5 mL	Orthographic variations in the names along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: There is an upstroke letter 'l' in the second letter position of the name Glydo that is not present in the name Cydec providing orthographic distinction. Differentiating product characteristics: Dosage form: Oral syrup versus topical jelly Route of administration: Oral versus topical/urethral Frequency of administration: Three to four times daily versus single administration during procedure

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
4	**Cylert** (Pemoline) Tablets Strength: 18.75 mg, 37.5 mg and 75 mg Dose: 18.75 mg to 75 mg daily	Orthographic similarities: The first letter 'C' can appear like the first letter 'G' when scripted, both names contain a downstroke letter 'y' and an upstroke letter 'l' versus 'd' similarly placed in the names. Overlapping product characteristics: None	Orthographic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: There is an upstroke/cross-stroke letter 't' in the last letter position of Cylert that is not present in Glydo and provides orthographic distinction. Varying product characteristics: No overlap in strength or dose Dosage form: Tablet versus topical jelly Route of administration: Oral versus topical
5	**Galzin** (Zinc Salts) capsules Strength: 25 mg and 50 mg Dose: 50 mg three times daily until wound healed	Orthographic similarities: Both names begin with the letter 'G', contain an upstroke letter 'l' and downstroke letter 'z' versus 'y' in the names. Overlapping product characteristics: Numeric overlap in 25 mg versus 25 mL dose	Orthographic differences in the names along with varying product characteristics minimize the potential for confusion. Orthographic differences: Although both names contain a downstroke letter 'z' versus 'y' and an upstroke letter 'l' versus d'd in the names, they appear in different letter positions in Galzin versus Glydo, providing orthographic distinction in the beginning of the names 'Gly' versus 'Gal'. Dosage form: Capsule versus topical jelly Single strength versus multiple strength availability Route of administration: Oral versus topical Frequency of administration: Three times daily versus once during procedure

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
6	**Gliadel** (Carmustine) Implant Strength: 7.7 mg Dose: Up to eight wafer implants placed at resection of cavity	Orthographic and phonetic similarities: Both names begin with the letter 'G' and contain the upstroke letter 'l' and the upstroke letter 'd' similarly placed. Both names have two syllables and contain the 'Gly' sound in the first syllable, and the second syllable sound 'do' can sound like the second syllable sound 'del' when pronounced. Overlapping product characteristics: Single strength availability	Orthographic and phonetic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic and Phonetic differences: There is an upstroke letter 'l' in Gliadel that is not present in Glydo, and there is a downstroke letter 't' in Glydo that is not present in Gliadel. Addionally, Gliadel is pronounced with three syllables while Glydo has only two syllables. Varying product characteristics: Dosage form: Implant wafer versus topical gel No overlap in dose Route of administration: Intrawound versus topical/urethral

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
7	**Glyate** (Guaifenesin) oral liquid Strength: 100 mg/5 mL Dose: 200 mg (10 mL) to 400 mg (20 mL) every four hours	Orthographic similarities: Both names begin with the letters 'Gly' and the upstroke letter 't' can appear like an upstroke letter 'd' when scripted.. Overlapping product characteristics: Single strength availability Dose: 10 mL	Orthographic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: The letter 'a' in the fifth letter position of Glyate separates the letter 'y' and 't' while there is no letter separating the upstroke 't' from the upstroke letter 'd' in Glydo, providing orthographic distinction when scripted. Varying product characteristics: Dosage form: Oral liquid versus topical gel Strength: 100 mg/5 mL versus 2% or 20 mg/mL Route of administration: Oral versus topical/urethral Frequency of administration: Every four hours versus one-time use during procedure
8	**Glyburide** (Glyburide) Strength: 1.25 mg, 2.5 mg, and 5 mg Dose: 1.25 mg to 20 mg daily	Orthographic similarities: Both names begin with the letters 'Gly' and the upstroke letter 'b' can appear like the upstroke letter 'd'. Overlapping product characteristics: Potential numeric overlap in dose (5 to 20)	Orthographic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: Glydo contains five letters while Glyburide contains nine letters making it appear much longer when scripted. Varying product characteristics: Dosage form: Tablet versus topical jelly Strength: 1.25 mg, 2.5 mg and 5 mg versus 2%

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
9	**Glycate** (Calcium Carbonate) Tablets Strength: 300 mg Dose: One to two tablets once daily	Orthographic similarities: Both names begin with the letters 'Gly' Overlapping product characteristics: Single strength availability Numeric overlap 30 mL versus 300 mg dose	Orthographic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: Glydo contains five letters while Glycate contains seven letters making it appear longer when scripted. Varying product characteristics: Dosage form: Tablet versus topical jelly Route of administration: Oral versus topical/urethral Frequency of administration: Once daily versus single administration during procedure
10	(b) (4)		

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
11	**Glycine** (Glycine Irrigation, USP) Strength: 1.5% in 3000 mL Dose: Administration by transurethral instillation; total volume used based on surgeon discretion	Orthographic similarities: Both names begin with the letters 'Gly'. Overlapping product characteristics: Single strength availability Similar route of administration Possible dose (mL) overlap	Orthographic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: Glydo contains five letters while Glycine contains seven letters making it appear longer when scripted. Additionally, Glydo contains an upstroke letter 'd' not present in the name Glycine. Varying product characteristics: Dosage form: Irrigant versus topical jelly
12	**Glycolax** (Polyethylene Glycol) Powder for Oral Solution Strength: 17 gram/ scoopful Dose: 17 gram dose once daily	Orthographic similarities: Both names begin with the letters 'Gly' Overlapping product characteristics: Single strength availability	Orthographic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: Glydo contains five letters while Glycolax contains eight letters with a cross-stroke letter 'x' in the last letter position making it appear longer and providing distinction when scripted. Varying product characteristics: Dosage form: Powder for oral solution versus topical jelly Dose: 17 grams or 'one scoopful' versus 3 mL to 30 mL Route of administration: Oral versus topical/urethral Frequency: Once daily versus single use during procedure

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
13	**Glyco-A** (Glycolid Acid) Gel Strength: 6% and 12% Dose: Apply to face or Use as directed	Orthographic and phonetic similarities: Both names begin with the letters 'Gly' and contain a letter 'o' in the last letter position of the name. Both names have two syllables in the root name and the root name 'Glydo' can sound similar to 'Glyco' with the beginning 'Gl' sound and hard 'i' sound. Overlapping product characteristics: Similar dosage form: Topical gel versus jelly Route of administration: Topical	Orthographic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: The added modifier, 'A' in Glyco-A provides orthographic and phonetic distinction from the name Glydo. Additionally, there is an upstroke letter 'd' in the fourth letter position of Glydo that is not presents in Glyco-A providing added distinction. Varying product characteristics: Strength: 6% and 12% versus 2% Dose: 'Apply to face' or 'Use as directed' versus 3 mL to 30 mL Area of use: Face versus Urethral or endotracheal Setting of use: Self administered daily versus clinical setting during a procedure under the supervision of a healthcare professional Frequency of administration: Once daily versus one time use during procedure

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
14	**Glynase** (Glyburide) Tablets Strength: 1.5 mg, 3 mg and 6 mg Dose: 1.5 mg to 6 mg once daily	Orthographic similarities: Both names begin with the letters 'Gly' Overlapping product characteristics: Numeric overlap in '3' mg versus '30' mL	Orthographic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: Glydo contains five letters while Glynase contains seven letters making it appear longer when scripted. Varying product characteristics: Dosage form: Tablet versus topical jelly Strength: 1.5 mg, 3 mg, 6 mg versus 2% Route of administration: Oral versus topical Frequency of administration: Once daily versus one time during procedure
15	**Glyset** (Miglitol) Tablets Strength: 25 mg, 50 mg and 100 mg Dose: 25 mg to 100 mg three times daily	Orthographic similarities: Both names begin with the letters 'Gly' Overlapping product characteristics: None	Orthographic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: The third upstroke letter t' versus 'd' appear in different letter positions of the names. Varying product characteristics: Dosage form: Tablet versus topical jelly No strength or dose overlap Route of administration: Oral versus topical Frequency of administration: Three times daily versus one time administration during procedure

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
16	**Glytone** (Salycylic Acid) Lotion, Foam, Self-foaming cleanser, Benzoyl Peroxide Gel Sulfur Cream Hydroquinone, USP Clarifying cream Strength: 1% Lotion 0.5% Aerosol Foam, 2% Facial Cleanser, 6.4% Cream , 4% Hydroquinone cream Dose: Lotion: Apply thin layer to face three times daily Foam: Apply to face or infected area twice daily	Orthographic and phonetic similarities: Both names begin with the letters 'Gly' and the upstroke letter 't' can appear like the upstroke letter 'd' followed by the letter 'o' in both names. Both names have two syllables and contain the 'Gly' sound in the first syllable followed by the 'o' sound in the second syllable. Overlapping product characteristics: Strength: 2% Similar Dosage form: Topical lotion or foam versus topical jelly Route of administration: Topical	Orthographic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: Glydo contains five letters while Glytone contains seven letters making it appear longer when scripted. The added letters 'ne' after the 'o' in Glytone provides distinction from the name Glydo. The 'n' sound at the end of the second syllable provides some phonetic distinction from the 'o' sound at the end of the second syllable in Glydo. Varying product characteristics: Dosage form: Topical lotion, aerosol foam, facial cleaner, cream, gel versus topical jelly only. Strength: While strength overlap exists (2%), there are multiple topical dosage forms for Glytone, therefore, words 'facial cleaner' would likely accompany the proprietary name 'Glytone'. Dose: Glydo is dosed in millilters or milligrams while Glytone is likely dosed 'use as directed' or 'apply to face'. Setting of use: Glytone is self administered while Glydo is administered by a healthcare professional during a clinical procedure.

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

	PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**	**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
	FAILURE MODE: Name Confusion	**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
17	[redacted] (b) (4)		
18	**Onxol** (Paclitaxel) Injection Strength: 30 mg/5 mL, 150 mg/25 mL, 300 mg/50 mL Dose: 135 mg/m^2 or 175 mg/m^2	Orthographic similarities: The first letter 'O' can appear like the first letter 'G' and the downstroke letter 'y' in Glydo can appear like the cross-stroke letter 'x' if the cross-stroke falls below the line. Overlapping product characteristics: Numeric overlap '30 mg/50 mL' and '300 mg/50 mL' versus 30 mg (15 m)	Orthographic differences along with varying product characteristics listed below minimize the potential for confusion: Orthographic differences: There is an upstroke letter 'l' in the second letter position of Glydo that is not present in Onxol and a upstroke letter 'l' that appears in the last letter position of Onxol that is not present in Glydo that provide orthographic distinction. Dosage form: Injection versus topical jelly No overlap in dose Route of administration: Intravenous versus topical

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
19	**Sprycel** (Dasatinib) Tablets Strength: 20 mg, 50 mg, 70 mg and 100 mg Dose: 20 mg to 180 mg once daily	Orthographic similarities include the letter 'S' can appear like the letter 'G' and both names contain a downstroke letter 'y' similarly placed in the name. Overlapping product characteristics: Numeric overlap in strength '20' % versus '2'%	Orthographic differences in the names along with varying product characteristics minimize the potential for confusion. Orthographic differences: There is a downstroke letter 'p' in the second letter position and an upstroke letter 'l' in the last letter position of Sprycel that are not present in Glydo. Differentiating product characteristics: Dosage form: Tablet versus topical jelly Route of administration: Oral versus topical Frequency: Once daily versus one time use during procedure
20	**Syeda**[***] (Drosperinone and Ethinyl Estradiol) Tablet Strength: 3 mg/0.03 mg Dose: Take one tablet once daily (Proposed name found acceptable by DMEPA in 2010 for ANDA 090114 still under review)***	Orthographic similarities include the first letter 'S' can appear like the first letter 'G', both names contain a downstroke letter 'y' similarly placed in the names, and contains the letters 'da' versus 'do' at the end of the name. Overlapping product characteristics: Single strength availability	Orthographic differences in the names, along with varying product characteristics minimize the potential for confusion. Orthographic differences: The upstroke letter 'l' positioned between the capital letter 'G' and the downstroke letter 'y' provides differentiation from the 'Sy' presentation in Syeda. Differentiating product characteristics: Dosage form: Tablet versus Topical Jelly Route of administration: Oral versus topical/urethral

[***] This document contains proprietary and confidential information that should not be released to the public.***

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
21	**Symlin** (Pramlintide Acetate) Injection Strength: 1000 mcg/mL Dose: 15 mcg to 120 mcg immediately prior to major meals (titrate to optimize glycemic control) via subcutaneous injection	Orthographic similarities include the first letter 'S' can appear like the first letter 'G' and both names contain a downstroke letter 'y' similarly placed in the names and there is an upstroke letter 'l' versus 'd' similarly placed in the names. Overlapping product characteristics: Single strength availability Numeric overlap in the dose of '15' mcg versus '15' mL	Orthographic differences in the names along with varying product characteristics minimize the potential for confusion. Orthographic differences: There is an upstroke letter 'l' in the second letter position of Glydo that is not present in Symlin and the letter 'm' in third letter position of Symlin elongates the name. Additionally, the ending letters 'in' in Symlin appear different than the ending letter 'o' in Glydo. Differentiating product characteristics: Dosage form: Injection versus topical jelly Route of administration: Subcutaneously versus topical
22	[redacted]		(b) (4)

Appendix E: Potentially confusing names with orthographic, phonetic or multiple differentiating product characteristics that decrease the risk of medication errors.

PROPOSED NAME: **Glydo** **(Lidocaine Hydrochloride) Jelly**		**STRENGTH:** **2%** **(20 mg/mL)**	**USUAL DOSE:** **DOSED IN MILLILITERS:** **Usual Dose: 5 mL to 30 mL prior to trans-urethral procedures (i.e. cystoscopy, catherization, TURP); Apply a moderate amount of jelly to external surface of endotracheal tube before use for lubrication** **MAX DOSE: No more than 60 mL in twenty-four hour period**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized including differentiating information including on outpatient and inpatient prescription orders)
23	**Zydone** (Hydrocodoneo Bitartrate and Acetaminophen) Tablet Strength: 5 mg/400 mg, 7.5 mg/400 mg, 10 mg/400 mg Dose: 5 mg/400 mg to 10 mg/400 mg every four to six hours	Orthographic similarities include the first letter 'Z' can appear like the first letter 'G', and both names contain a downstroke letter 'y' and an upstroke letter 'd' in the names. Overlapping product characteristics: Numeric overlap in dose for '5', '7.5' and '10' mg versus mL	Orthographic differences in the names along with varying product characteristics minimize the potential for confusion. Orthographic differences: There is an upstroke letter 'l' in the second letter position of Glydo that is not present in Zydone that provides orthographic distinction. Differentiating product characteristics: Dosage form: Tablet versus topical jelly Route of administration: Oral versus topical Frequency of administration: Every four to six hours versus one time use during procedure

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/s/

CATHY A MILLER
04/13/2011

ZACHARY A OLESZCZUK
04/13/2011

CAROL A HOLQUIST
04/13/2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201094Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

ROUTING SHEET

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

Division: I	Team: 13	PM: Mandy Kwong

Electronic ANDA: Yes ☒ No ☐

ANDA #:201094
Firm Name:Sagent Pharmaceuticals, Inc.
ANDA Name:Glydo (lidocaine hydrochloride jelly, USP), 2% Jelly
RLD Name:Xylocaine ® (lidocaine hydrochloride) Jelly, 2% of Oak Pharmaceuticals, Inc.

Electronic AP Routing Summary Located:
V:\Chemistry Division I\Team 13\Electronic AP Summary\201094.ARS.doc

AP/TA Letter Located:
V:\Chemistry Division I\Team 13\Approval Letters\201094.AP.doc

Project Manager Evaluation: **Date: 3-27-14 Initials:** MK

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

Original Rec'd date 12-23-09	Date of Application 12-23-09	Date Acceptable for Filing 12-23-09
Patent Certification (type) PII	Date Patent/Excl. expires N/A	Citizens' Petition/Legal Case? Yes☐ No ☒ (If YES, attach email from PM to CP coord)
First Generic Yes ☐ No ☒ **DMF#:** (b) (4) (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 ☐	

GDUFA User Fee Obligation Status: ☒ Met ☐ Unmet**:** ☐ Facility Fee not paid, ☐ Backlog fee not paid
EER Status: ☐ Pending ☐☐ ☒ Acceptable ☐ OAI *EES Date Acceptable: 4-18-14* ☐ 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) 4-10-12 Addendum Needed: Yes ☐ No ☒ Comment:
Date of Acceptable Bio 5-11-12 Bio reviews in DARRTS: Yes ☒ No ☐ (Volume location:)
Date of Acceptable Labeling 4-11-14 Attached labeling to Letter: Yes ☐ No ☐ Comment:
Date of Acceptable Sterility Assurance (Micro) 11-18-11

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: 4-18-14 REMS Required: Yes ☐ No ☒ REMS Acceptable: Yes ☐ No ☐

☒ Regulatory Support

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

☒ Division

☒ Bob West / Peter Rickman

☒ Kathleen Uhl

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

OGD APPROVAL ROUTING SUMMARY

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

Martin Shimer **Date: 4/25/2014**

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 =_____ NDA#_____ Date Checked _____ 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 Is a forfeiture memo needed: Yes ☐ No ☐ If yes, has it been completed	
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:ANDA submitted on 12/23/2009, BOS=Xylocaine NDA 08816, PII cert provided. ANDA ack for filing on 12/23/2009(LO dated 3/25/2010). There are no unexpired patents or exclusivities which protect the RLD. This ANDA is eligible for immediate Full Approval.	

2. ***Labeling Endorsement***

Reviewer, Betty Turner:
Date4-18-14

Labeling Team Leader, Angela Payne:
Date4-18-14

REMS required?
☐Yes ☒No

REMS acceptable?
☐Yes ☐No ☒n/a

Comments:
From: Payne, Angela
Sent: Friday, April 18, 2014 3:10 PM
To: Turner, Betty; Kwong, Mandy
Subject: RE: Request for Labeling Endorsement for ANDA # 201094 Lidocaine HCL Jelly

I concur.

Angela
ATL

From: Turner, Betty
Sent: Friday, April 18, 2014 2:43 PM
To: Kwong, Mandy; Payne, Angela
Subject: FW: Request for Labeling Endorsement for ANDA # 201094 Lidocaine HCL Jelly

Hi Mandy,

There are no new changes for the labeling since the last review was completed. I have checked the OB, DARRTS, USP and REMS and no updates are required.

Thanks,

Betty

From: Kwong, Mandy
Sent: Friday, April 18, 2014 1:57 PM
To: Turner, Betty; Payne, Angela
Subject: Request for Labeling Endorsement for ANDA # 201094 Lidocaine HCL Jelly

Hello Betty and Angela,

I'm not sure if I still need your endorsement for the full approval of this ANDA, since the labeling was just reviewed on 4/11/14. Could you please take a look? I have attached the latest labeling review and AP letter for your reference.

Thank you.

Mandy

3. ***Paragraph IV Evaluation*** **PIV's Only**
David Read **Date _____**
OGD Regulatory Counsel **Initials_____**
Pre-MMA Language included ☐
Post-MMA Language Included ☐
Comments:

4. ***Quality Division Director /Deputy Director Evaluation*** **Date 4/22/14**
Chemistry Div. **I (Raw)** **InitialsASR**
Comments:CMC Acceptable

OGD Office Management Evaluation

5. Peter Rickman **Date 4/28/14**
Director, DLPS **Initials wpr**
Para.IV Patent Cert: Yes☐ ☐ ☐ No☒
Pending Legal Action: Yes☐ ☐ No☒
Petition: Yes☐ No☒
Entered to APTrack database ☒
GDUFA User Fee Obligation Status Met☒ Unmet☐
Press Release Acceptable ☐
Date PETS checked for first generic drug _____

Comments: BOS=Xylocaine NDA 08816. Applicant provided a PII patent certification. There are no unexpired patents or exclusivities which protect the RLD. Chemistry acceptable 4/10/2012. Bio acceptable 5/11/2012 (waiver granted). Labeling acceptable 4/11/2014, TL sign-off 4/18/2014. Micro acceptable 11/18/2011. EER acceptable 4/18/2014. This ANDA is eligible for immediate Full Approval.

OR

6. Robert L. West **Date _____**
Deputy Director, OGD **Initials _____**
Para.IV Patent Cert: Yes☐ ☐ ☐ No☐
Pending Legal Action: Yes☐ ☐ No☐
Petition: Yes☐ No☐
Entered to APTrack database ☐
GDUFA User Fee Obligation Status Met☐ Unmet☐
Press Release Acceptable ☐
Date PETS checked for first generic drug _____

Comments:

7. ***OGD Director Evaluation***

Kathleen Uhl

Comments:

First Generic Approval ☐

PD or Clinical for BE ☐

Special Scientific or Reg. Issue ☐

Press Release Acceptable ☐

Comments:

8. Project Manager **Date 4-29-14**
Initials MK

Comments:called and faxed AP letter to ANDA holder.

Check Communication and Routing Summary into DARRTS

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/s/

MANDY C KWONG
04/29/2014

FDA FAX

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North VII
7620 Standish Place
Rockville, Maryland 20855

TO: SAGENT PHARMACEUTICALS INC TEL: (b) (6)

ATTN: Kalpesh Shroff FAX: 847-908-1601

This facsimile is in reference to your abbreviated new drug application(s), submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act.

This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

Pages (including cover): 4

SPECIAL INSTRUCTIONS:

DATE: 2/10/2014

TO: SAGENT PHARMACEUTICALS INC

ATTN: Kalpesh Shroff

E-Mail: kshroff@sagentpharma.com

FAX: 847-908-1601

RE: Update summary of filed and pending original ANDA(s)

Dear Sir or Madam:

The Office of Generic Drugs (OGD) in the Center for Drug Evaluation and Research, Food and Drug Administration (FDA), is providing you with this one-time communication on the status of your filed and pending original abbreviated new drug application(s) (ANDA) submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act. OGD is providing these updates as an interim measure to help applicants assess the status of their current submissions as we transition towards predictable goal times pursuant to the Generic Drug User Fee Amendments of 2012 (GDUFA).

Your status update is limited to available review information as of January 29, 2014. Any additional information regarding your ANDA collected after this date is neither considered nor provided. Furthermore, your ANDA status is subsequently subject to revision pending additional information or concerns raised by any of the discipline reviews (bioequivalence, clinical, chemistry, microbiology, labeling, facility), other unforeseen legal, scientific or regulatory issues, or inspectional results, which can also impact the status or ability to issue a complete response. Any applicable fees can also affect the status of your ANDA.

OGD is providing your ANDA status update in the attached chart with a list of applicable acronyms. The chart only contains current information regarding discipline review and does not forecast if and when OGD will issue a complete response, tentative approval, or final approval letter.

Please do not respond to this communication by asking FDA or your Regulatory Project Manager for additional or more detailed information. This is a one-time communication intended to assist you to ascertain the current status of submissions. It is not feasible for us to respond to a high volume of follow up inquiries.

Sincerely yours,

CAPT Aaron W. Sigler, USPHS
Chief, Review Support Branch

ANDA	DRUG NAME	CHEM	BIO	MICRO	LABEL	CLINICAL	FACILITY
(b) (4)							
201094	LIDOCAINE HYDROCHLORIDE	AQ	AQ	AQ	AQ	NA	PN
(b) (4)							

CHART ACRONYMS

Column Headings

ANDA - The application number for your Abbreviated New Drug Application
DRUG NAME - The official filed name of the drug associated with the ANDA number
CHEM - Product Quality Chemistry Review
BIO - Bioequivalence Review, typically including OSI, if applicable
MICRO - Microbiology Review
LABEL - Labeling Review
CLINICAL - Clinical Review
FACILITY - Overall Facility inspections summary. All facilities must be acceptable at the time of 29 JAN 14 in order to warrant an adequate notation. If one of more facility is not acceptable then the FACILITY column will be marked as such. OSI information is not considered.

Discipline Notations

IQ	- Inadequate. This particular discipline is currently found to be inadequate.
AQ	- Adequate. This particular discipline was found to be adequate when the information was gathered for this communication.
UR	- Under Review. This particular discipline is currently assigned OR under review with the discipline team.
NR	-Not Reviewed. This particular discipline is either currently not under review or assigned.
NA	- Not applicable. This particular discipline is not required for the approval of this ANDA.

Facility Notations

PN	- Pending, i.e., one or more facilities have been inspected and are pending an outcome.
AC	- All facilities are acceptable at the time of this publication.

*Please note that you may receive your updates in multiple communications over time, based on the number of ANDAs pending in OGD.

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/s/

SIMON S ENG on behalf of AARON W SIGLER
02/12/2014

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 201094

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Sagent Pharmaceuticals, Inc.
1901 N. Roselle Road, Suite 700
Schaumburg, IL 60195-3176

ATTENTION: Kalpesh Shroff
Associate Director, Regulatory Affairs

Dear Mr. Shroff:

Please refer to your Abbreviated New Drug Application (ANDA) dated and received December 23, 2009, and your resubmission, dated and received April 23, 2013, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lidocaine Hydrochloride Jelly USP, 2%.

We also refer to your July 3, 2013, correspondence, received July 5, 2013, and your amendment dated July 10, 2013, received July 11, 2013, requesting reconsideration of your proposed proprietary name, Glydo. We have completed our review of the proposed proprietary name, Glydo. Based on the information you submitted stating that Glyco has a unique distribution system and limited availability, we agree that the risk of confusion between Glydo and Glyco is minimal. Therefore, we have concluded that Glydo is acceptable.

If **any** of the proposed product characteristics as stated in your July 3, 2013 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Lisa Skarupa, Senior Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-2219. For any other information regarding this application, contact Tania Mazza, Regulatory Project Manager, in the Office of Generic Drugs at (240) 276-9344.

Sincerely,

{See appended electronic signature page}

Kellie A. Taylor, Pharm.D., MPH
Deputy Director
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
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/

TODD D BRIDGES on behalf of KELLIE A TAYLOR
01/09/2014

Thomas, Teena

From: Bourdage, Jill
Sent: Wednesday, May 01, 2013 3:43 PM
To: Thomas, Teena
Cc: Stephenson, Franklin; Jenkins, Darrell
Subject: FW: ANDA 201094 - Request for Reconsideration of GLYDO as the proprietary name for Lidocaine Hydrochloride Jelly, USP 2%

Teena

Below is an email trail for ANDA 201094 which I don't know if you received. Will you please place this in RCM AIMS?

Thanks

Jill R. Bourdage, RPh, PMP, CPM
Director, Project Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research
Food and Drug Administration
Email: jill.bourdage@fda.hhs.gov
Office: 301.796.5164

From: Jerry Phillips [mailto:jphillips@brandinstitute.com]
Sent: Tuesday, April 30, 2013 11:54 AM
To: Holquist, Carol A
Cc: Bourdage, Jill
Subject: RE: ANDA 201094 - Request for Reconsideration of GLYDO as the proprietary name for Lidocaine Hydrochloride Jelly, USP 2%

Yes, I understood that. Thanks.

From: Holquist, Carol A [mailto:Carol.Holquist@fda.hhs.gov]
Sent: Tuesday, April 30, 2013 10:51 AM
To: Jerry Phillips
Cc: Bourdage, Jill
Subject: RE: ANDA 201094 - Request for Reconsideration of GLYDO as the proprietary name for Lidocaine Hydrochloride Jelly, USP 2%

Jerry,

Let me make this clear. The information you sent in the e-mail is not an official submission and will not even be looked at until it is sumbitted formally to the ANDA.

Carol

From: Jerry Phillips [mailto:jphillips@brandinstitute.com]
Sent: Tuesday, April 30, 2013 11:51 AM
To: Holquist, Carol A
Cc: Bourdage, Jill
Subject: RE: ANDA 201094 - Request for Reconsideration of GLYDO as the proprietary name for Lidocaine Hydrochloride Jelly, USP 2%

Thanks. We'll submit this request to the ANDA also.
Jerry

From: Holquist, Carol A [mailto:Carol.Holquist@fda.hhs.gov]
Sent: Tuesday, April 30, 2013 10:48 AM
To: Jerry Phillips
Cc: Bourdage, Jill
Subject: RE: ANDA 201094 - Request for Reconsideration of GLYDO as the proprietary name for Lidocaine Hydrochloride Jelly, USP 2%

Jerry,
The Agency does not take requests for reconsideration via e-mail. If you and Sagent Pharmaceuticals wish to have this name re-evaluated you must submit it formally to the application. No expedited review is going to be granted. If you have further questions about how to submit the request for reconsideration to the ANDA please contact the OSE RPM point of contact for guidance. I have also attached the guidance for industry on contents of a complete submission that explains how you should identify this request on the cover letter of your submission http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075068.pdf.
Carol

From: Jerry Phillips [mailto:jphillips@brandinstitute.com]
Sent: Monday, April 29, 2013 5:44 PM
To: Holquist, Carol A
Subject: ANDA 201094 - Request for Reconsideration of GLYDO as the proprietary name for Lidocaine Hydrochloride Jelly, USP 2%

Dear Carol:
I am respectively requesting, on behalf of Sagent Pharmaceuticals, a reconsideration of the July 14, 2010 submission for the name GLYDO. The unacceptable letter for this name was dated April 15, 2011 (see attachment), which cited an objection based upon 21 CFR 201.10(5). When we received this letter in 2011, the Red Book listed GLYCO GEL (Glycolic Acid in 30%, 50% and 70% strengths) available by TOPIX Pharmaceuticals and thus we elected to move on to our next name submission, as we fully concurred with your excellent risk assessment and conclusion.
However, we have contacted Topix Pharmaceuticals today and they no longer have a product with that name. In CLINICAL PHARMACOLOGY, we do note a product called GLYCO for a company name Topiderm Pharmaceuticals. We inquired about the availability of GLYCO and they said that this Over-the-Counter product is available on 3 websites, but noting that they don't have a website nor do they sell it directly to consumers. These sites included: skinstore.com; dermstore.com; and dermadoctor.com. Upon searching these sites, we found nothing on Dermadoctor.com and found "Derma Quest Skin Therapy Glyco Creamy Cleanser 15%" on the other two sites. We believe that Derma Quest Therapy Glyco Creamy Cleanser is not similar to GLYDO and thus not confusingly similar in accord with 21 CFR 201.10(5). We also note that the Agency did not consider the product profile differences of these two products, which are quite different. In light of the upcoming ANDA approval and the four previous name rejections, we kindly ask for an expedited review of this new information so that Sagent Pharmaceuticals can launch this product under the brand name GLYDO. Thanks on behalf of Sagent Pharmaceuticals and we look forward to your reconsideration.
Sagent would be happy to follow-up this e-mail request with a written request to the ANDA, if requested.
Jerry

Jerry Phillips, R.Ph.
President & Chief Executive Officer

DSI
DrugSafetyInstitute
Where Great Brands BeginÂ®

www.drugsafetyinstitute.com | Austin
jphillips@brandinstitute.com
Tel: (305) 374-7233
Mobile: (305) 926-6680
Fax: (305) 374-2504

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/s/

TEENA THOMAS
05/02/2013

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/s/

CAROL A HOLQUIST
05/02/2013

MEMORANDUM of TELECONFERENCE

MEETING DATE: 05/01/2013
TIME: 10:10 am
APPLICATION: ANDA 201094
DRUG NAME: (b) (4)
TYPE OF MEETING: Teleconference

FDA ATTENDEES: *Franklin Stephenson, OSE SRPM, TL*
Teena Thomas, OSE SRPM

SPONSOR ATTENDEES:Kalpesh Shroff

BACKGROUND: Kalpesh Shroff had sent an email to Teena giving authorization to Jerry Philips for all proprietary name review matters. Today we called Kalpesh and asked him to submit the authorization letter officially to the document room. The teleconference lasted less than five minutes and Kalpesh promised to submit the authorization letter to the Document Room by 05/02/2013.

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/s/

TEENA THOMAS
05/01/2013

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/s/

CAROL A HOLQUIST
09/05/2012

Please send an email to the labeling reviewer (betty.turner@fda.hhs.gov) to confirm that you received the labeling comments

Labeling Comments

ANDA 201094

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773 (240-276-8728)

TO: Sagent Pharmaceuticals Inc.

TEL: (847) 908-1655

ATTN: Kalpesh Shroff

FAX: (847) 908-1601

FROM: Betty Turner

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 and signature page): 4

SPECIAL INSTRUCTIONS:

*Effective **01-Aug-2010**, the new mailing address for Abbreviated New Drug Application (ANDA) Regulatory Documents has become:*

Office of Generic Drugs
Document Control Room
7620 Standish Place
Rockville, Maryland 20855

ANDAs will only be accepted at the new mailing address listed above. For further information, please refer to the following websites prior to submitting your ANDA Regulatory documents: Office of Generic Drugs (OGD): http://www.fda.gov/cder/ogd or Federal Register: http://www.gpoaccess.gov/fr/

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/s/

CHI-ANN Y WU
08/22/2012
For Wm. Peter Rickman

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA See Attached

Date: 8/20/2012

Attention:
Department of Regulatory Affairs
SAGENT PHARMS
1901 NORTH ROSELLE RD STE 700
SCHAUMBURG, IL 60195

RE: Request to Withdraw Applications from the Generic Drug Backlog to Avoid Incurring Backlog Fee

Dear Sir or Madam:

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

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III), enacted on July 9, 2012, establish a one-time backlog fee for any ANDA that is pending at the US Food and Drug Administration (FDA) on October 1, 2012 and has not received a tentative approval.

FDA is issuing this letter to encourage applicants who have pending ANDAs for which the applicants no longer wish to seek approval to notify FDA of the request to withdraw those ANDAs (see Federal Register Notice Docket Number FDA-2012-N-0879). **Requests for withdrawal should be submitted in writing individually for each ANDA as a "Request for Withdrawal" to the affected ANDA**. A decision to withdraw the ANDA is without prejudice to refiling.

Any ANDA that is not withdrawn by September 28, 2012 will incur the obligation to pay the backlog fee. Payment of backlog fees will be due no later than 30 calendar days after publication in the Federal Register of a notice (to be issued by October 31, 2012) announcing the amount of the backlog fee. Applicants with original ANDAs that fail to pay the backlog fee by the due date will be placed on a publicly available arrears list, and FDA will not receive new ANDAs or supplements submitted by those applicants, or any affiliates of those applicants, until the outstanding fee is paid.

To avoid incurring the backlog fee for an application, you, the applicant, must submit a request to withdraw the application and that request must be received by the FDA on or before **September 28, 2012**. However, to expedite this process, you are encouraged to submit the request by **September 15, 2012**.

You should submit the request to withdraw your applications by standard application submission methods. If an application was submitted via the FDA electronic gateway, a request for withdrawal should be submitted to the application via the gateway. Alternatively, you should send written notification to the ANDA archival file at the following address: Office of Generic Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, Document Control Room, Metro Park North VII, 7620 Standish Pl., Rockville, MD 20855.

In addition, please provide electronic confirmation of all ANDAs you wish to withdraw by sending an email to OGDGDUFA@fda.hhs.gov within the timeframe specified above**.**

For your convenience, a list of pending ANDAs for which we have identified you as the applicant is attached. **However, this list may be incomplete. Therefore, it is important to note that the absence of an ANDA from this list does not exempt that ANDA from incurring a backlog fee. Please verify the list for completeness of all ANDAs you have submitted. Discrepancies should be reported to the email address noted above.**

The GDUFA statute exempts only generic Positron Emission Tomography (PET) products from the user fees. There are no additional exemptions or waivers for GDUFA fees beyond those in the statute.

If you have questions regarding this communication, contact Thomas Hinchliffe at OGDGDUFA@fda.hhs.gov.

Please direct general GDUFA questions to ASKGDUFA@fda.hhs.gov.

Sincerely,

{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

CC: Attached List of ANDAs

PENDING ANDAs
(List produced as of 8/20/2012)

ANDA #	Drug Name
(b) (4)	
201094	LIDOCAINE HYDROCHLORIDE
(b) (4)	

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/s/

CECELIA M PARISE
08/22/2012

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

ANDA 201094

PROPRIETARY NAME REQUEST
UNACCEPTABLE

Sagent Pharmaceuticals, Inc.
1901 Roselle Road, Suite 700
Schaumburg, IL 60195

ATTENTION: Kalpesh Shroff, RAC
Associate Director, Regulatory Affairs

Dear Mr. Shroff:

Please refer to your Abbreviated New Drug Application (ANDA) dated December 23, 2009, received December 23, 2009, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lidocaine Jelly, USP, 2%.

We also refer to your July 29, 2011 correspondence, received August 1, 2011, requesting review of your proposed proprietary name, (b) (4) We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons:

(b) (4)

We note that you have not proposed an alternate proprietary name for review. If you intend to have a proprietary name for this product, we recommend that you submit a new request for a proposed proprietary name review. (See the Guidance for Industry, *Contents of a Complete Submission for the Evaluation of Proprietary Names,* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf and "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012".)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Danyal Chaudhry, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301)-796-3813. For any other information regarding this application contact Trang Tran, Product Quality Regulatory Project Manager in the Office of Generic Drugs (OGD), at (240) 276-8518.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

AZEEM D CHAUDHRY
06/27/2012

CAROL A HOLQUIST
06/28/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION			REQUEST FOR CONSULTATION	
TO *(Division/Office)* Division of Clinical Review, Office of Generic Drugs			FROM: - HFD-613 - Labeling Review Branch HFD-600 Office of Generic Drugs Thuyanh Vu, labeling reviewer	
DATE: 4/17/2012	IND NO.	ANDA NO. 201094	TYPE OF DOCUMENT Safety Consult	DATE OF DOCUMENT 4/17/2012
NAME OF DRUG Lidocaine Hydrochloride Jelly, 2%		PRIORITY CONSIDERATION HIGH	CLASSIFICATION OF DRUG Local anesthetics	DESIRED COMPLETION DATE ASAP
NAME OF FIRM Sagent Pharmaceuticals				

REASON FOR REQUEST

I. GENERAL

NEW PROTOCOL	PRE NDA MEETING	RESPONSE TO DEFICPENCY LETTER
PROGRESS REPORT	END OF PHASE II MEETING	FINAL PRINTED LABELING
NEW CORRESPONDENCE	RESUBMISSION	LABELING REVISION
DRUG ADVERTISING	SAFETY/EFFICACY	ORIGINAL NEW CORRESPONDENCE
ADVERSE REACTION REPORT	PAPER NDA	FORMULATIVE REVIEW
MANUFACTURING CHANGE/ADDITION	CONTROL SUPPLEMENT	X *OTHER ('specify below)*

MEETING PLANNED BY _____

II.BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
TYPE A OR B NDA REVIEW END QF PHASE II MEETING CONTROLLED STUDI ES PROTOCOL REVIEW OTHER	CHEMISTRY PHARMACOLOGY BIOPHARMACEUTICS OTHER

III.BIOPHARMACEUTICS

DISSOLUTION	DEFICIENCY LETTER RESPONSE
PROTOCOL-- BIOPHARMACEUTICS	BIOAVAILABILITY STUDIES
IN--VIVO WAIVER REQUEST	PHASE IV STUDIES

IV.DRUG EXPERIENCE

PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL	REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES	SUMMARY OF ADVERSE EXPERIENCE
CASE REPORTS OF SPECIFIC *REACTIONS(List below)*	POISON RISK ANALYSIS
COMPARATIVE RISK ASSESSEMENT ON GENERIC DRUG GROUP	

V. SCIENTIFIC INVESTIGATIONS

CLINICAL PRECLINICAL

The RLD is Abraxis' Xyclocaine 2% Jelly (NDA 08816). The RLD is currently marketed in a 30 mL aluminum tube (with a detachable applicator cone and a key for expressing the contents) and a 5 mL plastic tube. In the past, the RLD was also marketed in 10 mL polypropylene and 20 mL polypropylene syringe. IMS (ANDA) currently markets single-use 5 mL, 10 mL and 20 mL lidocaine hydrochloride Jelly packaged in glass vials. IMS provides Uro-Jet vial injectors to use with the glass vials.

Sagent proposes to market the jelly in prefilled 6 mL an 11 mL (b) (4) syringes. Sagent's product is not packaged with a plastic cone. (b) (4)

(b) (4)

SIGNATURE OF REQUESTER Thuyanh Vu	METHOD OF DELIVERY **DAARTS**
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

FORM FDA 3291 (7/83)

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/s/

THUYANH VU
04/17/2012

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20852

To:	John Peters, M.D., Director, Division of Clinical Review, Office of Generic Drugs
From:	Wayne DeHaven, Reviewer, Team 8, Division of Bioequivalence I, Office of Generic Drugs
Through:	Hoainhon Nguyen, Acting Deputy Director, Division of Bioequivalence I (DBI), Office of Generic Drugs
Re:	Request the opinion on the clinical significance of the viscosity difference seen between the Test and Reference product as reported in ANDA 201094, Sagent Pharmaceuticals' Lidocaine Hydrochloride Jelly, 2%

Introduction:

Sagent Pharmaceuticals, Inc. originally submitted a waiver of *in vivo* bioequivalence (BE) study requirements under 21 CFR 320.24 (b) (6) for its test product, Lidocaine Hydrochloride Jelly, 2%. The reference listed drug (RLD) is Xylocaine®, 2% (NDA #008816) manufactured by Oak Pharmaceuticals Inc (transfer of ownership from APP Pharmaceuticals) and is a Drug Efficacy Study Implementation (DESI) effective drug product [coded "AT" in the Orange Book (OB)].

The proposed test product is a preservative-free formulation (see Section III: Formulation), packaged in a ready-to-use prefilled syringe as a single-use, sterile product. In contrast, the RLD contains (b) (4) Methylparaben and Propylparaben. There is an approved ANDA (#086283) which also is packaged as a single-use product, (b) (4) The test product formulation does not need to be Q1/Q2 the same as the RLD with respect to (b) (4) The test product meets USP potency assay specification for lidocaine hydrochloride jelly of 95%.00 to 105.00%[2].

The viscosity of the current test product is not comparable to that of the reference product (b) (4) (b) (4) The viscosity difference between the test and RLD could lead to different surface retention of the lidocaine, and thus possibly different local drug absorption. Therefore, the Division of Bioequivalence I (DBI) recommended Sagent justify for such difference, as well as the wide viscosity specification range given (b) (4) The DBI also recommended Sagent submit additional viscosity data from additional batches to establish a more accurate viscosity range for the test product[3].

Sagent responded in an amendment dated 03/23/2012[4]. In the amendment, the firm justified the viscosity difference by comparing measured viscosities of other approved lidocaine jelly products available in the U.S market. The firm argued that approved lidocaine jelly drug products have a wide range of viscosity which "*suggests that the viscosity may not have a significant impact or may not lead to different surface retention of the active pharmaceutical ingredient (API), and thus different local drug absorption.*" The following table summarizes the viscosity results of the various products as determined by Sagent:

(b) (4)

[redacted]

[1] DARRTS: ANDA 201094 REV-BIOEQ-01(General Review); Submit/Final Date 11/10/2011, Page 10-11
[2] USP 34-NF 29 Official Monograph, Page 3308 – 3309 (http://www.uspnf.com/uspnf/login) Last Accessed: 04.04.2012
[3] DARRTS: ANDA 201094 REV-BIOEQ-01(General Review); Submit/Final Date 11/10/2011
[4] DARRTS: ANDA 201094 Bioequivalence/Response to Information Request #13 and 14; Submit Date 03/23/2012

(b) (4)

Additionally, Sagent submitted *in vitro* drug release testing data (see Appendix) comparing the Test product to the RLD, as well as other US marketed products, using the European Pharmacopoeia (EP) method 2.9.4 (DISSOLUTION TEST FOR TRANSDERMAL PATCHES). However, currently the DBI does not recommend drug release testing for semi-solid drug products as methods for such testing have not been standardized.

Issue: The DBI requests a clinical consult to determine whether the viscosity difference observed between the test and RLD products (Lidocaine Hydrochloride Jelly, 2%) should be of a safety and/or efficacy concern.

Section I: OGD History of This Drug Product

According to the Orange Book (OB), the following are approved for Lidocaine Jelly, 2%:

Appl No	TE Code	RLD	Proprietary Name	Applicant	Approval date
A040433	AT	No	LIDOCAINE HCl	AKORN	2/12/2003
A040837	AT	No	LIDOCAINE HCl	HI TECH PHARMA	3/23/2011
A086283	AT	No	LIDOCAINE HCl	INTL MEDICATION	08/07/1979
N008816	AT	Yes	XYLOCAINE	OAK PHARMS	03/12/1953
A080429	AT	No	ANESTACON	POLYMEDICA	04/11/1974
A081318	AT	No	LIDOCAINE HCl	TEVA PHARMS	4/29/1993

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…"

The following ANDAs are listed in DARRTS:

ANDA #	Submitter	Current Status	Status Date
040433	AKORN INC	Approved	2/12/2003
086283	INTERNATIONAL MED SYST	Approved	8/7/1979
081318	TEVA	Approved	4/29/1993
201094	SAGENT	Pending	12/23/2009
040837	HI TECH	Approved	3/23/2011
080429	POLYMEDICA	Approved	4/11/1974

(b) (4)

Highlighted yellow is the current product under review

Section II: Additional Drug Product Information

Test Product	Lidocaine Hydrochloride Jelly, 2%
Reference Product[5]	Xylocaine® Jelly (Lidocaine Hydrochloride), 2%
RLD Manufacturer	Oak Pharmaceuticals Inc (transfer of ownership from APP Pharmaceuticals)
NDA No.	008816
RLD Approval Date	03/12/1953
TE Code	AT
Indication[6]	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).

PK/PD Information[7]

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.
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 cm2 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
Tmax	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

[5] http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=008816&TABLE1=OB_Rx
[6] http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=33063#nlm34067-9
[7] http://www.clinicalpharmacology-ip.com/Forms/search.aspx?s=xylocaine

Section III: Comparative Formulations:

FIRM:		RLD (Oak Pharm)	(b) (4)	Sagent (transferred from Farco-Pharma GMBH)
ANDA/NDA #:		8816		201094
Volume of Packaged Product:		5mL and 30mL		6mL and 11mL
Packaging:		tube + Applicator		Single use syringe
		mg/mL		quantity per 100 grams
Lidocaine HCl	Active	2% (20mg/mL)		2.0g (20mg/mL)[8]
Methylparaben	Inactive	(b) (4)		
Propylparaben	Inactive			
Hydroxypropylmethylcellulose	Inactive			(b) (4)
Carboxymethylcellulose Sodium	Inactive			
Purified Water	Inactive			QS[10]
Hydrochloric Acid	Inactive			
Sodium Hydroxide	Inactive			ADJUST PH[11]
Sodium Chloride	Inactive			[12]
Benzalkonium Chloride	Inactive			

(b) (4)

Appendix:
The following is copied from the firm's deficiency letter response:[13]

In order to demonstrate the equivalence of the subject drug product with the RLD (Rate of drug release through a membrane), we have performed in vitro dissolution testing with the approved Lidocaine Jelly drug products currently available in US market.

In vitro testing is a well accepted method used to characterize performance characteristics of a finished topical dosage form. In general, in-vitro testing can be used as an indicator of in-vivo bioavailability. Important changes in the characteristics of a drug product formula or the thermodynamic properties of the drug(s) it contains should show up as a difference in drug release.

The test method used is based on the European Pharmacopoeia (EP) method 2.9.4 (DISSOLUTION TEST FOR TRANSDERMAL PATCHES). The in vitro dissolution test method is provided in section 3.2.P.3.2. This test was performed on two different temperatures as listed below covering average temperature range from tip to core of urethra.

1. *at 32°C (skin temperature)*
2. *at 37°C (Core body temperature)*

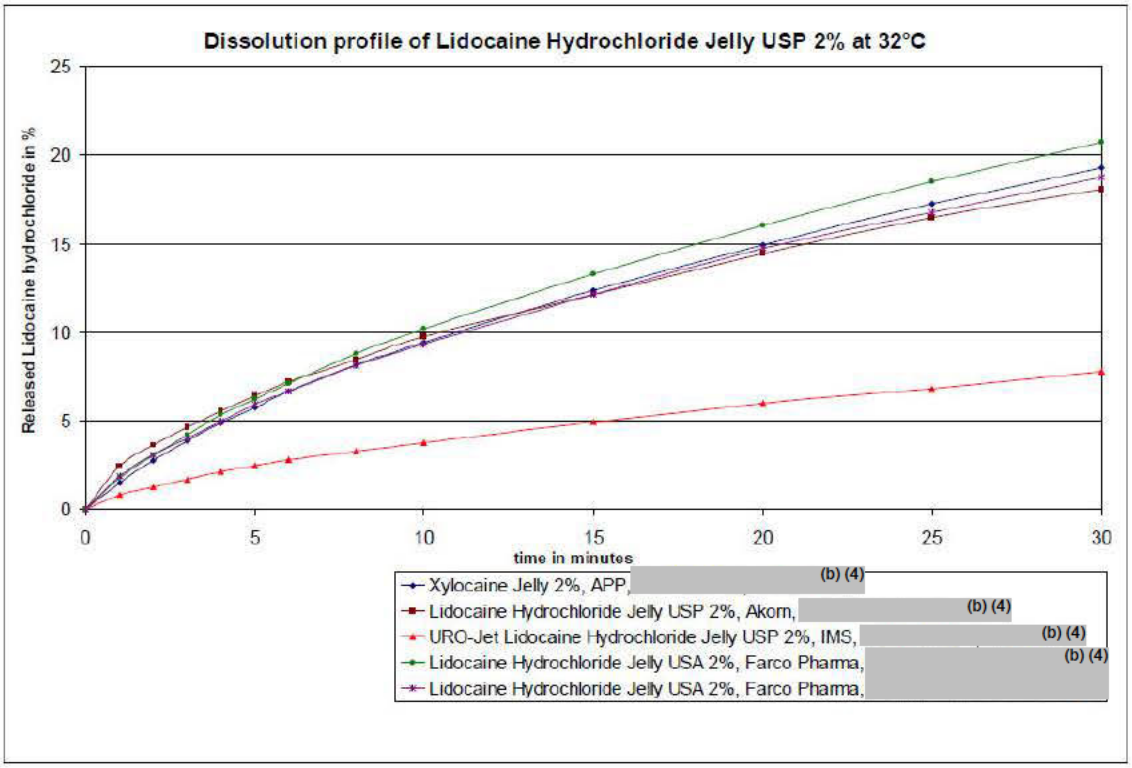
The comparative in vitro dissolution data is presented in the following table.

Dissolution profile of Lidocaine Hydrochloride Jelly USP 2%, at 32°C (skin temperature),

Time [min]	Lidocaine Hydrochloride concentration in the acceptor medium in %				
	Xylocaine Jelly 2%, APP (b) (4)	Lidocaine HCl Jelly USP2%, Akorn (b) (4)	URO-Jet Lidocaine HCl Jelly USP2% (b) (4)	Lidocaine HCl Jelly USA 2%, Farco-Pharma, (b) (4)	Lidocaine HCl Jelly USA 2%, Farco-Pharma, (b) (4)
0	0.00	0.00	0.00	0.00	0.00
1	1.51	2.48	0.82	1.81	1.88
2	2.76	3.63	1.25	3.06	3.08
3	3.89	4.65	1.69	4.19	4.02
4	4.90	5.54	2.14	5.35	4.98
5	5.77	6.45	2.47	6.23	5.97
6	6.66	7.22	2.80	7.13	6.69
8	8.18	8.47	3.27	8.80	8.14
10	9.43	9.75	3.76	10.21	9.34
15	12.37	12.15	4.93	13.31	12.15
20	14.93	14.44	6.00	16.03	14.73
25	17.24	16.47	6.82	18.51	16.80

[13] DARRTS: ANDA 201094 Bioequivalence/Response to Information Request #13 and 14; Submit Date 03/23/2012

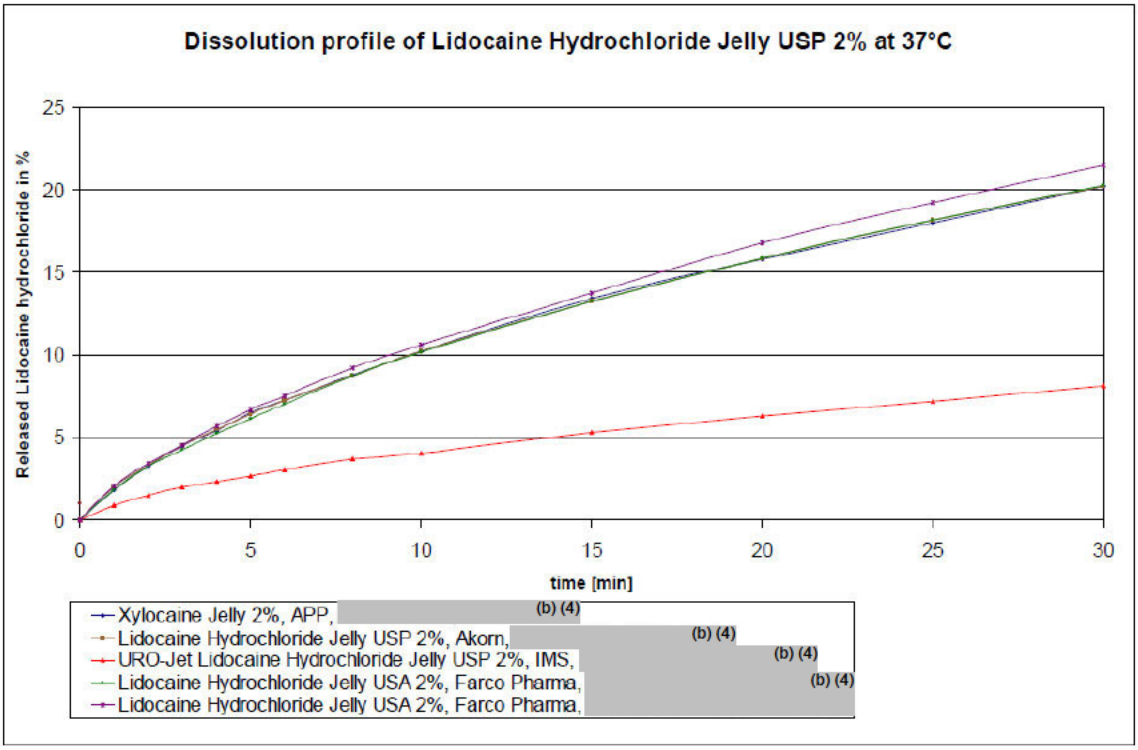
30	19.29	18.08	7.80	20.73	18.77
F1=		8	55	8	4
F2=		92	58	93	98



Dissolution profile of Lidocaine Hydrochloride Jelly USP 2%, at 37°C (Core body temperature)

Time [min]	*Lidocaine Hydrochloride concentration in the acceptor medium in %*				
	Xylocaine Jelly 2%, APP, (b) (4)	Lidocaine HCl Jelly USP 2%, Akorn, (b) (4)	URO-Jet Lidocaine HCl Jelly USP 2%, IMS (b) (4)	Lidocaine HCl Jelly USA 2%, Farco-Pharma,	Lidocaine HCl Jelly USA 2%, Farco-Pharma, (b) (4)
0	0.0	0.0	0.00	0.00	0.00
1	1.8	1.9	0.88	1.82	2.04
2	3.2	3.3	1.49	3.24	3.45
3	4.4	4.5	1.97	4.23	4.55
4	5.4	5.4	2.31	5.25	5.68
5	6.5	6.4	2.66	6.13	6.66
6	7.2	7.2	3.01	7.04	7.50
8	8.7	8.7	3.67	8.7	9.20
10	10.24	10.2	4.05	10.14	10.60
15	13.40	13.2	5.31	13.26	13.73

20	15.80	15.82	6.32	15.84	16.76
25	17.97	18.14	7.19	18.1	19.18
30	20.1	20.1	8.09	20.2	21.48
F1 =		3	55	6	2
F2=		9	58	96	100



The above in vitro dissolution test data demonstrates that viscosity does not have an impact on release of drug substance through the membrane for the drug product with similar formulation.

As it is demonstrated from the in vitro dissolution test data that viscosity does not have an impact on availability of the drug, for the drug product with similar formulation, we are of the opinion that the wide viscosity specification range given (b) (4) for the test product, should not affect the availability of the drug product.

(b) (4)

Reviewer's Note on the Dissolution Method: Per the current ANDA amendment, the release test was based on measurement of the drug release from an extraction cell containing the semi-solid sample preparation and through a Nephrophan dialysis cellulose membrane, into the acceptor medium (water), which was kept at two different temperatures, covering the temperature range of the urethra outside and inside the body (32 °C respectively 37 °C). The cell was attached to the bottom end of a vertical rod of the blade agitator, rotating at a speed of 100 rpm, and samples of the medium were taken at different time intervals to measure the drug release.

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/s/

WAYNE I DEHAVEN
04/16/2012

APRIL C BRADDY
04/17/2012

HOAINHON N CARAMENICO
04/17/2012

BIOEQUIVALENCE AMENDMENT

ANDA 201094

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North VII
7620 Standish Pl.
Rockville, MD 20855-2810

APPLICANT: Sagent Pharmaceuticals, Inc. TEL: (847) 908-1655

ATTN: Kalpesh Shroff FAX: (847) 908-1601

FROM: Teresa Ramson FDA CONTACT PHONE: (240) 276-8782

Dear Sir or Madam:

This facsimile is in reference to the bioequivalence data submitted on December 23, 2009, pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lidocaine Hydrochloride Jelly, 2%.

The Division of Bioequivalence has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached 2 pages. This facsimile is to be regarded as an official FDA communication and unless requested, a hard-copy will not be mailed.

You should submit a response to these deficiencies in accord with 21 CFR 314.96. Your amendment should respond to all the deficiencies listed. **Facsimiles or partial replies will not be considered for review.** Your cover letter should clearly indicate:

Bioequivalence Response to Information Request

If applicable, please clearly identify any new studies (i.e., fasting, fed, multiple dose, dissolution data, waiver or dissolution waiver) that might be included for each strength. We also request that you include a copy of this **communication with your response.**
Please submit a copy of your amendment in an archival (blue) jacket and unless submitted electronically through the gateway, a review (orange) jacket. Please direct any questions concerning this communication to the project manager identified above.

Please remember that when changes are requested to your proposed dissolution methods and/or specifications by the Division of Bioequivalence, an amendment to the Division of Chemistry should also be submitted to revise the release and stability specification. We also recommend that supportive dissolution data or scientific justification be provided in the CMC submission to demonstrate that the revised dissolution specification will be met over the shelf life of the drug product.

SPECIAL INSTRUCTIONS:

*Effective **01-Aug-2010**, the new mailing address for Abbreviated New Drug Application (ANDA) Regulatory Documents is:*

Office of Generic Drugs
Document Control Room, Metro Park North VII
7620 Standish Place
Rockville, Maryland 20855-2810

ANDAs will only be accepted at the new mailing address listed above. For further information, please refer to the following websites prior to submitting your ANDA Regulatory documents: Office of Generic Drugs (OGD): http://www.fda.gov/cder/ogd or Federal Register: http://www.gpoaccess.gov/fr/

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

ANDA: 201094

APPLICANT: Sagent Pharmaceuticals Inc

DRUG PRODUCT: Lidocaine Hydrochloride Jelly, 2%

The Division of Bioequivalence (DBE) has completed its review and the following deficiency has been identified:

You have provided the following physicochemical property data for the test and reference products:

(b) (4)

[redacted]

Based on the above data, the DBE is concerned that the significant viscosity difference between the test and RLD as shown here could lead to different surface retention of the active pharmaceutical ingredient (API), and thus different local drug absorption. Therefore, please justify for such difference, as well as the wide viscosity specification range given [redacted] (b) (4) for the test product. Please submit additional viscosity data from additional batches to establish a more accurate viscosity range of your product.

Sincerely yours,

{See appended electronic signature page}

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

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/s/

DALE P CONNER
11/17/2011

FAX – Microbiology Deficiencies Enclosed

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North VII
7620 Standish Place
Rockville, Maryland 20855 (240-276-8408)

TO: Thomas J Moutvic		**FROM:** Kun Shen
Sagent Pharmaceuticals, Inc.		Microbiology Project Manager
PHONE: (b) (6)		**PHONE:** (240) 276-8722
FAX: (847) 908-1601		**FAX:** (240) 276-8725

Total number of pages, excluding this cover sheet: ____

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7620 Standish Place
Rockville, Maryland 20855

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Microbiology Deficiencies:

Enclosed are the microbiology deficiencies for **ANDA 201094, Lidocaine Hydrochloride Jelly 2%**. The submission reviewed was submitted on May 27, 2011. 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 your microbiology project manager.

LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS:

ANDA: 201094 APPLICANT: Sagent Pharmaceuticals, Inc

DRUG PRODUCT: Lidocaine Hydrochloride Jelly 2%

A. Microbiology Deficiencies:

1. We acknowledge the BI data provided for the validation and requalification studies for [redacted] (b) (4) of the product filled syringes. However, population confirmation study results are not provided. Please indicate the confirmed population of the BIs used in these studies.

2. Regarding production and validation [redacted] (b) (4) parameters, while the acceptance criteria appear to indicate identical parameters in the sterilization cycles for both production and validation, it is implied that [redacted] (b) (4) Please clarify and identify any differences between validation and production conditions for sterilization of the subject drug product. Please provide the rationale for any difference, as necessary.

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

Please consider revising the Jelly Bioburden acceptance limit (10^4 cfu/g) to more closely reflect the actual bioburden determined from screen batches [redacted] (b) (4)

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}

CDR Paul Dexter, M.S.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

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/s/

PAUL L DEXTER
08/17/2011

Labeling Comments

ANDA 20l094

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
240-276-8991

TO: Sagent Pharmaceuticals Inc. TEL: (b) (6)

ATTN: Kalpesh Shrof FAX: 847-908-1601

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 Jelly USP, 2%,

Pages (including cover):4

Labeling comments enclosed

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

ANDA Number: 201094 Date of Submission: December 23, 2009

Applicant's Name: Sagent Pharmaceuticals Inc.

Established Name: Lidocaine Hydrochloride Jelly USP, 2%

Labeling Deficiencies:

1. GENERAL COMMENTS

   a. We note that the proprietary name “Glydo” is unacceptable by Division of Medication Error Prevention and Analysis. If you do not intend to submit the alternate proprietary name (b) (4) then submit the labels, and labeling using the established name.

   b. Please note that the appearance of a person's name on a drug product label without qualification is a representation that the named person is the sole manufacturer of the product. FARCO-PHARMA GmbH is NOT the manufacturer of this drug product, Please clarify. See 21 CFR 201.1 for guidance.

2. SYRINGE –6 mL and 11 mL

   a. Revise the storage temperature to read (b) (4)

   b. Please put in bold and capitalize “TOPICAL” in “Sterile Topical Anesthetic”.

3. BLISTER

   Please refer to SYRINGE comment b.

4. CARTON – (10s)

   a. Inside Top Panel: (b) (4)

   b. The consumer may overlook the text printed in the “inside top panel”. Please relocate the text to the top (large) panel instead.

   c. (b) (4)

   d. Please refer to SYRINGE comment b.

3. INSERT

a. DOSAGE AND ADMINISTRATION: revise the subsection as follow:

For surface anesthesia of the male adult urethra

The outer orifice is washed and disinfected. The plastic tip is introduced into the orifice, where it is firmly held in position. The jelly is instilled by an easy syringe-like action, until the patient has a feeling of tension or until about 15 mL (i.e., 300 mg of lidocaine hydrochloride) is instilled. A penile clamp is then applied for several minutes at the corona and then additional jelly (about 15 mL) 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 (i.e.,600 mg) is usually required to fill and dilate the male urethra. Prior to catheterization, smaller volumes of 5 to 10 mL (100-200 mg) are usually adequate for lubrication.

b. HOW SUPPLIED

(b) (4)

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

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/s/

JOHN F GRACE
07/29/2011

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

ANDA 201094

PROPRIETARY NAME REQUEST
UNACCEPTABLE

Sagent Pharmaceuticals, Inc.
1901 Roselle Road, Suite 700
Schaumburg, IL 60195

ATTENTION: Kalpesh Shroff
Associate Director, Regulatory Affairs

Dear Mr. Shroff:

Please refer to your Abbreviated New Drug Application (ANDA) dated December 23, 2009, received December 23, 2009, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act for Lidocaine Hydrochloride Jelly USP, 2%.

We also refer to your July 14, 2010, correspondence, received July 15, 2010, requesting review of your proposed proprietary name, Glydo. We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons:

The proposed name, Glydo, is similar to the currently marketed product Glyco, pursuant to 21 CFR 201.10(5) which states "designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient."

We note that you have proposed an alternate proprietary name in your submission dated July 14, 2010. In order to initiate the review of the alternate proprietary name, (b) (4) submit a new complete request for proprietary name review. The review of this alternate name will not be initiated until the new submission is received.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Danyal Chaudhry, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3813. For any other information regarding this application contact the Office of Generic Drugs (OGD) Regulatory Project Manager, Ted Palat at 240 276-8982.

Sincerely,
{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

CAROL A HOLQUIST
04/15/2011

FAX – Microbiology Deficiencies Enclosed

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North VII
7620 Standish Place
Rockville, Maryland 20855 (240-276-8408)

TO: Kalpesh Shroff		**FROM:** Kun Shen
Sagent Pharmaceuticals, Inc		Microbiology Project Manager
PHONE: 547-908-1600		**PHONE:** (240) 276-8722
FAX: 847-908-1601		**FAX:** (240) 276-8725

Total number of pages, excluding this cover sheet: ____

SPECIAL INSTRUCTIONS:

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Document Control Room, Metro Park North VII
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Rockville, Maryland 20855

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Microbiology Deficiencies:

Enclosed are the microbiology deficiencies for **ANDA 201094, Lidocaine Hydrochloride Jelly 2%**. The submission reviewed was submitted on December 23, 2009. 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 your microbiology project manager.

LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS:

ANDA: 201094 APPLICANT: Sagent Pharmaceuticals, Inc

DRUG PRODUCT: Lidocaine Hydrochloride Jelly 2%

Microbiology Deficiencies:

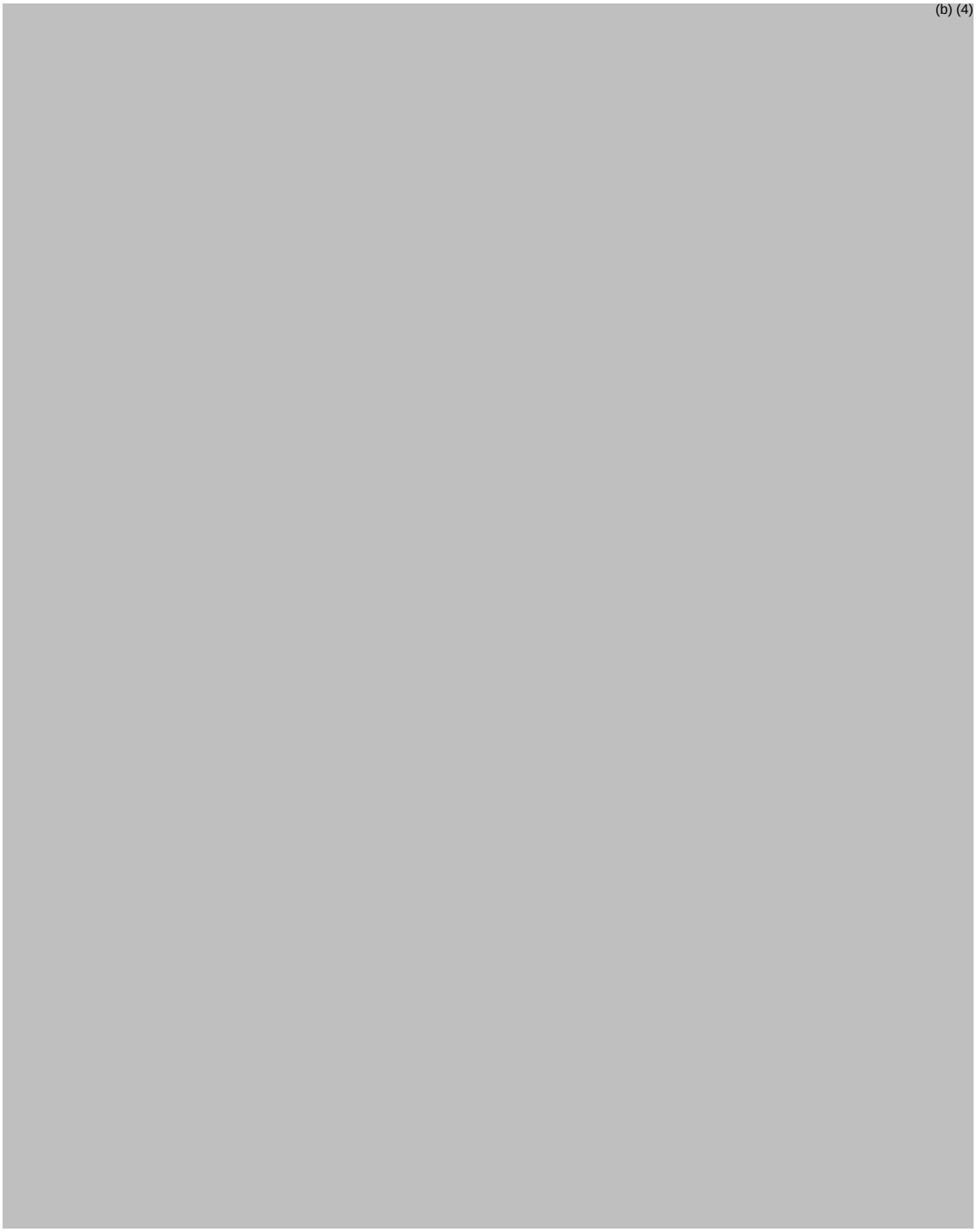
1. Regarding container/closure integrity: the data provided for the container/closure integrity test does not adequately assess the integrity of the subject container/closure. The description of the bacterial challenge (b) (4) Please provide test results to adequately validate container closure integrity, including the method of detection and the sensitivity of the testing method. (b) (4) (b) (4) (b) (4) Please confirm the container closure system used during validation is the same or equivalent as that used for the commercial batch of the drug. If any component is different from the subject drug product container/closure, please provide justification or rationale for its use.

2. (b) (4)

3.

4. Please provide bioburden alert and action levels for purified water.

5. (b) (4)



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}

CDR Paul Dexter, M.S.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

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/s/

BRENDA A PILLARI
03/07/2011

ANDA CHECKLIST FOR CTD or eCTD FORMAT
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION FOR FILING

For More Information on Submission of an ANDA in Electronic Common Technical Document (eCTD) Format please go to: http://www.fda.gov/cder/regulatory/ersr/ectd.htm
***For a Comprehensive Table of Contents Headings and Hierarchy please go to:**
http://www.fda.gov/cder/regulatory/ersr/5640CTOC-v1.2.pdf
**** For more CTD and eCTD informational links see the final page of the ANDA Checklist**
***** A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage http://www.fda.gov/cder/ogd/ *****

ANDA #: 201094 **FIRM NAME**: FARCO PHARMA GMBH

PIV: NO **Electronic or Paper Submission:** ELECTRONIC (GATEWAY)

RELATED APPLICATION(S): (b) (4)

First Generic Product Received? NO

DRUG NAME: LIDOCAINE HYDROCHLORIDE
DOSAGE FORM: JELLY USP, 2%

Review Team: (Bolded/Italicized & Checked indicate Assignment or DARRTS designation)

Quality Team: DC3 Team 12 ☒ ***Activity***	***Bio Team 6: Bing Li*** ☒ ***Activity***
ANDA/Quality RPM: Leign Ann Bradford ☒ ***FYI***	Bio PM: Nam J. Chun (Esther) ☐ ***FYI***
Quality Team Leader: Iser, Robert No assignment needed in DARRTS	***Clinical Endpoint Team Assignment: (No)*** ☐ ***Activity***
Labeling Reviewer: Thuyanh (Ann) Vu ☒ ***Activity***	***Micro Review (No)*** ☐ ***Activity***

*****Document Room Note: for New Strength amendments and supplements, if specific reviewer(s) have already been assigned for the original, please assign to those reviewer(s) instead of the default random team(s). *****

Letter Date: DECEMBER 23, 2009 **Received Date**: DECEMBER 23, 2009

Comments: EC - 1 YES **On Cards:** YES
Therapeutic Code: 6040400 LOCAL ANESTHETICS, TOPICAL

Archival copy: ELECTRONIC (GATEWAY) **Sections** I
Review copy: NA E-Media Disposition: NA
Not applicable to electronic sections

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 Ted Palat **Date 02/26/2010**	**Recommendation:** ☒ **FILE** ☐ **REFUSE to RECEIVE**

Supervisory Concurrence/Date: _____ **Date:** _____

1. Edit Application Property Type in DARRTS where applicable for
   a. First Generic Received
      ☐ Yes ☒ No
   b. Market Availability
      ☒ Rx ☐ OTC
   c. Pepfar
      ☐ Yes ☒ No
   d. Product Type
      ☐ Small Molecule Drug (usually for most ANDAs except protein drug products)
   e. USP Drug Product (at time of filing review)
      ☒ Yes ☐ No
2. Edit Submission Patent Records
   ☒ Yes
3. Edit Contacts Database with Bioequivalence Recordation where applicable
   ☐ Yes
4. Requested EER
   ☐ Yes

ADDITIONAL COMMENTS REGARDING THE ANDA: Audrey Zaweski 516-222-6222
1. submit reprocessing statement. – comment placed in ACK letter
2. The drug product is packaged in syringes for topical use. The RLD is packaged in tubes for topical use. This is considered a change in packaging and not a change in dosage form.

MODULE 1
ADMINISTRATIVE

		ACCEPTABLE
1.1	**1.1.2 Signed and Completed Application Form (356h) (original signature)** (Check Rx/OTC Status) RX YES	☒
1.2	**Cover Letter** Dated: DECEMBER 23, 2009	☒
1.2.1	**Form FDA 3674 (PDF) YES**	☒
*	**Table of Contents (paper submission only)** YES	☒
1.3.2	**Field Copy Certification (original signature)** NA **(N/A for E-Submissions)**	☒
1.3.3	**Debarment Certification-GDEA (Generic Drug Enforcement Act)/Other:** 1. Debarment Certification (original signature) YES SEE SECTION 1.3.3 2. List of Convictions statement (original signature) SAME	☒
1.3.4	**Financial Certifications** Bioavailability/Bioequivalence Financial Certification (Form FDA 3454) NA Disclosure Statement (Form FDA 3455, submit copy to Regulatory Branch Chief) NA	☒

1.3.5	**1.3.5.1 Patent Information** Patents listed for the RLD in the Electronic Orange Book Approved Drug Products with Therapeutic Equivalence Evaluations **1.3.5.2 Patent Certification** 1. Patent number(s) **Patent and Exclusivity Search Results from query on Appl No 008816 Product 001 in the OB_Rx list.** **There are no unexpired patents for this product in the Orange Book Database.** **There is no unexpired exclusivity for this product.** 2. Paragraph: (Check all certifications that apply) MOU ☐ PI ☐ PII ☒ PIII ☐ PIV ☐ (Statement of Notification) ☐ 3. Expiration of Patent(s): NA a. Pediatric exclusivity submitted? b. Expiration of Pediatric Exclusivity? 4. Exclusivity Statement: YES no exlcusivity	☒
1.4.1	**References** Letters of Authorization 1. DMF letters of authorization a. Type II DMF authorization letter(s) or synthesis for Active Pharmaceutical Ingredient YES Type II DMF No. (b) (4) b. Type III DMF authorization letter(s) for container closure YES 2. US Agent Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) YES	☒

(b) (4)

[redacted]

1.12.11	**Basis for Submission** **OK** NDA# : 008816 Ref Listed Drug: XYLOCAINE Firm: APP PHARMS ANDA suitability petition required? NA If Yes, then is change subject to PREA (change in dosage form, route or active ingredient) see section 1.9.1	☒

MODULE 1 (Continued)
ADMINISTRATIVE

ACCEPTABLE

1.12.12	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use SAME 2. Active ingredients SAME 3. Inactive ingredients SAME minus (b) (4) 4. Route of administration SAME 5. Dosage Form SAME 6. Strength SAME	☒
1.12.14	**Environmental Impact Analysis Statement** YES SEE SECTION 1.12.14	☒
1.12.15	**Request for Waiver** Request for Waiver of In-Vivo BA/BE Study(ies): YES SEE SECTION 1.12.15 A Biowaiver was granted for 040837 Lidocaine 2% Jelly by Hi-Tech. also see ANDA 40-911 Additional Comments regarding the ANDA: **As per OGD Internal meeting conducted on 2/2/2000 and emails conducted between OGD management, it was concluded that "…topical products already coded AT we were going to continue waiving. The rationale being that it would be time-consuming and disruptive to ask for in-vivo studies for all of these products. For post-62 RLDs single source products, we were going to request in-vivo studies. From COMIS, the original RLD from Astra Zeneca was approved in 1951 (pre-62) and withdrawn in 2003. Since we have waived in-vivo for this product and coded it AT, we will waive. " (as per email from Lizzie Sanchez).** **Note: Firm also supplied container closure information (e.g. materials, dimensions) in C1.4, 3.2.P.2.4.** **Enter Review Productivity and Generate Report** http://cdsogd1/bioprod **Application Number Search Results from "OB_Rx" table for query on "008816."**	☒

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
N008816	AT	Yes	LIDOCAINE HYDROCHLORIDE	JELLY; TOPICAL	2%	XYLOCAINE	APP PHARMS

1.14.1	**Draft Labeling (Mult Copies N/A for E-Submissions)** **1.14.1.1** 4 copies of draft (each strength and container) YES **1.14.1.2** 1 side by side labeling comparison of containers and carton with all differences annotated and explained YES **1.14.1.3** 1 package insert (content of labeling) submitted electronically YES ***Was a proprietary name request submitted? YES (If yes, send email to Labeling Reviewer indicating such.)	☒
1.14.3	**Listed Drug Labeling** **1.14.3.1** 1 side by side labeling (package and patient insert) comparison with all differences annotated and explained YES **1.14.3.3** 1 RLD label and 1 RLD container label YES	☒

MODULE 2
SUMMARIES ACCEPTABLE

2.3	**Quality Overall Summary (QOS)** **E-Submission: PDF** YES **Word Processed e.g., MS Word** YES A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage http://www.fda.gov/cder/ogd/ **Question based Review (QbR)** YES **2.3.S** **Drug Substance (Active Pharmaceutical Ingredient)** YES **2.3.S.1 General Information** **2.3.S.2 Manufacture** **2.3.S.3 Characterization** **2.3.S.4 Control of Drug Substance** **2.3.S.5 Reference Standards or Materials** **2.3.S.6 Container Closure System** **2.3.S.7 Stability** **2.3.P** **Drug Product** YES **2.3.P.1 Description and Composition of the Drug Product** **2.3.P.2 Pharmaceutical Development** **2.3.P.2.1 Components of the Drug Product** **2.3.P.2.1.1 Drug Substance** **2.3.P.2.1.2 Excipients** **2.3.P.2.2 Drug Product** **2.3.P.2.3 Manufacturing Process Development** **2.3.P.2.4 Container Closure System** **2.3.P.3 Manufacture** **2.3.P.4 Control of Excipients** **2.3.P.5 Control of Drug Product** **2.3.P.6 Reference Standards or Materials** **2.3.P.7 Container Closure System** **2.3.P.8 Stability**	☒
2.7	**Clinical Summary (Bioequivalence) NA** **Model Bioequivalence Data Summary Tables** **E-Submission: PDF** **Word Processed e.g., MS Word** **2.7.1 Summary of Biopharmaceutic Studies and Associated Analytical Methods** **2.7.1.1 Background and Overview** Table 1. Submission Summary Table 4. Bioanalytical Method Validation Table 6. Formulation Data YES **2.7.1.2 Summary of Results of Individual Studies** Table 5. Summary of In Vitro Dissolution **2.7.1.3 Comparison and Analyses of Results Across Studies** Table 2. Summary of Bioavailability (BA) Studies Table 3. Statistical Summary of the Comparative BA Data **2.7.1.4 Appendix** **2.7.4.1.3 Demographic and Other Characteristics of Study Population** Table 7. Demographic Profile of Subjects Completing the Bioequivalence Study **2.7.4.2.1.1 Common Adverse Events** Table 8. Incidence of Adverse Events in Individual Studies	☐

MODULE 3

3.2.S DRUG SUBSTANCE ACCEPTABLE

3.2.S.1	**General Information** **3.2.S.1.1 Nomenclature** **3.2.S.1.2 Structure** **3.2.S.1.3 General Properties**	☒
3.2.S.2	**Manufacturer** **3.2.S.2.1** **Manufacturer(s) (This section includes contract manufacturers and testing labs)** **Drug Substance (Active Pharmaceutical Ingredient)** 1. Name and Full Address(es)of the Facility(ies) **Who manufactures the drug substance?** (b) (4) 2. Function or Responsibility YES 3. Type II DMF number for API YES 4. CFN or FEI numbers YES	☒
3.2.S.3	**Characterization**	☒
3.2.S.4	**Control of Drug Substance (Active Pharmaceutical Ingredient)** **3.2.S.4.1 Specification** Testing specifications and data from drug substance manufacturer(s) YES **3.2.S.4.2 Analytical Procedures** YES **3.2.S.4.3 Validation of Analytical Procedures** 1. Spectra and chromatograms for reference standards and test samples YES 2. Samples-Statement of Availability and Identification of: a. Drug Substance YES b. Same lot number(s) YES **3.2.S.4.4 Batch Analysis** 1. COA(s) specifications and test results from drug substance mfgr(s) YES 2. Applicant certificate of analysis YES **3.2.S.4.5 Justification of Specification**	☒
3.2.S.5	**Reference Standards or Materials**	☒
3.2.S.6	**Container Closure Systems**	☒
3.2.S.7	**Stability**	☒

MODULE 3

3.2.P DRUG PRODUCT ACCEPTABLE

3.2.P.1	**Description and Composition of the Drug Product** 1. Unit composition The quantitative composition and function of each component in the drug product is listed below. (b) (4) 2. Inactive ingredients and amounts are appropriate per IIG YES	☒

IIG Table:

(b) (4)

3.2.P.2	**Pharmaceutical Development** Pharmaceutical Development Report YES	☒
3.2.P.3	**Manufacture** **3.2.P.3.1 Manufacture(s)** (Finished Dosage Manufacturer and Outside Contract Testing Laboratories) 1. Name and Full Address(es)of the Facility(ies) **2.3.P.3 Manufacture** **Who manufactures the drug product?** (b) (4) 2. CGMP Certification: YES SEE SECTION 3.2.P.3.1 3. Function or Responsibility YES 4. CFN or FEI numbers YES **3.2.P.3.2 Batch Formula** YES **3.2.P.3.3 Description of Manufacturing Process and Process Controls** (b) (4) **3.2.P.3.4 Controls of Critical Steps and Intermediates** **3.2.P.3.5 Process Validation and/or Evaluation** 1. Microbiological sterilization validation YES 2. Filter validation (if aseptic fill) NA	☒
3.2.P.4	**Controls of Excipients (Inactive Ingredients)** Source of inactive ingredients identified YES **3.2.P.4.1 Specifications** 1. Testing specifications (including identification and characterization) YES 2. Suppliers' COA (specifications and test results) YES **3.2.P.4.2 Analytical Procedures** **3.2.P.4.3 Validation of Analytical Procedures** **3.2.P.4.4 Justification of Specifications** Applicant COA YES	☒

MODULE 3

3.2.P DRUG PRODUCT

ACCEPTABLE

3.2.P.5	**Controls of Drug Product** **3.2.P.5.1 Specification(s)** YES **3.2.P.5.2 Analytical Procedures** YES **3.2.P.5.3 Validation of Analytical Procedures** Samples - Statement of Availability and Identification of: 1. Finished Dosage Form YES 2. Same lot numbers YES **3.2.P.5.4 Batch Analysis** Certificate of Analysis for Finished Dosage Form YES **3.2.P.5.5 Characterization of Impurities** **3.2.P.5.6 Justification of Specifications**	☒
3.2.P.7	**Container Closure System** 1. Summary of Container/Closure System (if new resin, provide data) YES 2. Components Specification and Test Data YES 3. Packaging Configuration and Sizes **HOW SUPPLIED** LIDOCAINE HYDROCHLORIDE JELLY (lidocaine HCl) 2% is supplied in the listed dosage forms. NDC xxxxxxxxxx 6 mL syringes, in sterile blister packs Boxes of 10 NDC xxxxxxxxxx 11 mL syringes, in sterile blister packs Boxes of 10 4. Container/Closure Testing YES 5. Source of supply and suppliers address YES	☒
3.2.P.8	**3.2.P.8.1 Stability (Finished Dosage Form)** 1. Stability Protocol submitted YES 2. Expiration Dating Period 24 months **3.2.P.8.2 Post-approval Stability and Conclusion** Post Approval Stability Protocol and Commitments YES **3.2.P.8.3 Stability Data** 1. 3 month accelerated stability data YES 2. Batch numbers on stability records the same as the test batch **YES**	☒

MODULE 3

3.2.R Regional Information

ACCEPTABLE

3.2.R (Drug Substance)	**3.2.R.1.S Executed Batch Records for drug substance (if available) NO** **3.2.R.2.S Comparability Protocols NO** **3.2.R.3.S Methods Validation Package YES** Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☒

3.2.R (Drug Product)	**3.2.R.1.P.1** **Executed Batch Records** Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures) Batch Reconciliation and Label Reconciliation YES **What is the reconciliation of the exhibit batch?** (b) (4) [redacted] **3.2.R.1.P.2 Information on Components** YES **3.2.R.2.P Comparability Protocols** NO **3.2.R.3.P Methods Validation Package** YES Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☒

MODULE 5

CLINICAL STUDY REPORTS NA

ACCEPTABLE

5.2	**Tabular Listing of Clinical Studies**	☐

5.3.1 (complete study data)	**Bioavailability/Bioequivalence** **1. Formulation data same?** a. Comparison of all Strengths (check proportionality of multiple strengths) b. Parenterals, Ophthalmics, Otics and Topicals per 21 CFR 314.94 (a)(9)(iii)-(v) **2. Lot Numbers of Products used in BE Study(ies):** **3. Study Type: IN-VIVO PK STUDY(IES)** (Continue with the appropriate study type box below)	☐
	5.3.1.2 Comparative BA/BE Study Reports 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. Summary Bioequivalence tables: Table 10. Study Information Table 12. Dropout Information Table 13. Protocol Deviations **5.3.1.3** **In Vitro-In-Vivo Correlation Study Reports** 1. Summary Bioequivalence tables: Table 11. Product Information Table 16. Composition of Meal Used in Fed Bioequivalence Study **5.3.1.4** **Reports of Bioanalytical and Analytical Methods for Human Studies** 1. Summary Bioequivalence table: Table 9. Reanalysis of Study Samples Table 14. Summary of Standard Curve and QC Data for Bioequivalence Sample Analyses Table 15. SOPs Dealing with Bioanalytical Repeats of Study Samples **5.3.7** **Case Report Forms and Individual Patient Listing**	☐
5.4	**Literature References**	☐
	Possible Study Types:	
Study Type	**IN-VIVO BE STUDY(IES) with PK ENDPOINTS** (i.e., fasting/fed/sprinkle) NA 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted: NA 3. In-Vitro Dissolution: NO	☐
Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** NO 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria: 90% CI of the proportional difference in success rate between test and reference must be within (-0.20, +0.20) for a binary/dichotomous endpoint. For a continuous endpoint, the test/reference ratio of the mean result must be within (0.80, 1.25). 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted	☐

Study Type	**IN-VITRO BE STUDY(IES)** (i.e., in vitro binding assays) NO 1. Study(ies) meets BE criteria (90% CI of 80-125) 2. EDR Email: Data Files Submitted: 3. In-Vitro Dissolution:	☐
Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** 1. Solutions (Q1/Q2 sameness): a. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming) 2. Suspensions (Q1/Q2 sameness): a. In-Vivo PK Study 1. Study(ies) meets BE Criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted b. In-Vivo BE Study with Clinical End Points 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria (90% CI within +/- 20% of 80-125) 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted c. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming)	☐
Study Type	**IN-VIVO BE STUDY(IES) with PD ENDPOINTS** (e.g., topical corticosteroid vasoconstrictor studies) 1. Pilot Study (determination of ED50) 2. Pivotal Study (study meets BE criteria 90%CI of 80-125)	☐
Study Type	**TRANSDERMAL DELIVERY SYSTEMS** 1. In-Vivo PK Study 1. Study(ies) meet BE Criteria (90% CI of 80-125, C max, AUC) 2. In-Vitro Dissolution 3. EDR Email: Data Files Submitted 2. Adhesion Study 3. Skin Irritation/Sensitization Study	☐

Updated 10/19/2009

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-201094	ORIG-1	FARCO PHARMA GMBH	LIDOCAINE HYDROCHLORIDE

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/s/

TED C PALAT
03/19/2010

MARTIN H Shimer
03/25/2010

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 201094

Lachman Consultant Services, Inc.
US Agent for Farco Pharma GmbH
Attention: Audrey Zaweski
1600 Stewart Avenue
Suite 604
Westbury, NY 11590

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, 2%

DATE OF APPLICATION: December 23, 2009

DATE (RECEIVED) ACCEPTABLE FOR FILING: December 23, 2009

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.

In the interim, please submit a reprocessing statement.

Should you have questions concerning this application, contact:

Leigh Ann Bradford
Project Manager
240-276-8453

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-201094	ORIG-1	FARCO PHARMA GMBH	LIDOCAINE HYDROCHLORIDE

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/s/

MARTIN H Shimer
03/25/2010
Signing for Wm Peter Rickman