CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 91-306

Name: Fluocinolone Acetonide Topical Oil, 0.01% (Ear Drops)

Sponsor: Identi Pharmaceuticals Inc.

Approval Date: October 17, 2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 91-306

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 91-306

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 091306

SciRegs International, Inc.
U.S. Agent for: Identi Pharmaceuticals Inc.
Attention: Jeanne Taborsky
President & CEO
6333 Summercrest Drive
Columbia, MD 21045

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated April 16, 2009, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Fluocinolone Acetonide Topical Oil, 0.01% (Ear Drops).

Reference is also made to your amendments dated August 26, August 27, and October 6, 2009; July 8, August 12, August 17, September 20, October 1, December 15, and December 17, 2010; and March 16, March 22, June 8, August 19, September 29, and October 4, 2011.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Fluocinolone Acetonide Topical Oil, 0.01% (Ear Drops) to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug, DermOtic Ear Drops, 0.01%, of Hill Dermaceuticals, 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 505-1(i).

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

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

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

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

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

The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

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

/s/

ROBERT L WEST

10/17/2011

Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 91-306

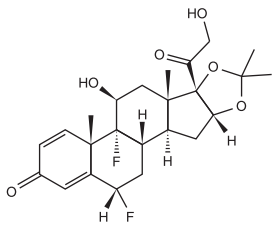
LABELING

Fluocinolone Acetonide Oil 0.01% Ear Drops

For Otic Use Only-
Not for Ophthalmic Use

DESCRIPTION

Fluocinolone Acetonide Oil 0.01% Ear Drops contain fluocinolone acetonide {(6α, 11β, 16α)-6,9-difluoro-11,21-dihydroxy-16,17[(1-methylethylidene)bis(oxy)]-pregna-1,4-diene-3,20-dione, cyclic 16,17 acetal with acetone}, a synthetic corticosteroid. Chemically, fluocinolone acetonide is C_{24} H_{30} F_2O_6 anhydrous. It has the following structural formula:



Fluocinolone acetonide in Fluocinolone Acetonide Oil 0.01% has a molecular weight of 452.49. It is a white crystalline powder that is odorless, stable in light, and melts at 270°C with decomposition; soluble in alcohol, acetone and methanol; slightly soluble in chloroform; insoluble in water.

Each gram of Fluocinolone Acetonide Oil 0.01% contains approximately 0.11 mg of fluocinolone acetonide in a blend of oils, which contains isopropyl alcohol, isopropyl myristate, light mineral oil, oleth-2, and refined peanut oil NF.

CLINICAL PHARMACOLOGY

Like other topical corticosteroids, fluocinolone acetonide has anti-inflammatory, antipruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of the topical steroids, in general, is unclear. However, corticosteroids are thought to act by the induction of phospholipase A_2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A_2.

Pharmacokinetics: The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle and the integrity of the epidermal barrier. Occlusion of topical corticosteroids can enhance penetration. Topical corticosteroids can be absorbed from normal intact skin. Also, inflammation and/or other disease processes in the skin can increase percutaneous absorption.

Fluocinolone Acetonide Oil 0.01% is in the low to medium range of potency as compared with other topical corticosteroids.

CLINICAL STUDIES

Efficacy in a placebo-controlled study for the treatment of chronic eczematous external otitis on 154 patients (adults and children 2 years of age and older) treated with five drops per ear of fluocinolone acetonide oil 0.01% twice daily, after 7 days of treatment, showed fluocinolone acetonide oil 0.01% to be superior to placebo in clearing the signs and symptoms of eczematous external otitis.

Clinical safety studies were conducted on the same formulation of fluocinolone acetonide oil 0.01%, marketed as Fluocinolone Acetonide 0.01% Topical Oil. Open-label safety studies on 33 children (20 subjects ages 2 to 6 years, 13 subjects ages 7 to 12 years) with moderate to severe stable atopic dermatitis, and baseline body surface area involvement greater than 75% in 18 patients, and 50% to 75% in 15 patients, were treated with Fluocinolone Acetonide 0.01% Topical Oil twice daily for 4 weeks. Morning pre-stimulation cortisol level and post-Cortrosyn stimulation cortisol level were obtained in each subject at the beginning of the trial and at the end of 4 weeks of treatment. At the end of treatment, 4 out of 18 subjects aged 2 to 5 years showed low pre-stimulation cortisol levels (3.2 to 6.6 mcg/dL; normal: cortisol > 7mcg/dL) but all had normal responses to 0.25 mg of Cortrosyn stimulation (cortisol > 18 mcg/dL).

A clinical study was conducted to assess the safety of Fluocinolone Acetonide 0.01% Topical Oil, which contains refined peanut oil, on subjects with known peanut allergies. The study enrolled 13 patients with atopic dermatitis, 6 to 17 years of age. Of the 13 patients, 9 were Radioallergosorbent Test (RAST) positive to peanuts and 4 had no peanut sensitivity (controls). The study evaluated the responses to both prick test and patch test utilizing peanut oil NF, Fluocinolone Acetonide 0.01% Topical Oil and histamine/saline controls on the 13 individuals. These subjects were also treated with Fluocinolone Acetonide 0.01% Topical Oil twice daily for 7 days. Prick test and patch test results for all 13 patients were negative to Fluocinolone Acetonide 0.01% Topical Oil and the refined peanut oil. One of the 9 peanut-sensitive patients experienced an exacerbation of atopic dermatitis after 5 days of Fluocinolone Acetonide 0.01% Topical Oil use. Importantly, the bulk peanut oil NF, used in Fluocinolone Acetonide 0.01% Oil is heated at 475°F for at least 15 minutes, which should provide for adequate decomposition of allergenic proteins.

INDICATION AND USAGE

Fluocinolone Acetonide Oil 0.01% is a low to medium potency corticosteroid indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years old and older.

CONTRAINDICATIONS

Fluocinolone Acetonide Oil 0.01% is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

This product contains refined peanut oil NF (See PRECAUTIONS).

PRECAUTIONS

General: Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment.

Patients applying a topical steroid to a large surface area or to areas under occlusion should be evaluated periodically for evidence of HPA axis suppression. This may be done by using the ACTH stimulation, A.M. plasma cortisol, and urinary free cortisol tests.

If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent corticosteroid. Infrequently, signs and symptoms of glucocorticoid insufficiency may occur requiring supplemental systemic corticosteroids. For information on systemic supplementation, see prescribing information for those products.

Children may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. (See PRECAUTIONS-Pediatric use)

Allergic contact dermatitis to any component of topical corticosteroids is usually diagnosed by a failure to heal rather than noting a clinical exacerbation, which may occur with most topical products not containing corticosteroids. Such an observation should be corroborated with appropriate diagnostic testing.

If wheal and flare type reactions (which may be limited to pruritus) or other manifestations of hypersensitivity develop, fluocinolone acetonide oil 0.01% should be discontinued immediately and appropriate therapy instituted.

If concomitant skin infections are present or develop, an appropriate antifungal or antibacterial agent should be used. If a favorable response does not occur promptly, use of fluocinolone acetonide oil 0.01% should be discontinued until the infection has been adequately controlled.

Fluocinolone acetonide oil 0.01% is formulated with 48% refined peanut oil NF. Physicians should use caution in prescribing Fluocinolone Acetonide Oil 0.01% for peanut-sensitive individuals.

Information for Patients: Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external ear use only. Do not use occlusive dressings.

2. Avoid contact with the eyes. In case of contact, wash eyes liberally with water.

3. This medication should not be used for any disorder other than that for which it was prescribed.

4. Patients should promptly report to their physician any worsening of their skin condition.

5. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, contact the physician.

Laboratory Tests: The following tests may be helpful in evaluating patients for HPA axis suppression:
ACTH stimulation test
A.M. plasma cortisol test
Urinary free cortisol test

Carcinogenesis, mutagenesis, and impairment of fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of fluocinolone acetonide oil 0.01%. Studies have not been performed to evaluate the mutagenic potential of fluocinolone acetonide, the active ingredient in fluocinolone acetonide oil 0.01%. Some corticosteroids have been found to be genotoxic in various genotoxicity tests (i.e. the *in vitro* human peripheral blood lymphocyte chromosome aberration assay with metabolic activation, the *in vivo* mouse bone marrow micronucleus assay, the Chinese hamster micronucleus test and the *in vitro* mouse lymphoma gene mutation assay).

Pregnancy: Teratogenic effects: Pregnancy category C: Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application in laboratory animals.

There are no adequate and well-controlled studies in pregnant women on teratogenic effects from fluocinolone acetonide oil 0.01%. Therefore, fluocinolone acetonide oil 0.01% should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when fluocinolone acetonide oil 0.01% is administered to a nursing woman.

Pediatric Use: Fluocinolone acetonide oil 0.01% may be used twice daily for up to 2 weeks in pediatric patients 2 years of age and older with chronic eczematous external otitis.

Fluocinolone acetonide oil 0.01% is not recommended for use on the face (See ADVERSE REACTIONS section).

Because of a higher ratio of skin surface area to body mass, children are at a greater risk than adults of HPA-axis-suppression when they are treated with topical corticosteroids. They are therefore also at greater risk of glucocorticosteroid insufficiency after withdrawal of treatment and of Cushing's syndrome while on treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children. (See PRECAUTIONS).

HPA axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Children may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Fluocinolone acetonide oil 0.01% is formulated with 48% refined peanut oil NF. Physicians should use caution in prescribing Fluocinolone Acetonide Oil 0.01% for peanut-sensitive individuals.

ADVERSE REACTIONS

The following local adverse reactions have been reported infrequently with topical corticosteroids. They may occur more frequently with the use of occlusive dressings, especially with higher potency corticosteroids. These reactions are listed in an approximate decreasing order of occurrence: burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, skin atrophy, striae, and miliaria.

OVERDOSAGE

Topically applied fluocinolone acetonide oil 0.01% can be absorbed in sufficient amounts to produce systemic effects (See PRECAUTIONS).

DOSAGE AND ADMINISTRATION

For the treatment of chronic eczematous external otitis, using the supplied ear-dropper, apply 5 drops of fluocinolone acetonide oil 0.01% into the affected ear. To apply, tilt head to one side so that the ear is facing up. Then gently pull the ear lobe backward and upward and apply 5 drops of fluocinolone acetonide oil 0.01% into the ear. Keep head tilted for about a minute to allow fluocinolone acetonide oil 0.01% to penetrate lower into the ear canal. Gently pat excess material dripping out of the ear using a clean cotton ball. Follow these instructions twice each day for 7 to 14 days.

HOW SUPPLIED

Fluocinolone Acetonide Oil 0.01% Ear Drops is supplied in 1 fluid ounce bottles with a net contents of 20 mL (Dropper Included) (NDC # 65162-702-94).

Keep tightly closed. Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

CAUTION: Rx only

Manufactured by:
Amneal Pharmaceuticals
Branchburg, NJ 08876

Distributed by:
Amneal Pharmaceuticals
Glasgow, KY 42141

Rev. 09-2011

702-985

Fluocinolone Acetonide Oil 0.01% Ear Drops

Rx Only
Rev. 09-2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 91-306

LABELING REVIEWS

APPROVAL SUMMARY #1

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

ANDA Number: 91-306
Date of Submission: **October 4, 2011**
Applicant's Name: Identi Pharmaceuticals, LLC.
Established Name: Fluocinolone Acetonide Oil, 0.01% (Ear Drops)

REMS required? NO

MedGuides and/or PPIs (505-1(e))	☐ **Yes** ☐ No
Communication plan (505-1(e))	☐ Yes ☐ No
Elements to assure safe use (ETASU) (505-1(f)(3))	☐ Yes ☐ No
Implementation system if certain ETASU (505-1(f)(4))	☐ Yes ☐ No
Timetable for assessment (505-1(d))	☐ Yes ☐ No

ANDA REMS acceptable?
☐ **Yes** ☐ No ☒ n/a

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

1. CONTAINER (20 mL in 1 oz bottle) - Satisfactory in Final Print as of October 4, 2011 electronic submission.

2. **CARTON (20 mL) -** Satisfactory in Final Print as of October 4, 2011 electronic submission.

3. **PACKAGE INSERT** – Satisfactory in Final Print as of October 4, 2011 electronic submission

BASIS OF APPROVAL:

- Was this approval based upon a petition? No
- What is the RLD on the 356(h) form: Derma-Smoothe/FS Topical Oil, 0.01% (ear drops)
- NDA Number: 19-452
- NDA Drug Name: Fluocinolone Acetonide Topical Oil, 0.01% (ear drops)
- NDA Firm: Hill Laboratories, Inc.
- Date of Approval of NDA Insert and supplement: NDA 19-452
- Has this been verified by the MIS system for the NDA? Yes
- Was this approval based upon an OGD labeling guidance? No
- Basis of Approval for the Container Labels: Side-by-side comparison
- Basis of Approval for the Carton Labeling: Side-by-side comparison
- Revisions needed post-approval: NO
- Comments: The firm has revised their insert labeling, submitted March 22, 2011, to remove the labeling statements describing the testing methodology for peanut proteins as per guidance from the agency.
- Patents/Exclusivities: Refer to chart below.

Patent Data – NDA 19-452

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
			There are no unexpired patents for this product in the Orange Book Database.	II	none

Exclusivity Data– NDA 19-452

Code	Reference	Expiration	Labeling Impact
NONE	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	NONE

QUESTION to Chemist: Emailed question to Jim Fan: The firm states that the statement which is in the RLD labeling **"Importantly, the bulk peanut oil NF, used in fluocinolone acetonide oil is heated at 475° F for at least 15 minutes, which should provide for adequate decomposition of allergenic proteins" does pertain to their Fluocinolone Acetonide Oil products.**

The firm states that their bulk peanut oil is also heated at 475° F for at least 15 minutes.

Can you please confirm that the above statement is correct. (Answer below)

ANSWER: Hi, Beverly

We have asked the firm about the manufacturing process for the refined peanut oil in our Review#1 (see deficiency below):
Please provide a process description, including the processing temperature for the refined peanut oil, NF. Also, please provide a commitment statement to pledge that a supplemental application is required to change peanut oil suppliers.

In Review#2, the firm provide their response, which clearly describes the heating at 475° F for at least 15 minutes.

The firm's response: While conducting our search for raw material suppliers, we discovered a patent held by Hill Dermaceuticals for fluorouracil in topical cream containing peanut oil. A copy of the patent is provided in Module 3.3 Literature On page 2, item number 10, this patent lists Peanut Oil from Welch, Holme and Clark as one of interest that is suitable for use. Since Hill is the manufacturer of the RLD, we concluded that they are most likely using this (b) (4) Peanut Oil, NF is heated at 475° F for at least 15 minutes. Identi commits to file a supplemental application in the event that we need to change the Peanut Oil, NF vendor.

Reviewer's assessment: The firm provided a commitment statement to pledge that a supplement application is required to change peanut oil suppliers. The firm also included the processing temperature for refine peanut oil (475° F=246.1° C), which is in the temperature range specified in USP (230° C to 260° C). Based on the firm's investigation, it is quite possible, but not certain that Hill, the manufacturer of the RLD uses peanut oil from Welch, Holme and Clark. The firm's response is acceptable.

Therefore, the refined peanut oil used by Identi Pharma is indeed heated at 475° F for at least 15 minutes, according to their amendment.

Richard Chang

FOR THE RECORD:

1. MODEL LABELING
Labeling review based on the labeling of the reference listed drug, Derma-Smoothe/FS Topical Oil, 0.01% manufactured by Hill Laboratories, Inc., (NDA19-452: Approved November 9, 2005).

LABELING PEANUT OIL TEST METHOD ISSUE – Memorandum to File (in DARRTS): This Memo was regarding the basis for the ANDA labeling carve-out of information relating to peanut protein in the labeling for fluocinolone products that reference Hill Dermaceutical's Dema-Smoothe (NDA 19-452). (b) (4) The office of Generic Drugs recommended the statements regarding the amount of residual peanut protein and test method be removed from the insert labeling.

FDA has determined that there is no validated assay for residual peanut protein. FDA has further determined that any peanut oil that is fully refined in accordance with the USP NF process is sufficiently safe for use in topical fluocinolone products and cannot be reliably determined to be safer for peanut allergic individuals than any other peanut oil refined in accordance with the USP NF process. As a result, when manufacturers use peanut oil that is fully refined in accordance with the USP NF process, FDA has

determined that the addition of a test to quantitate protein in refined peanut oil would not improve the safety of products formulated with this excipient and will not be required. (CP response at 30.) Accordingly, FDA has determined that no product, NDA or ANDA, should reference in its labeling an unvalidated assay for peanut protein (such as the S-ELISA test or the amino acid test) that implies an additional safety benefit that has not been shown to exist.

In this case, the Hill fluocinolone labeling includes information about assays for peanut protein that have not been validated and FDA has asked Hill to remove references to these assays from the Derma-Smoothe labeling. Although Hill has not yet complied with FDA's request, FDA stands by its conclusion that, based on the information before it, the references to unvalidated assays in the Derma-Smoothe labeling are misleading and should be removed. Given FDA's conclusions about peanut oil in general and the unvalidated nature of the S-ELISA and amino acid assays as described in the Hill CP response (b) (4) FDA believes that ANDA applicants referencing Derma-Smoothe should not be required to include this unnecessary and misleading information in their labeling.

Accordingly, FDA concludes that ANDA applicants can remove references to assays for residual peanut protein from their labeling to comply with the labeling guidelines that FDA has provided to Hill. The resulting difference between ANDA and RLD labeling is a permitted difference due to difference in manufacturer within the meaning of the statute and regulations.

Labeling outcome: It has been recommended that the generic firms do not include in their labeling the statements describing the testing methodology for peanut proteins.

Remove:
Body Oil: The peanut oil used in Derma-Smooth/FS is tested for peanut proteins through amino acid analysis which can detect the quantity of amino acids to below 0.5 parts per million

and

Scalp Oil or Ear Drops: "Peanut oil used in this product is routinely tested for peanut proteins using a sandwich enzyme-linked immunosorbent assay test(S-ELISA) kit, which can detect peanut proteins to as low as 2.5 parts per million (ppm)"

2. PATENTS/EXCLUSIVITIES

Patent Data – NDA 19-452

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
			There are no unexpired patents for this product in the Orange Book Database.	II	none

Exclusivity Data– NDA 19-452

Code	Reference	Expiration	Labeling Impact
NONE	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	NONE

3. PACKAGING CONFIGURATION

- **RLD:** 20 mL fill in 1 oz (b) (4) bottle with (b) (4) . The dropper assembly consists of a black cap fitted with a black rubber and glass pipette.
- **ANDA**: 20 mL fill in 1 oz white round soft-shoulder (b) (4) bottle with (b) (4).

4. CONTAINER/CLOSURE

Summary of Container Closure System with Configuration and Composition	
Package	**Configuration**
20 mL fill	• 1 ounce white round (b) (4) bottle with a (b) (4) neck finish • (b) (4) continuous thread white (b) (4) closure with (b) (4) foam liner • Dropper Assembly in a plastic wrapper (straight-point glass pipette, white rubber bulb, white (b) (4) cap) • Container label • Insert • Carton

5 . INACTIVE INGREDIENTS - There does not appear to be a discrepancy in inactives between the DESCRIPTION and the composition statement. The proposed formulation falls within the FDA guidelines for all components and contains the same components as the RLD.

6. STORAGE TEMPERATURE RECOMMENDATION COMPARISON

RLD – Store at 25ºC (68º-77ºF); excursions permitted to 15-30ºC (59-86ºF). [see USP Controlled Room Temperature] Keep tightly closed.
ANDA – Store at 25ºC (77ºF); excursions permitted to 15-30ºC (59-86ºF). [see USP Controlled Room Temperature] Keep tightly closed.

7. FINISHED DOSAGE FORM

- RLD – Oil
- ANDA - A colorless to yellow colored oil.

8. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM

Amneal Pharmaceuticals
Branchburgh, NJ 08876

Date of Submission: October 4, 2011

Primary Reviewer: Beverly Weitzman **Date:**

Team Leader: John Grace **Date:**

0126027A

For Otic Use Only
Not for Ophthalmic Use

Dosage and Administration:
For the treatment of **chronic eczematous external otitis**: itching, dryness, and redness of the ear. Using the supplied ear-dropper, apply 5 drops of Fluocinolone Acetonide Oil 0.01% into the affected ear. To apply, tilt head to one side so that the ear is facing up. Then gently pull the ear lobe backward and upward and apply 5 drops of Fluocinolone Acetonide Oil 0.01% into the ear. Keep head tilted for about a minute to allow Fluocinolone Acetonide Oil 0.01% to penetrate lower into the ear canal. Gently pat excess material dripping out of the ear using a clean cotton ball. Follow these instructions twice each day for 7 to 14 days.

CONTAINS: Active: Fluocinolone Acetonide (0.01%).
Inactive: Isopropyl Alcohol, Isopropyl Myristrate, Light Mineral Oil, Oleth-2 and Refined Peanut Oil

CONTENTS OF PACKAGE:
20 mL in 1 oz bottle
1 Dropper

See package insert for full prescribing information.

STORAGE: Keep tightly closed. Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F).

KEEP OUT OF REACH OF CHILDREN.

FLUOCINOLONE ACETONIDE OIL
Ear Drops

NDC 65162-**702**-94

FLUOCINOLONE ACETONIDE OIL Ear Drops

For Otic Use Only
Not For Ophthalmic Use

LOT:

EXP:

Rx only
Rev. 09-2011

Net Contents 20 mL

FLUOCINOLONE ACETONIDE OIL
Ear Drops

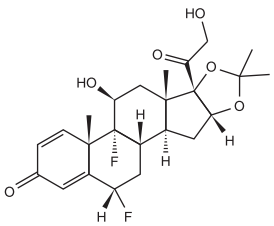
(b) (4)

Fluocinolone Acetonide Oil 0.01% Ear Drops

For Otic Use Only-
Not for Ophthalmic Use

DESCRIPTION

Fluocinolone Acetonide Oil 0.01% Ear Drops contain fluocinolone acetonide {(6α, 11β, 16α)-6,9-difluoro-11,21-dihydroxy-16,17[(1-methylethylidene)bis(oxy)]-pregna-1,4-diene-3,20-dione, cyclic 16,17 acetal with acetone}, a synthetic corticosteroid. Chemically, fluocinolone acetonide is C_{24} H_{30} F_2O_6 anhydrous. It has the following structural formula:



Fluocinolone acetonide in Fluocinolone Acetonide Oil 0.01% has a molecular weight of 452.49. It is a white crystalline powder that is odorless, stable in light, and melts at 270°C with decomposition; soluble in alcohol, acetone and methanol; slightly soluble in chloroform; insoluble in water.

Each gram of Fluocinolone Acetonide Oil 0.01% contains approximately 0.11 mg of fluocinolone acetonide in a blend of oils, which contains isopropyl alcohol, isopropyl myristate, light mineral oil, oleth-2, and refined peanut oil NF.

CLINICAL PHARMACOLOGY

Like other topical corticosteroids, fluocinolone acetonide has anti-inflammatory, antipruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of the topical steroids, in general, is unclear. However, corticosteroids are thought to act by the induction of phospholipase A_2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A_2.

Pharmacokinetics: The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle and the integrity of the epidermal barrier. Occlusion of topical corticosteroids can enhance penetration. Topical corticosteroids can be absorbed from normal intact skin. Also, inflammation and/or other disease processes in the skin can increase percutaneous absorption.

Fluocinolone Acetonide Oil 0.01% is in the low to medium range of potency as compared with other topical corticosteroids.

CLINICAL STUDIES

Efficacy in a placebo-controlled study for the treatment of chronic eczematous external otitis on 154 patients (adults and children 2 years of age and older) treated with five drops per ear of fluocinolone acetonide oil 0.01% twice daily, after 7 days of treatment, showed fluocinolone acetonide oil 0.01% to be superior to placebo in clearing the signs and symptoms of eczematous external otitis.

Clinical safety studies were conducted on the same formulation of fluocinolone acetonide oil 0.01%, marketed as Fluocinolone Acetonide 0.01% Topical Oil. Open-label safety studies on 33 children (20 subjects ages 2 to 6 years, 13 subjects ages 7 to 12 years) with moderate to severe stable atopic dermatitis, and baseline body surface area involvement greater than 75% in 18 patients, and 50% to 75% in 15 patients, were treated with Fluocinolone Acetonide 0.01% Topical Oil twice daily for 4 weeks. Morning pre-stimulation cortisol level and post-Cortrosyn stimulation cortisol level were obtained in each subject at the beginning of the trial and at the end of 4 weeks of treatment. At the end of treatment, 4 out of 18 subjects aged 2 to 5 years showed low pre-stimulation cortisol levels (3.2 to 6.6 mcg/dL; normal: cortisol > 7mcg/dL) but all had normal responses to 0.25 mg of Cortrosyn stimulation (cortisol > 18 mcg/dL).

A clinical study was conducted to assess the safety of Fluocinolone Acetonide 0.01% Topical Oil, which contains refined peanut oil, on subjects with known peanut allergies. The study enrolled 13 patients with atopic dermatitis, 6 to 17 years of age. Of the 13 patients, 9 were Radioallergosorbent Test (RAST) positive to peanuts and 4 had no peanut sensitivity (controls). The study evaluated the responses to both prick test and patch test utilizing peanut oil NF, Fluocinolone Acetonide 0.01% Topical Oil and histamine/saline controls on the 13 individuals. These subjects were also treated with Fluocinolone Acetonide 0.01% Topical Oil twice daily for 7 days. Prick test and patch test results for all 13 patients were negative to Fluocinolone Acetonide 0.01% Topical Oil and the refined peanut oil. One of the 9 peanut-sensitive patients experienced an exacerbation of atopic dermatitis after 5 days of Fluocinolone Acetonide 0.01% Topical Oil use. Importantly, the bulk peanut oil NF, used in Fluocinolone Acetonide 0.01% Oil is heated at 475°F for at least 15 minutes, which should provide for adequate decomposition of allergenic proteins.

INDICATION AND USAGE

Fluocinolone Acetonide Oil 0.01% is a low to medium potency corticosteroid indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years old and older.

CONTRAINDICATIONS

Fluocinolone Acetonide Oil 0.01% is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

This product contains refined peanut oil NF (See PRECAUTIONS).

PRECAUTIONS

General: Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment.

Patients applying a topical steroid to a large surface area or to areas under occlusion should be evaluated periodically for evidence of HPA axis suppression. This may be done by using the ACTH stimulation, A.M. plasma cortisol, and urinary free cortisol tests.

If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent corticosteroid. Infrequently, signs and symptoms of glucocorticoid insufficiency may occur requiring supplemental systemic corticosteroids. For information on systemic supplementation, see prescribing information for those products.

Children may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. (See PRECAUTIONS-Pediatric use)

Allergic contact dermatitis to any component of topical corticosteroids is usually diagnosed by a failure to heal rather than noting a clinical exacerbation, which may occur with most topical products not containing corticosteroids. Such an observation should be corroborated with appropriate diagnostic testing.

If wheal and flare type reactions (which may be limited to pruritus) or other manifestations of hypersensitivity develop, fluocinolone acetonide oil 0.01% should be discontinued immediately and appropriate therapy instituted.

If concomitant skin infections are present or develop, an appropriate antifungal or antibacterial agent should be used. If a favorable response does not occur promptly, use of fluocinolone acetonide oil 0.01% should be discontinued until the infection has been adequately controlled.

Fluocinolone acetonide oil 0.01% is formulated with 48% refined peanut oil NF. Physicians should use caution in prescribing Fluocinolone Acetonide Oil 0.01% for peanut-sensitive individuals.

Information for Patients: Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external ear use only. Do not use occlusive dressings.

2. Avoid contact with the eyes. In case of contact, wash eyes liberally with water.

3. This medication should not be used for any disorder other than that for which it was prescribed.

4. Patients should promptly report to their physician any worsening of their skin condition.

5. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, contact the physician.

Laboratory Tests: The following tests may be helpful in evaluating patients for HPA axis suppression:
ACTH stimulation test
A.M. plasma cortisol test
Urinary free cortisol test

Carcinogenesis, mutagenesis, and impairment of fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of fluocinolone acetonide oil 0.01%. Studies have not been performed to evaluate the mutagenic potential of fluocinolone acetonide, the active ingredient in fluocinolone acetonide oil 0.01%. Some corticosteroids have been found to be genotoxic in various genotoxicity tests (i.e. the *in vitro* human peripheral blood lymphocyte chromosome aberration assay with metabolic activation, the *in vivo* mouse bone marrow micronucleus assay, the Chinese hamster micronucleus test and the *in vitro* mouse lymphoma gene mutation assay).

Pregnancy: Teratogenic effects: Pregnancy category C: Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application in laboratory animals.

There are no adequate and well-controlled studies in pregnant women on teratogenic effects from fluocinolone acetonide oil 0.01%. Therefore, fluocinolone acetonide oil 0.01% should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when fluocinolone acetonide oil 0.01% is administered to a nursing woman.

Pediatric Use: Fluocinolone acetonide oil 0.01% may be used twice daily for up to 2 weeks in pediatric patients 2 years of age and older with chronic eczematous external otitis.

Fluocinolone acetonide oil 0.01% is not recommended for use on the face (See ADVERSE REACTIONS section).

Because of a higher ratio of skin surface area to body mass, children are at a greater risk than adults of HPA-axis-suppression when they are treated with topical corticosteroids. They are therefore also at greater risk of glucocorticosteroid insufficiency after withdrawal of treatment and of Cushing's syndrome while on treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children. (See PRECAUTIONS).

HPA axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Children may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Fluocinolone acetonide oil 0.01% is formulated with 48% refined peanut oil NF. Physicians should use caution in prescribing Fluocinolone Acetonide Oil 0.01% for peanut-sensitive individuals.

ADVERSE REACTIONS

The following local adverse reactions have been reported infrequently with topical corticosteroids. They may occur more frequently with the use of occlusive dressings, especially with higher potency corticosteroids. These reactions are listed in an approximate decreasing order of occurrence: burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, skin atrophy, striae, and miliaria.

OVERDOSAGE

Topically applied fluocinolone acetonide oil 0.01% can be absorbed in sufficient amounts to produce systemic effects (See PRECAUTIONS).

DOSAGE AND ADMINISTRATION

For the treatment of chronic eczematous external otitis, using the supplied ear-dropper, apply 5 drops of fluocinolone acetonide oil 0.01% into the affected ear. To apply, tilt head to one side so that the ear is facing up. Then gently pull the ear lobe backward and upward and apply 5 drops of fluocinolone acetonide oil 0.01% into the ear. Keep head tilted for about a minute to allow fluocinolone acetonide oil 0.01% to penetrate lower into the ear canal. Gently pat excess material dripping out of the ear using a clean cotton ball. Follow these instructions twice each day for 7 to 14 days.

HOW SUPPLIED

Fluocinolone Acetonide Oil 0.01% Ear Drops is supplied in 1 fluid ounce bottles with a net contents of 20 mL (Dropper Included) (NDC # 65162-702-94).

Keep tightly closed. Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

CAUTION: Rx only

Manufactured by:
Amneal Pharmaceuticals
Branchburg, NJ 08876

Distributed by:
Amneal Pharmaceuticals
Glasgow, KY 42141

Rev. 09-2011

702-985

Fluocinolone Acetonide Oil 0.01% Ear Drops

Rx Only
Rev. 09-2011

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

/s/

BEVERLY WEITZMAN
10/12/2011

JOHN F GRACE
10/12/2011

REVIEW OF PROFESSIONAL LABELING #1
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 91-306

Date of Submission: April 16, 2009, July 8, 2010, March 16, 2011 and March 22, 2011

Applicant's Name: Identi Pharmaceuticals, LLC.

Established Name: Fluocinolone Acetonide Oil, 0.01% (Ear Drops)

Labeling Deficiencies:

1. **CONTAINER:** Revise "Net Contents 20 mL (1 fl oz)" to read as "Net Contents 20 mL"
2. **INSERT: CLINICAL STUDIES:** Revise to include this section in its entirety except for the last sentence **"Importantly, the bulk peanut oil NF, used in fluocinolone acetonide oil is heated at 475° F for at least 15 minutes, which should provide for adequate decomposition of allergenic proteins".** This information is product specific and should not be included in your labeling if it does not pertain to your drug product.

Labeling Comments:

1. **CARTON: (20 mL): Satisfactory in Final Print.**

Revise your labeling, as instructed above, and submit final printed 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 submission, with all differences annotated and explained.

REMS required? NO

MedGuides and/or PPIs (505-1(e))	☐ **Yes** ☐ No
Communication plan (505-1(e))	☐ Yes ☐ No
Elements to assure safe use (ETASU) (505-1(f)(3))	☐ Yes ☐ No
Implementation system if certain ETASU (505-1(f)(4))	☐ Yes ☐ No
Timetable for assessment (505-1(d))	☐ Yes ☐ No

ANDA REMS acceptable?

☐ **Yes** ☐ No ☒ n/a

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

1. CONTAINER (20 mL in 1 oz bottle) - Satisfactory in Final Print as of March 23, 2010 electronic submission.

2. **CARTON (20 mL)**

3. **PACKAGE INSERT** – Satisfactory in Final Print as of electronic submission

BASIS OF APPROVAL:

- Was this approval based upon a petition? No
- What is the RLD on the 356(h) form: Derma-Smoothe/FS Topical Oil, 0.01% (ear drops)
- NDA Number: 21-930:
- NDA Drug Name: Fluocinolone Acetonide Topical Oil, 0.01% (ear drops)
- NDA Firm: Hill Laboratories, Inc.
- Date of Approval of NDA Insert and supplement: NDA 21- 930
- Has this been verified by the MIS system for the NDA? Yes
- Was this approval based upon an OGD labeling guidance? No
- Basis of Approval for the Container Labels: Side-by-side comparison
- Basis of Approval for the Carton Labeling: Side-by-side comparison
- Revisions needed post-approval: NO
- Comments: The firm has revised their insert labeling, submitted March 22, 2011, to remove the labeling statements describing the testing methodology for peanut proteins as per guidance from the agency.
- Patents/Exclusivities: Refer to chart below.

Patent Data – NDA 21-930

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
			There are no unexpired patents for this product in the Orange Book Database.	II	none

Exclusivity Data– NDA 21-930

Code	Reference	Expiration	Labeling Impact
NONE	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	NONE

Comment to Chemist: The firm was asked to include the Clinical Studies section to be the same as the RLD, Derma-Smooth/FS Topical Oil except for the last sentence “Importantly, the bulk peanut oil NF, used in fluocinolone acetonide oil is heated at 475° F for at least 15 minutes, which should provide for adequate decomposition of allergenic proteins”. The firm was asked not to include the last sentence, which is product specific, if it does not pertain to their drug product. Spoke with James Fan, Chemistry Division, September 23, 2011, regarding the last sentence and he is in agreement.

FOR THE RECORD:

1. MODEL LABELING

Labeling review based on the labeling of the reference listed drug, Derma-Smoothe/FS Topical Oil, 0.01% manufactured by Hill Laboratories, Inc., (NDA19-452: Approved November 9, 2005.

LABELING PEANUT OIL TEST METHOD ISSUE – Memorandum to File (in DARRTS): This Memo was regarding the basis for the ANDA labeling carve-out of information relating to peanut protein in the labeling for fluocinolone products that reference Hill Dermaceutical's Dema-Smoothe (NDA 19-452). (b) (4) The office of Generic Drugs recommended the statements regarding the amount of residual peanut protein and test method be removed from the insert labeling.

FDA has determined that there is no validated assay for residual peanut protein. FDA has further determined that any peanut oil that is fully refined in accordance with the USP NF process is sufficiently safe for use in topical fluocinolone products and cannot be reliably determined to be safer for peanut allergic individuals than any other peanut oil refined in accordance with the USP NF process. As a result, when manufacturers use peanut oil that is fully refined in accordance with the USP NF process, FDA has determined that the addition of a test to quantitate protein in refined peanut oil would not improve the safety of products formulated with this excipient and will not be required. (CP response at 30.) Accordingly, FDA has determined that no product, NDA or ANDA, should reference in its labeling an unvalidated assay for peanut protein (such as the S-ELISA test or the amino acid test) that implies an additional safety benefit that has not been shown to exist.

In this case, the Hill fluocinolone labeling includes information about assays for peanut protein that have not been validated and FDA has asked Hill to remove references to these assays from the Derma-Smoothe labeling. Although Hill has not yet complied with FDA's request, FDA stands by its conclusion that, based on the information before it, the references to unvalidated assays in the Derma-Smoothe labeling are misleading and should be removed. Given FDA's conclusions about peanut oil in general and the unvalidated nature of the S-ELISA and amino acid assays as described in the Hill CP response (b) (4) FDA believes that ANDA applicants referencing Derma-Smoothe should not be required to include this unnecessary and misleading information in their labeling.

Accordingly, FDA concludes that ANDA applicants can remove references to assays for residual peanut protein from their labeling to comply with the labeling guidelines that FDA has provided to Hill. The resulting difference between ANDA and RLD labeling is a permitted difference due to difference in manufacturer within the meaning of the statute and regulations.

Labeling outcome: It has been recommended that the generic firms do not include in their labeling the statements describing the testing methodology for peanut proteins.

Remove:

Body Oil: The peanut oil used in Derma-Smooth/FS is tested for peanut proteins through amino acid analysis which can detect the quantity of amino acids to below 0.5 parts per million

and

Scalp Oil or Ear Drops: "Peanut oil used in this product is routinely tested for peanut proteins using a sandwich enzyme-linked immunosorbent assay test(S-ELISA) kit, which can detect peanut proteins to as low as 2.5 parts per million (ppm)"

2. PATENTS/EXCLUSIVITIES

Patent Data – NDA 19-452

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
			There are no unexpired patents for this product in the Orange Book Database.	II	none

Exclusivity Data– NDA 19-452

Code	Reference	Expiration	Labeling Impact
NONE	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	NONE

4. PACKAGING CONFIGURATION

- **RLD:** 20 mL fill in 1 oz (b) (4) bottle with (b) (4) neck finish with (b) (4) closure fitted with a (b) (4) The dropper assembly consists of a black cap fitted with a black rubber and glass pipette.
- **ANDA**: 20 mL fill in 1 oz white round soft-shoulde (b) (4) bottle with (b) (4) neck finish.

5. CONTAINER/CLOSURE

Summary of Container Closure System with Configuration and Composition	
Package	**Configuration**
20 mL fill	• 1 ounce white round (b) (4) bottle with a (b) (4) neck finish • (b) (4) continuous thread white (b) (4) closure with (b) (4) foam liner • Dropper Assembly in a plastic wrapper (straight-point glass pipette, white rubber bulb, white (b) (4) cap) • Container label • Insert • Carton

6 . **INACTIVE INGREDIENTS -** There does not appear to be a discrepancy in inactives between the DESCRIPTION and the composition statement. The proposed formulation falls within the FDA guidelines for all components and contains the same components as the RLD.

7. STORAGE TEMPERATURE RECOMMENDATION COMPARISON

RLD – Store at 25ºC (68º-77ºF); excursions permitted to 15-30ºC (59-86ºF). [see USP Controlled Room Temperature] Keep tightly closed.
ANDA – Store at 25ºC (77ºF); excursions permitted to 15-30ºC (59-86ºF). [see USP Controlled Room Temperature] Keep tightly closed.

8. FINISHED DOSAGE FORM

- RLD – Oil
- ANDA - A colorless to yellow colored oil.

9. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM

Amneal Pharmaceuticals
Branchburgh, NJ 08876

Date of Submission: April 16, 2009, July 8, 2010, March 16, 2011 and March 22, 2011

Primary Reviewer: Beverly Weitzman **Date:**

Team Leader: John Grace **Date:**

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

/s/

BEVERLY WEITZMAN
09/27/2011

JOHN F GRACE
09/27/2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 91-306

CHEMISTRY REVIEWS

ANDA 091306

Fluocinolone Acetonide Oil, 0.01% Ear Drops

Identi Pharmaceuticals Inc.

Richard Chang
Chemistry I

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Chemistry Assessment **10**

Chemistry Review Data Sheet

1. ANDA 091306

2. REVIEW #: 7

3. REVIEW DATE: October 03, 2011

4. REVIEWER: Richard Chang

5. PREVIOUS DOCUMENTS:

Submission(s) Reviewed	Document Date
Original submission	April 16, 2009
Acceptable for filing	April 20, 2009
Amendment	August 26, 2009
Amendment	August 27, 2009
Amendment	October 6, 2009
Amendment	July 08, 2010
Gratuitous Amendment	August 12, 2010
Gratuitous Amendment	August 17, 2010
Amendment	September 20, 2010
Amendment	October 1, 2010
Gratuitous Amendment	December 15, 2010
Gratuitous Amendment	December 17, 2010
Amendment	March 16, 2011
Gratuitous Amendment	June 08, 2011
Telephone Amendment	August 19, 2011

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Telephone Amendment	September 29, 2011

7. NAME & ADDRESS OF APPLICANT:

Name: Identi Pharmaceuticals Inc.
Address: 2224 W. Northern Ave.
Suite# D-300
Phoenix, Arisona 85021

Chemistry Review Data Sheet

US Agent: SciRegs International, Inc.
6333 Summercrest Drive
Columbia, MD 21045
Contact person: Jeanne Taborsky
Telephone: 410-309-3145

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
Non-Proprietary Name (USAN): Fluocinolone Acetonide Oil, 0.01 % Ear Drops

9. LEGAL BASIS FOR SUBMISSION:

The Reference Listed Drug is Hill's DermOtic® Oil (fluocinolone acetonide oil, 0.01%)(NDA 019452 and NDA 021930)

PATENT CERTIFICATION STATEMENT

Identi Pharmaceuticals provided a statement of patent certification for the Abbreviated New Drug Application for Fluocinolone Acetonide Oil, 0.01%.

Also presented is a marketing exclusivity statement required under 21 CFR Section 314.94(a)(3)(ii).

PATENT INFORMATION

Identi Pharmaceuticals' proposed drug product is the generic version of Hill Dermaceuticals' DermOtic®, pursuant to NDA 021930 and NDA 019452. There are no unexpired patents for this drug product in the FDA listing titled Electronic Orange Book- Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as Orange Book). Identi Pharmaceuticals provided a Paragraph II certification for their drug product, Fluocinolone Acetonide Oil, 0.01%.

EXCLUSIVITY STATEMENT

The firm also provided an exclusivity statement to state that there is no unexpired exclusivity for this drug product.

10. PHARMACOL. CATEGORY:
Glucocorticoid and indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years old and older.

11. DOSAGE FORM: Topical-otic

12. STRENGTH/POTENCY: 0.01%

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:

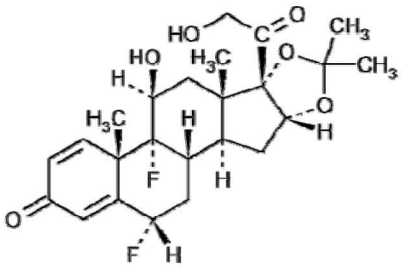
Compendial name: fluocinolone acetonide, USP

Chemical name: Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α,11β,16α)-6α,9-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with acetone

Molecular formula: $C_{24}H_{30}F_2O_6$ (anhydrous)

Molecular weight: 452.50

Structure:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	Type	Item referenced	Holder	Code[1]/ Status[2]	Date review completed	Comments
[redacted]			(b) (4)			
				1/Adequate	02/28/11	Reviewed by Richard Chang
				4		
				4		

Chemistry Review Data Sheet

(b) (4)	4
	4
	4
	4
	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 REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	12/17/10	
Methods Validation	N/A		
Labeling	Acceptable	10/12/11	B. Weitzman
Bioequivalence	Acceptable	08/31/10	J. Osterhout
EA	Satisfactory (exclusion requested)		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

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

The Chemistry Review for ANDA 091306

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on approvability

This ANDA is 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
Fluocinolone Acetonide Oil, 0.01% contains fluocinolone acetonide which is a synthetic, fluorinated corticosteroid. It is intended for topical dermatologic use for the relief of the inflammatory and pruritic manifestation of atopic dermatitis in patients 1 year or older.
Each gram of Fluocinolone Acetonide Oil, 0.01% contains 0.11 (b) (4) mg fluocinolone acetonide in an oil consisting of isopropyl alcohol USP, refined peanut oil NF, isopropyl myristate NF, and light mineral oil NF.

Fluocinolone Acetonide Oil, 0.01% is a clear, colorless to light straw colored liquid. Fluocinolone acetonide oil will be marketed in the following package; (b) (4) mL (1 oz) white round soft-shoulder bottle with a (b) (4) white, fine ribbed cap and a dropper.

It is to be stored in controlled room temperature and shipped at cool or refrigerated conditions. The proposed expiration dating for the drug product is 24 months.

Drug substance
The chemical name of fluocinolone acetonide is Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α,11β,16α)-6α,9-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with acetone. The drug substance is listed in the USP Monograph. It is a white to practically white crystalline powder. It is insoluble in water, freely soluble in acetone and glacial acetic acid, sparingly soluble in chloroform and methanol, and very slightly soluble in ether.

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

Fluocinolone Acetonide Oil, 0.01%, should be applied five drops to the affected ear(s) twice daily for seven to fourteen days.

Maximum daily dose (MDD)

The MDD is calculated below based on the package insert information from DermOtic® Oil for Fluocinolone Acetonide Oil, 0.01%, which states that the product be applied to the affected ear(s) for maximum 14 days. In addition, the bottle for the firm's drug product is 20 mL fill.
MDD= (b) (4)
assuming 100% absorption

	IT	QT
DS	(b) (4)	
DP		

C. Basis for approvability or Not-approval Recommendation

This ANDA is approvable.

Review Note:

Gratuitous Amendment (dated December 15, 2010)

On December 15, 2010, the firm submitted a Gratuitous Amendment to request the withdrawal of Amneal Pharmaceuticals as a testing laboratory for the active pharmaceutical ingredient. Post approval, once the method transfer protocol is executed/, Identi will submit a post approval supplement to add Amneal Pharmaceutical as a testing facility for the API.

Gratuitous Amendment (dated December 17, 2010)

On December 17, 2010, the firm submitted a Gratuitous Amendment for the following: (b) (4) was provided as a testing facility for the drug substance and drug product release and stability for the test batch in the original submission. (b) (4) was approved for this testing in the ANDA. (b) (4) waswithdrawn in eCTD 0007 because the testing was being transferred to an alternate facility, Amneal Pharmaceuticals. Amneal is in the process of completing the methods transfer validation. Identi is requesting that (b) (4) be re-instated in the ANDA for drug substance and drug product testing.
The firm also included the debarment certification and cGMP certifications in the submission.

Additionally, we decided to submit (b) (4)

(b) (4)

The warning on Peanut content was already part of the insert, and Peanut Oil is clearly listed on the carton as an ingredient, as it is on the innovator carton.

Reviewer's assessment:
The firm follows our suggestion [redacted] The firm's response is satisfactory.

Review Note for Gratuitous Amendment dated June 08, 2011

On June 08, 2011, the firm submitted a gratuitous amendment to transfer the testing of the active ingredient from [redacted] to Amneal Pharmaceuticals. The firm stated that Amneal will not be transferring the [redacted] method for assay or impurities, but rather using the USP regulatory method to test assay and the API supplier method to test impurities. Amneal is already approved as the manufacturer, and as the testing lab for inactive ingredients and the finished product. Amneal was satisfactorily inspected in July 2010. The cGMP and Debarment Certifications are already on file in the AND A. On August 09, 2011, the firm was communicated with the following deficiency:
Please submit a test method verification report by Amneal for API impurities determination using the supplier's test method.

Review Note for Telephone Amendment dated August 19, 2011

To respond to the deficiency, the firm submitted [redacted]

Review Note for Telephone Amendment dated September 29, 2011

On September 26, 2011, the following deficiencies were communicated with the firm and the firm responded on September 29, 2011:
1. Please submit a revised Refined Peanut Oil Specifications in compliance with the USP monograph and in line with ANDA 201759 and 201764.
As requested, the revised Refined Peanut Oil Specifications in compliance with the USP monograph and in line with ANDA 201759 and 201764 are provided in Section 3.2.P.4.1 Specifications.

Reviewer's assessment: As requested, the firm revised the Refined Peanut Oil specifications in compliance with USP monograph.

2. Please remove the following tests and specifications from your drug product release and stability specifications: [redacted] Please submit a revised drug product release and stability specifications.
As requested, Identi removed the following tests and specifications from our drug product release and stability specifications: [redacted] and submitted revised drug product release specifications in Section 3.2.P.5.1 Specifications and stability specifications in Section

3.2.P.8.1 Stability The method for related compounds and assay has also been revised to reflect the changes to the impurities reporting. The revised method 701-AS-RC is provided herein.

Reviewer's assessment: The firm revised their drug product release and stability specifications, as requested.

The ANDA 091306 (CMC) is approvable.

16 pages have been withheld immediately following this page as b4

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

/s/

RICHARD CHANG
10/13/2011

TRANG Q TRAN
10/13/2011

JAMES M FAN
10/13/2011

ANDA 091306

Fluocinolone Acetonide Oil, 0.01% Ear Drops

Identi Pharmaceuticals Inc.

Richard Chang
Chemistry I

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Chemistry Review Data Sheet

1. ANDA 091306

2. REVIEW #: 6

3. REVIEW DATE: August 22, 2011

4. REVIEWER: Richard Chang

5. PREVIOUS DOCUMENTS:

Submission(s) Reviewed	Document Date
Original submission	April 16, 2009
Acceptable for filing	April 20, 2009
Amendment	August 26, 2009
Amendment	August 27, 2009
Amendment	October 6, 2009
Amendment	July 08, 2010
Gratuitous Amendment	August 12, 2010
Gratuitous Amendment	August 17, 2010
Amendment	September 20, 2010
Amendment	October 1, 2010
Gratuitous Amendment	December 15, 2010
Gratuitous Amendment	December 17, 2010
Amendment	March 16, 2011

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Gratuitous Amendment	June 08, 2011
Telephone Amendment	August 19, 2011

7. NAME & ADDRESS OF APPLICANT:

Name: Identi Pharmaceuticals Inc.
Address: 2224 W. Northern Ave.
Suite# D-300
Phoenix, Arisona 85021

US Agent: SciRegs International, Inc.
6333 Summercrest Drive

Columbia, MD 21045
Contact person: Jeanne Taborsky
Telephone: 410-309-3145

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
Non-Proprietary Name (USAN): Fluocinolone Acetonide Oil, 0.01 % Ear Drops

9. LEGAL BASIS FOR SUBMISSION:

The Reference Listed Drug is Hill's DermOtic® Oil (fluocinolone acetonide oil, 0.01%)(NDA 019452 and NDA 021930)

PATENT CERTIFICATION STATEMENT

Identi Pharmaceuticals provided a statement of patent certification for the Abbreviated New Drug Application for Fluocinolone Acetonide Oil, 0.01%.

Also presented is a marketing exclusivity statement required under 21 CFR Section 314.94(a)(3)(ii).

PATENT INFORMATION

Identi Pharmaceuticals' proposed drug product is the generic version of Hill Dermaceuticals' DermOtic®, pursuant to NDA 021930 and NDA 019452. There are no unexpired patents for this drug product in the FDA listing titled Electronic Orange Book- Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as Orange Book). Identi Pharmaceuticals provided a Paragraph II certification for their drug product, Fluocinolone Acetonide Oil, 0.01%.

EXCLUSIVITY STATEMENT

The firm also provided an exclusivity statement to state that there is no unexpired exclusivity for this drug product.

10. PHARMACOL. CATEGORY:
Glucocorticoid and indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years old and older.

11. DOSAGE FORM: Topical-otic

12. STRENGTH/POTENCY: 0.01%

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:

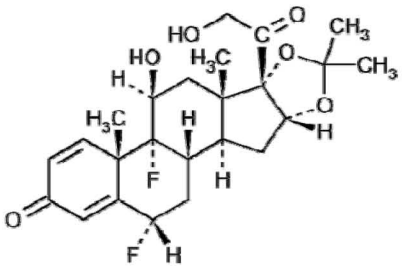
Compendial name: fluocinolone acetonide, USP

Chemical name: Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α,11β,16α)-6α,9-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with acetone

Molecular formula: $C_{24}H_{30}F_2O_6$ (anhydrous)

Molecular weight: 452.50

Structure:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	Type	Item referenced	Holder	Code[1]/ Status[2]	Date review completed	Comments
			(b) (4)			
				1/Adequate	02/28/11	Reviewed by Richard Chang
				4		
				4		

Chemistry Review Data Sheet

(b) (4)	4
	4
	4
	4
	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 REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	12/17/10	
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Acceptable	08/31/10	J. Osterhout
EA	Satisfactory (exclusion requested)		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

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

The Chemistry Review for ANDA 091306

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on approvability

CMC is approvable. Bioequivalence review and EES are acceptable. Labeling is pending.

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
Fluocinolone Acetonide Oil, 0.01% contains fluocinolone acetonide which is a synthetic, fluorinated corticosteroid. It is intended for topical dermatologic use for the relief of the inflammatory and pruritic manifestation of atopic dermatitis in patients 1 year or older.
Each gram of Fluocinolone Acetonide Oil, 0.01% contains 0.11 (b) (4) mg fluocinolone acetonide in an oil consisting of isopropyl alcohol USP, refined peanut oil NF, isopropyl myristate NF, and light mineral oil NF.

Fluocinolone Acetonide Oil, 0.01% is a clear, colorless to light straw colored liquid. Fluocinolone acetonide oil will be marketed in the following package; (b) (4) mL (1 oz) white round soft-shoulder bottle with a (b) (4) white, fine ribbed cap and a dropper.

It is to be stored in controlled room temperature and shipped at cool or refrigerated conditions. The proposed expiration dating for the drug product is 24 months.

Drug substance
The chemical name of fluocinolone acetonide is Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α,11β,16α)-6α,9-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with acetone. The drug substance is listed in the USP Monograph. It is a white to practically white crystalline powder. It is insoluble in water, freely soluble in acetone and glacial acetic acid, sparingly soluble in chloroform and methanol, and very slightly soluble in ether.

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

Fluocinolone Acetonide Oil, 0.01%, should be applied five drops to the affected ear(s) twice daily for seven to fourteen days.

Maximum daily dose (MDD)

The MDD is calculated below based on the package insert information from DermOtic® Oil for Fluocinolone Acetonide Oil, 0.01%, which states that the product be applied to the affected ear(s) for maximum 14 days. In addition, the bottle for the firm's drug product is 20 mL fill.
MDD= (b) (4)
assuming 100% absorption

	IT	OT
DS	(b) (4)	
DP		

C. Basis for approvability or Not-approval Recommendation

CMC is approvable. Bioequivalence review and EES are acceptable. Labeling review is pending.

Review Note:

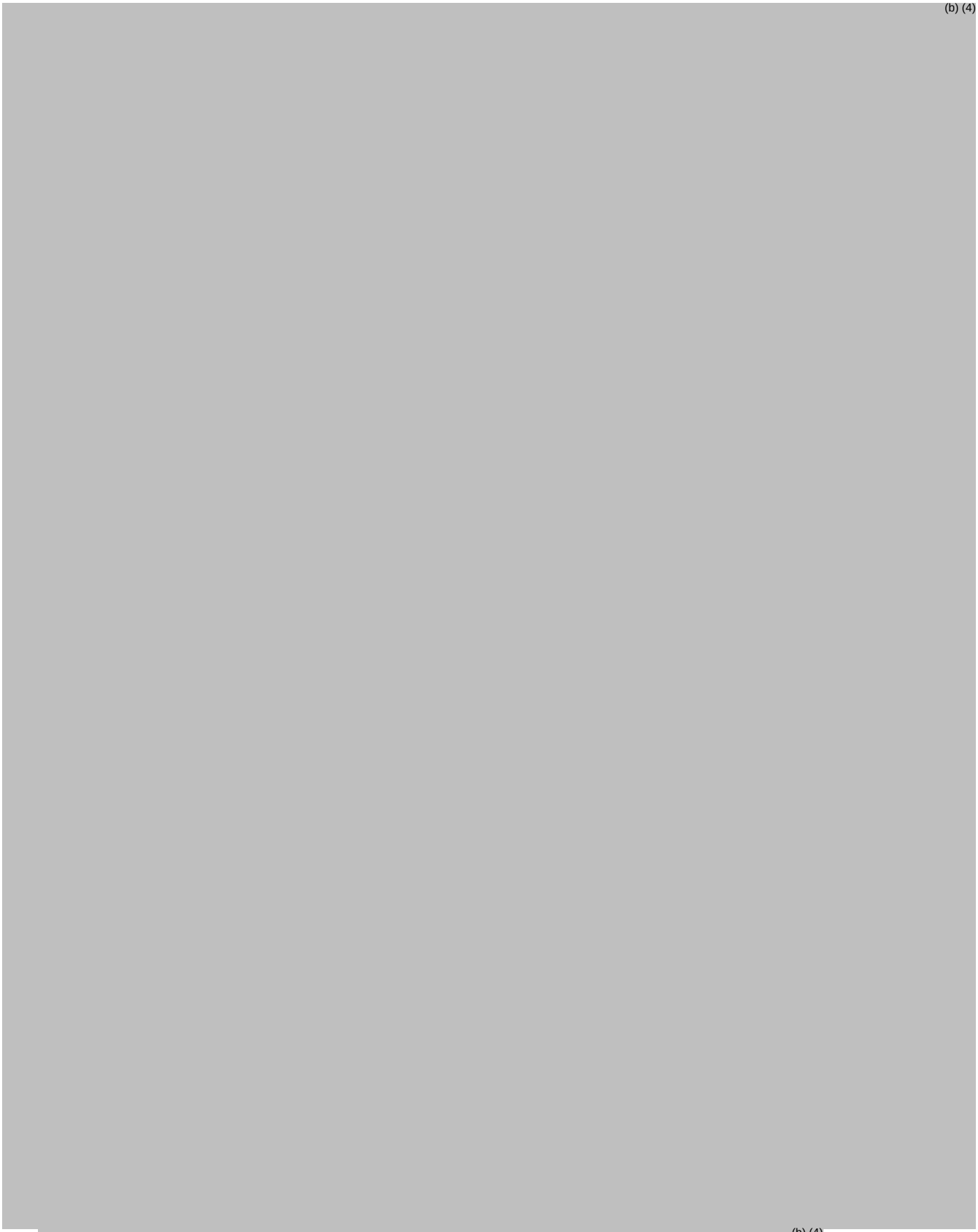
Gratuitous Amendment (dated December 15, 2010)

On December 15, 2010, the firm submitted a Gratuitous Amendment to request the withdrawal of Amneal Pharmaceuticals as a testing laboratory for the active pharmaceutical ingredient. Post approval, once the method transfer protocol is executed/, Identi will submit a post approval supplement to add Amneal Pharmaceutical as a testing facility for the API.

Gratuitous Amendment (dated December 17, 2010)

On December 17, 2010, the firm submitted a Gratuitous Amendment for the following: Analytical Solutions Inc. ((b) (4) was provided as a testing facility for the drug substance and drug product release and stability for the test batch in the original submission. (b) (4) was approved for this testing in the ANDA. (b) (4) waswithdrawn in eCTD 0007 because the testing was being transferred to an alternate facility, Amneal Pharmaceuticals. Amneal is in the process of completing the methods transfer validation. Identi is requesting that (b) (4) be re-instated in the ANDA for drug substance and drug product testing.
The firm also included the debarment certification and cGMP certifications in the submission.

Additionally, we decided to submi (b) (4)



The warning on Peanut content was already part of the insert, and Peanut Oil is clearly listed on

the carton as an ingredient, as it is on the innovator carton.

Reviewer's assessment:

(b) (4)

The firm's response is satisfactory.

Review Note for Gratuitous Amendment dated June 08, 2011

On June 08, 2011, the firm submitted a gratuitous amendment to transfer the testing of the active ingredient from (b) (4) to Amneal Pharmaceuticals. The firm stated that Amneal will not be transferring the (b) ( ) method for assay or impurities, but rather using the USP regulatory method to test assay and the API supplier method to test impurities. Amneal is already approved as the manufacturer, and as the testing lab for inactive ingredients and the finished product. Amneal was satisfactorily inspected in July 2010. The cGMP and Debarment Certifications are already on file in the AND A. On August 09, 2011, the firm was communicated with the following deficiency:
Please submit a test method verification report by Amneal for API impurities determination using the supplier's test method.

Review Note for Telephone Amendment dated August 19, 2011

To respond to the deficiency, (b) (4)

The ANDA 091306 (CMC) is approvable.

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/s/

RICHARD CHANG
09/08/2011

TRANG Q TRAN
09/08/2011

JAMES M FAN
09/09/2011

ANDA 091306

Fluocinolone Acetonide Oil, 0.01% Ear Drops

Identi Pharmaceuticals Inc.

Richard Chang
Chemistry I

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Chemistry Assessment **10**

Chemistry Review Data Sheet

1. ANDA 091306

2. REVIEW #: 5

3. REVIEW DATE: March 22, 2011

4. REVIEWER: Richard Chang

5. PREVIOUS DOCUMENTS:

Submission(s) Reviewed	Document Date
Original submission	April 16, 2009
Acceptable for filing	April 20, 2009
Amendment	August 26, 2009
Amendment	August 27, 2009
Amendment	October 6, 2009
Amendment	July 08, 2010
Gratuitous Amendment	August 12, 2010
Gratuitous Amendment	August 17, 2010
Amendment	September 20, 2010
Amendment	October 1, 2010
Gratuitous Amendment	December 15, 2010
Gratuitous Amendment	December 17, 2010

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	March 16, 2011

7. NAME & ADDRESS OF APPLICANT:

Name: Identi Pharmaceuticals Inc.
Address: 2224 W. Northern Ave.
Suite# D-300
Phoenix, Arisona 85021

US Agent: SciRegs International, Inc.
6333 Summercrest Drive

Columbia, MD 21045
Contact person: Jeanne Taborsky
Telephone: 410-309-3145

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
Non-Proprietary Name (USAN): Fluocinolone Acetonide Oil, 0.01 % Ear Drops

9. LEGAL BASIS FOR SUBMISSION:

The Reference Listed Drug is Hill's DermOtic® Oil (fluocinolone acetonide oil, 0.01%)(NDA 019452 and NDA 021930)

PATENT CERTIFICATION STATEMENT

Identi Pharmaceuticals provided a statement of patent certification for the Abbreviated New Drug Application for Fluocinolone Acetonide Oil, 0.01%.

Also presented is a marketing exclusivity statement required under 21 CFR Section 314.94(a)(3)(ii).

PATENT INFORMATION

Identi Pharmaceuticals' proposed drug product is the generic version of Hill Dermaceuticals' DermOtic®, pursuant to NDA 021930 and NDA 019452. There are no unexpired patents for this drug product in the FDA listing titled Electronic Orange Book- Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as Orange Book). Identi Pharmaceuticals provided a Paragraph II certification for their drug product, Fluocinolone Acetonide Oil, 0.01%.

EXCLUSIVITY STATEMENT

The firm also provided an exclusivity statement to state that there is no unexpired exclusivity for this drug product.

10. PHARMACOL. CATEGORY:
Glucocorticoid and indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years old and older.

11. DOSAGE FORM: Topical-otic

12. STRENGTH/POTENCY: 0.01%

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:

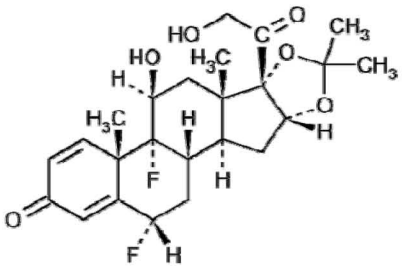
Compendial name: fluocinolone acetonide, USP

Chemical name: Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α,11β,16α)-6α,9-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with acetone

Molecular formula: $C_{24}H_{30}F_2O_6$ (anhydrous)

Molecular weight: 452.50

Structure:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	Type	Item referenced	Holder	Code[1]/ Status[2]	Date review completed	Comments
			(b) (4)			
				1/Adequate	02/28/11	Reviewed by Richard Chang
				4		
				4		

Chemistry Review Data Sheet

(b) (4)	4
	4
	4
	4
	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 REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	12/17/10	
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Acceptable	08/31/10	J. Osterhout
EA	Satisfactory (exclusion requested)		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

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

The Chemistry Review for ANDA 091306

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on approvability

CMC is approvable. Bioequivalence review and EES are acceptable. Labeling is pending.

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
Fluocinolone Acetonide Oil, 0.01% contains fluocinolone acetonide which is a synthetic, fluorinated corticosteroid. It is intended for topical dermatologic use for the relief of the inflammatory and pruritic manifestation of atopic dermatitis in patients 1 year or older.
Each gram of Fluocinolone Acetonide Oil, 0.01% contains 0.11 (b) (4) mg fluocinolone acetonide in an oil consisting of isopropyl alcohol USP, refined peanut oil NF, isopropyl myristate NF, and light mineral oil NF.

Fluocinolone Acetonide Oil, 0.01% is a clear, colorless to light straw colored liquid. Fluocinolone acetonide oil will be marketed in the following package; (b) (4) mL (1 oz) white round soft-shoulder bottle with a (b) (4) white, fine ribbed cap and a dropper.

It is to be stored in controlled room temperature and shipped at cool or refrigerated conditions. The proposed expiration dating for the drug product is 24 months.

Drug substance
The chemical name of fluocinolone acetonide is Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α,11β,16α)-6α,9-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with acetone. The drug substance is listed in the USP Monograph. It is a white to practically white crystalline powder. It is insoluble in water, freely soluble in acetone and glacial acetic acid, sparingly soluble in chloroform and methanol, and very slightly soluble in ether.

B. Description of How the Drug Product is Intended to be Used
Fluocinolone Acetonide Oil, 0.01%, should be applied five drops to the affected ear(s) twice daily for seven to fourteen days.

Maximum daily dose (MDD)

The MDD is calculated below based on the package insert information from DermOtic® Oil for Fluocinolone Acetonide Oil, 0.01%, which states that the product be applied to the affected ear(s) for maximum 14 days. In addition, the bottle for the firm's drug product is 20 mL fill.
MDD= (b) (4)
assuming 100% absorption

	IT	OT
DS	(b) (4)	
DP		

C. Basis for approvability or Not-approval Recommendation

CMC is approvable. Bioequivalence review and EES are acceptable. Labeling review is pending.

Review Note:

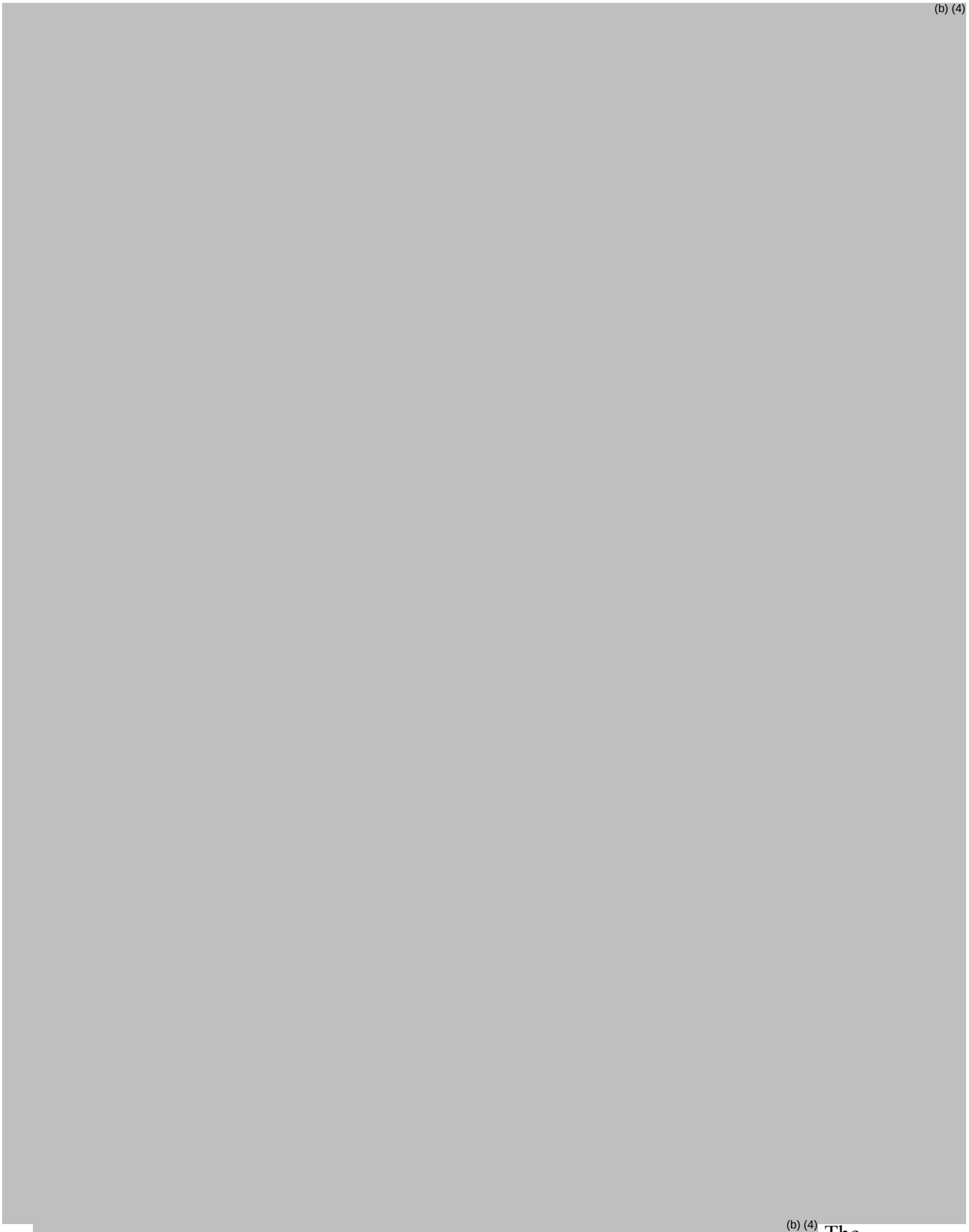
Gratuitous Amendment (dated December 15, 2010)

On December 15, 2010, the firm submitted a Gratuitous Amendment to request the withdrawal of Amneal Pharmaceuticals as a testing laboratory for the active pharmaceutical ingredient. Post approval, once the method transfer protocol is executed/, Identi will submit a post approval supplement to add Amneal Pharmaceutical as a testing facility for the API.

Gratuitous Amendment (dated December 17, 2010)

On December 17, 2010, the firm submitted a Gratuitous Amendment for the following: (b) (4) was provided as a testing facility for the drug substance and drug product release and stability for the test batch in the original submission. (b) (4) was approved for this testing in the ANDA. (b) (4) waswithdrawn in eCTD 0007 because the testing was being transferred to an alternate facility, Amneal Pharmaceuticals. Amneal is in the process of completing the methods transfer validation. Identi is requesting that (b) (4) be re-instated in the ANDA for drug substance and drug product testing.
The firm also included the debarment certification and cGMP certifications in the submission.

Additionally, we decided to submit (b) (4)



The warning on Peanut content was already part of the insert, and Peanut Oil is clearly listed on

the carton as an ingredient, as it is on the innovator carton.

Reviewer's assessment:

(b) (4)

The firm's response is satisfactory.

15 pages have been withheld immediately following this page as b4

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

/s/

RICHARD CHANG
04/01/2011

TRANG Q TRAN
04/01/2011

JAMES M FAN
04/01/2011

ANDA 091306

Fluocinolone Acetonide Oil, 0.01% Ear Drops

Identi Pharmaceuticals Inc.

Richard Chang
Chemistry I

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C. Basis for Approvability or Not-approval Recommendation 9

Chemistry Assessment **10**

Chemistry Review Data Sheet

1. ANDA 091306

2. REVIEW #: 4

3. REVIEW DATE: January 10, 2011

4. REVIEWER: Richard Chang

5. PREVIOUS DOCUMENTS:

Submission(s) Reviewed	Document Date
Original submission	April 16, 2009
Acceptable for filing	April 20, 2009
Amendment	August 26, 2009
Amendment	August 27, 2009
Amendment	October 6, 2009
Amendment	July 08, 2010
Gratuitous Amendment	August 12, 2010
Gratuitous Amendment	August 17, 2010
Amendment	September 20, 2010
Amendment	October 1, 2010

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Gratuitous Amendment	December 15, 2010
Gratuitous Amendment	December 17, 2010

7. NAME & ADDRESS OF APPLICANT:

Name: Identi Pharmaceuticals Inc.
Address: 2224 W. Northern Ave.
Suite# D-300
Phoenix, Arisona 85021

US Agent: SciRegs International, Inc.
6333 Summercrest Drive
Columbia, MD 21045

Chemistry Review Data Sheet

Contact person: Jeanne Taborsky
Telephone: 410-309-3145

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
Non-Proprietary Name (USAN): Fluocinolone Acetonide Oil, 0.01 % Ear Drops

9. LEGAL BASIS FOR SUBMISSION:

The Reference Listed Drug is Hill's DermOtic® Oil (fluocinolone acetonide oil, 0.01%)(NDA 019452 and NDA 021930)

PATENT CERTIFICATION STATEMENT

Identi Pharmaceuticals provided a statement of patent certification for the Abbreviated New Drug Application for Fluocinolone Acetonide Oil, 0.01%.

Also presented is a marketing exclusivity statement required under 21 CFR Section 314.94(a)(3)(ii).

PATENT INFORMATION

Identi Pharmaceuticals' proposed drug product is the generic version of Hill Dermaceuticals' DermOtic®, pursuant to NDA 021930 and NDA 019452. There are no unexpired patents for this drug product in the FDA listing titled Electronic Orange Book- Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as Orange Book). Identi Pharmaceuticals provided a Paragraph II certification for their drug product, Fluocinolone Acetonide Oil, 0.01%.

EXCLUSIVITY STATEMENT

The firm also provided an exclusivity statement to state that there is no unexpired exclusivity for this drug product.

10. PHARMACOL. CATEGORY:
Glucocorticoid and indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years old and older.

11. DOSAGE FORM: Topical-otic

12. STRENGTH/POTENCY: 0.01%

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:

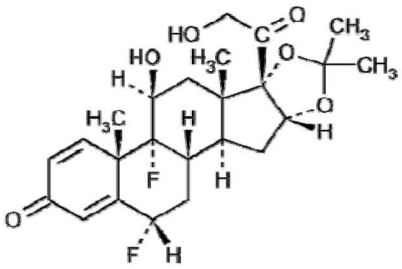
Compendial name: fluocinolone acetonide, USP

Chemical name: Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α,11β,16α)-6α,9-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with acetone

Molecular formula: $C_{24}H_{30}F_2O_6$ (anhydrous)

Molecular weight: 452.50

Structure:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	Type	Item referenced	Holder	Code[1]/ Status[2]	Date review completed	Comments
			(b) (4)			
				1/Adequate	02/26/10	Reviewed by Richard Chang
				4		
				4		

Chemistry Review Data Sheet

(b) (4)	4
	4
	4
	4
	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 REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	12/17/10	
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Acceptable	08/31/10	J. Osterhout
EA	Satisfactory (exclusion requested)		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

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

The Chemistry Review for ANDA 091306

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on approvability

This ANDA is not approvable. Bioequivalence review and EES are acceptable. Labeling is pending.

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
Fluocinolone Acetonide Oil, 0.01% contains fluocinolone acetonide which is a synthetic, fluorinated corticosteroid. It is intended for topical dermatologic use for the relief of the inflammatory and pruritic manifestation of atopic dermatitis in patients 1 year or older.
Each gram of Fluocinolone Acetonide Oil, 0.01% contains 0.11 (b) (4) mg fluocinolone acetonide in an oil consisting of isopropyl alcohol USP, refined peanut oil NF, isopropyl myristate NF, and light mineral oil NF.

Fluocinolone Acetonide Oil, 0.01% is a clear, colorless to light straw colored liquid. Fluocinolone acetonide oil will be marketed in the following package; (b) (4) mL (1 oz) white round soft-shoulder bottle with a (b) (4) white, fine ribbed cap and a dropper.

It is to be stored in controlled room temperature and shipped at cool or refrigerated conditions. The proposed expiration dating for the drug product is 24 months.

Drug substance
The chemical name of fluocinolone acetonide is Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α,11β,16α)-6α,9-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with acetone. The drug substance is listed in the USP Monograph. It is a white to practically white crystalline powder. It is insoluble in water, freely soluble in acetone and glacial acetic acid, sparingly soluble in chloroform and methanol, and very slightly soluble in ether.

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

Fluocinolone Acetonide Oil, 0.01%, should be applied five drops to the affected ear(s) twice daily for seven to fourteen days.

Maximum daily dose (MDD)

The MDD is calculated below based on the package insert information from DermOtic® Oil for Fluocinolone Acetonide Oil, 0.01%, which states that the product be applied to the affected ear(s) for maximum 14 days. In addition, the bottle for the firm's drug product is 20 mL fill.
MDD= (b) (4)
assuming 100% absorption

	IT	QT
DS	(b) (4)	
DP		

C. Basis for approvability or Not-approval Recommendation

The ANDA (CMC) is not approvable, due to the unacceptable test method for Total Amino Acids in Peanut Oil. Bioequivalence review and EES are acceptable. Labeling review is pending.

Review Note:

Gratuitous Amendment (dated December 15, 2010)

On December 15, 2010, the firm submitted a Gratuitous Amendment to request the withdrawal of Amneal Pharmaceuticals as a testing laboratory for the active pharmaceutical ingredient. Post approval, once the method transfer protocol is executed/, Identi will submit a post approval supplement to add Amneal Pharmaceutical as a testing facility for the API.

Gratuitous Amendment (dated December 17, 2010)

On December 17, 2010, the firm submitted a Gratuitous Amendment for the following: (b) (4) was provided as a testing facility for the drug substance and drug product release and stability for the test batch in the original submission. (b) (4) was approved for this testing in the ANDA. (b) (4) waswithdrawn in eCTD 0007 because the testing was being transferred to an alternate facility, Amneal Pharmaceuticals. Amneal is in the process of completing the methods transfer validation. Identi is requesting that (b) (4) be re-instated in the ANDA for drug substance and drug product testing.
The firm also included the debarment certification and cGMP certifications in the submission.

Additionally, we decided to submit (b) (4)

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/s/

RICHARD CHANG
01/21/2011

TRANG Q TRAN
01/21/2011

JAMES M FAN
01/22/2011

DEPARTMENT OF HEALTH & HUMAN SERVICES
Food and Drug Administration

Center for Drug Evaluation and Research
Division of Pharmaceutical Analysis
St. Louis, MO 63101
Tel. (314) 539-2174

Date: January 7, 2011

To: Richard Chang, Ph.D., Review Chemist

Through: B. J. Westenberger, Deputy Director, Division of Pharmaceutical Analysis

From: Hongping Ye, Ph.D., Chemist

Subject: (b) (4)

(b) (4)

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/s/

BENJAMIN J WESTENBERGER
01/07/2011

DEPARTMENT OF HEALTH & HUMAN SERVICES
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pharmaceutical Analysis
1114 Market Street, Room 1002
St. Louis, MO 63101
Tel. (314) 539-3813
FAX (314) 539-2113

December 9, 2010

C. Jeanne Taborsky
US Regulatory Agent
SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045

Re: Receipt of Sample materials for ANDA 091-306
Fluocinolone Acetonide Otic Oil, Ear Drops

Dear C. Jeanne Taborsky:

We acknowledge receipt on December 6, 2010 of the sample materials and documentation that SciRegs International, Inc., sent to the Division of Pharmaceutical Analysis (DPA) in St. Louis.

If you have questions, you may contact me by telephone (314-539-3813) or email (james.allgire@fda.hhs.gov).

Sincerely,

James Allgire
Division of Pharmaceutical Analysis

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/s/

JAMES F ALLGIRE
12/11/2010

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ANDA 091306

Fluocinolone Acetonide Oil, 0.01% Ear Drops

Identi Pharmaceuticals Inc.

Richard Chang
Chemistry I

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B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable 8

II. Summary of Chemistry Assessments 8

A. Description of the Drug Product(s) and Drug Substance(s) 8

B. Description of How the Drug Product is Intended to be Used 8

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Chemistry Assessment **10**

Chemistry Review Data Sheet

1. ANDA 091306

2. REVIEW #: 3

3. REVIEW DATE: September 27, 2010

4. REVIEWER: Richard Chang

5. PREVIOUS DOCUMENTS:

Submission(s) Reviewed	Document Date
Original submission	April 16, 2009
Acceptable for filing	April 20, 2009
Amendment	August 26, 2009
Amendment	August 27, 2009
Amendment	October 6, 2009

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	July 08, 2010
Gratuitous Amendment	August 12, 2010
Gratuitous Amendment	August 17, 2010
Amendment	September 20, 2010
Amendment	October 1, 2010

7. NAME & ADDRESS OF APPLICANT:

Name: Identi Pharmaceuticals Inc.
Address: 2224 W. Northern Ave.
Suite# D-300
Phoenix, Arisona 85021

US Agent: SciRegs International, Inc.
6333 Summercrest Drive
Columbia, MD 21045
Contact person: Jeanne Taborsky
Telephone: 410-309-3145

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A

Non-Proprietary Name (USAN): Fluocinolone Acetonide Oil, 0.01 % Ear Drops

9. LEGAL BASIS FOR SUBMISSION:

The Reference Listed Drug is Hill's DermOtic® Oil (fluocinolone acetonide oil, 0.01%)(NDA 019452 and NDA 021930)

PATENT CERTIFICATION STATEMENT

Identi Pharmaceuticals provided a statement of patent certification for the Abbreviated New Drug Application for Fluocinolone Acetonide Oil, 0.01%.

Also presented is a marketing exclusivity statement required under 21 CFR Section 314.94(a)(3)(ii).

PATENT INFORMATION

Identi Pharmaceuticals' proposed drug product is the generic version of Hill Dermaceuticals' DermOtic®, pursuant to NDA 021930 and NDA 019452. There are no unexpired patents for this drug product in the FDA listing titled Electronic Orange Book- Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as Orange Book). Identi Pharmaceuticals provided a Paragraph II certification for their drug product, Fluocinolone Acetonide Oil, 0.01%.

EXCLUSIVITY STATEMENT

The firm also provided an exclusivity statement to state that there is no unexpired exclusivity for this drug product.

10. PHARMACOL. CATEGORY:

Glucocorticoid and indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years old and older.

11. DOSAGE FORM: Topical-otic

12. STRENGTH/POTENCY: 0.01%

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:

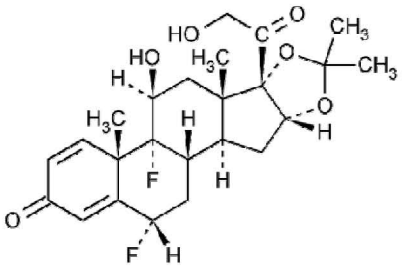
Compendial name: fluocinolone acetonide, USP

Chemical name: Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α,11β,16α)-6α,9-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with acetone

Molecular formula: $C_{24}H_{30}F_2O_6$ (anhydrous)

Molecular weight: 452.50

Structure:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	Type	Item referenced	Holder	Code[1]/ Status[2]	Date review completed	Comments
(b) (4)						
				/Adequate	02/26/10	Reviewed by Richard Chang
				4		
				4		
				4		

(b) (4)	4
	4
	4
	4

[1] Action codes for DMF Table: 1 – DMF Reviewed.
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B. Other Documents: N/A

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Pending		
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Acceptable	08/31/10	J. Osterhout
EA	Satisfactory (exclusion requested)		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

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

The Chemistry Review for ANDA 091306

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on approvability

This ANDA (CMC) is approvable. Bioequivalence review is acceptable. Labeling and EES are pending.

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
Fluocinolone Acetonide Oil, 0.01% contains fluocinolone acetonide which is a synthetic, fluorinated corticosteroid. It is intended for topical dermatologic use for the relief of the inflammatory and pruritic manifestation of atopic dermatitis in patients 1 year or older.
Each gram of Fluocinolone Acetonide Oil, 0.01% contains 0.11 (b) (4) mg fluocinolone acetonide in an oil consisting of isopropyl alcohol USP, refined peanut oil NF, isopropyl myristate NF, and light mineral oil NF.

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It is to be stored in controlled room temperature and shipped at cool or refrigerated conditions. The proposed expiration dating for the drug product is 24 months.

Drug substance
The chemical name of fluocinolone acetonide is Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α,11β,16α)-6α,9-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with acetone. The drug substance is listed in the USP Monograph. It is a white to practically white crystalline powder. It is insoluble in water, freely soluble in acetone and glacial acetic acid, sparingly soluble in chloroform and methanol, and very slightly soluble in ether.

B. Description of How the Drug Product is Intended to be Used
Fluocinolone Acetonide Oil, 0.01%, should be applied five drops to the affected ear(s) twice daily for seven to fourteen days.

Maximum daily dose (MDD)

The MDD is calculated below based on the package insert information from DermOtic® Oil for Fluocinolone Acetonide Oil, 0.01%, which states that the product be applied to the affected ear(s) for maximum 14 days. In addition, the bottle for the firm's drug product is 20 mL fill.
MDD= (b) (4)
assuming 100% absorption

	IT	QT
DS	(b) (4)	
DP		

C. Basis for approvability or Not-approval Recommendation

The ANDA (CMC) is approvable. Bioequivalence review is acceptable. Labeling review and EES are pending.

38 pages have been withheld immediately following this page as b4

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

/s/

RICHARD CHANG
10/18/2010

TRANG Q TRAN
10/18/2010

JAMES M FAN
10/18/2010

ANDA 091306

Fluocinolone Acetonide Oil, 0.01% Ear Drops

Identi Pharmaceuticals Inc.

Richard Chang
Chemistry I

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A. Description of the Drug Product(s) and Drug Substance(s) 8

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C. Basis for Approvability or Not-approval Recommendation 9

Chemistry Assessment **10**

Chemistry Review Data Sheet

1. ANDA 091306

2. REVIEW #: 2

3. REVIEW DATE: September 3, 2010

4. REVIEWER: Richard Chang

5. PREVIOUS DOCUMENTS:

Submission(s) Reviewed	Document Date
Original submission	April 16, 2009
Acceptable for filing	April 20, 2009
Amendment	August 26, 2009
Amendment	August 27, 2009
Amendment	October 6, 2009

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	July 08, 2010
Gratuitous Amendment	August 12, 2010
Gratuitous Amendment	August 17, 2010

7. NAME & ADDRESS OF APPLICANT:

Name: Identi Pharmaceuticals Inc.
Address: 2224 W. Northern Ave.
Suite# D-300
Phoenix, Arisona 85021

US Agent: SciRegs International, Inc.
6333 Summercrest Drive
Columbia, MD 21045
Contact person: Jeanne Taborsky
Telephone: 410-309-3145

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A

Non-Proprietary Name (USAN): Fluocinolone Acetonide Oil, 0.01 % Ear Drops

9. LEGAL BASIS FOR SUBMISSION:

The Reference Listed Drug is Hill's DermOtic® Oil (fluocinolone acetonide oil, 0.01%)(NDA 019452 and NDA 021930)

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Identi Pharmaceuticals provided a statement of patent certification for the Abbreviated New Drug Application for Fluocinolone Acetonide Oil, 0.01%.

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The firm also provided an exclusivity statement to state that there is no unexpired exclusivity for this drug product.

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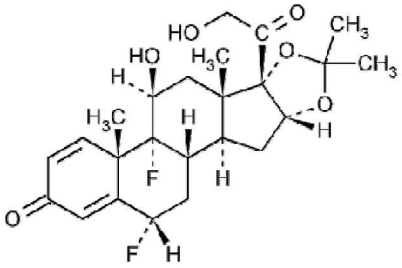
Molecular formula: $C_{24}H_{30}F_2O_6$ (anhydrous)

Molecular weight: 452.50

Structure:



17. RELATED/SUPPORTING DOCUMENTS:

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				4		
				4		
				4		
				4		

(b) (4)	
	4
	4
	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 REVIEWS	RECOMMENDATION	DATE	REVIEWER
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EES	Pending		
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Acceptable	08/31/10	J. Osterhout
EA	Satisfactory (exclusion requested)		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

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

The Chemistry Review for ANDA 091306

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on approvability

This ANDA is presently non-approvable. The minor chemistry deficiencies listed in the review should be addressed before the application can be approved. Bioequivalence review is acceptable. Labeling and EES are pending.

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
Fluocinolone Acetonide Oil, 0.01% contains fluocinolone acetonide which is a synthetic, fluorinated corticosteroid. It is intended for topical dermatologic use for the relief of the inflammatory and pruritic manifestation of atopic dermatitis in patients 1 year or older.
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MDD= (b) (4)
assuming 100% absorption

	IT	QT
DS	(b) (4)	
DP		

C. Basis for approvability or Not-approval Recommendation

The ANDA is non-approvable due to minor deficiencies. Bioequivalence review is acceptable. Labeling review and EES are pending.

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CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 091306 APPLICANT: Identi Pharmaceuticals Inc.

DRUG PRODUCT: Fluocinolone Acetonide Oil, 0.01% Ear Drops

The deficiencies presented below represent MINOR deficiencies.

Deficiencies:

(b) (4)

5. We noticed that the stability data generated for the test batch from (b) (4) and Amneal Pharmaceuticals are quite different. Please explain.

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

1. Information related to labeling is under review. After the reviews are completed, any deficiencies found will be communicated to you separately.

2. All facilities referenced in your ANDA should be in compliance with cGMP at the time of approval.

3. (b) (4)

Sincerely yours,

{See appended electronic signature page}

Paul Schwartz, Ph.D.
Acting Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 091306
ANDA DUP 091306
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-627/R. Chang/Review Chemist/07/16/2010, 08/31/2010

HFD-627/J. Fan/ Team Leader/07/29/10, 09/02/10

HFD-617/T. Tran/Project Manager/07/30/10, 09/02/10

V:\Chemistry Division I\Team 3\FIRMSAM\Identi\LTRS&REV\091306.rev2.DOC

TYPE OF LETTER: NOT APPROVABLE - MINOR

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-91306	ORIG-1	IDENTI PHARMACEUTICALS	FLUOCINOLONE ACETONIDE

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

/s/

RICHARD CHANG
09/03/2010

TRANG Q TRAN
09/03/2010

JAMES M FAN
09/03/2010

ANDA 091306

Fluocinolone Acetonide Oil, 0.01% Ear Drops

Identi Pharmaceuticals Inc.

Richard Chang
Chemistry I

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Chemistry Review Data Sheet

1. ANDA 091306

2. REVIEW #: 1

3. REVIEW DATE: November 17, 2009

4. REVIEWER: Richard Chang

5. PREVIOUS DOCUMENTS: N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original submission	April 16, 2009
Acceptable for filing	April 20, 2009
Amendment	August 26, 2009
Amendment	August 27, 2009
Amendment	October 6, 2009

7. NAME & ADDRESS OF APPLICANT:

Name: Identi Pharmaceuticals Inc.
Address: 2224 W. Northern Ave.
Suite# D-300
Phoenix, Arisona 85021

US Agent: SciRegs International, Inc.
6333 Summercrest Drive
Columbia, MD 21045
Contact person: Jeanne Taborsky

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
Non-Proprietary Name (USAN): Fluocinolone Acetonide Oil, 0.01 % Ear Drops

9. LEGAL BASIS FOR SUBMISSION:

The Reference Listed Drug is Hill's DermOtic® Oil (fluocinolone acetonide oil, 0.01%)(NDA 019452 and NDA 021930)

PATENT CERTIFICATION STATEMENT

Identi Pharmaceuticals provided a statement of patent certification for the Abbreviated New Drug Application for Fluocinolone Acetonide Oil, 0.01%.

Also presented is a marketing exclusivity statement required under 21 CFR Section 314.94(a)(3)(ii).

PATENT INFORMATION

Identi Pharmaceuticals' proposed drug product is the generic version of Hill Dermaceuticals' DermOtic®, pursuant to NDA 021930 and NDA 019452. There are no unexpired patents for this drug product in the FDA listing titled Electronic Orange Book- Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as Orange Book). Identi Pharmaceuticals provided a Paragraph II certification for their drug product, Fluocinolone Acetonide Oil, 0.01%.

EXCLUSIVITY STATEMENT

The firm also provided an exclusivity statement to state that there is no unexpired exclusivity for this drug product.

10. PHARMACOL. CATEGORY:
    Glucocorticoid and indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years old and older.

11. DOSAGE FORM: Topical-otic

12. STRENGTH/POTENCY: 0.01%

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:

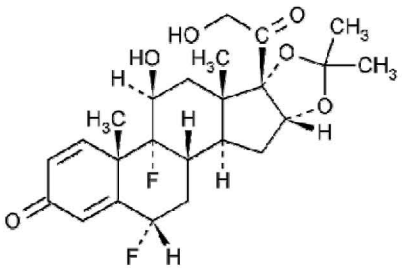
Compendial name: fluocinolone acetonide, USP

Chemical name: Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α,11β,16α)-6α,9-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with acetone

Molecular formula: $C_{24}H_{30}F_2O_6$ (anhydrous)

Molecular weight: 452.50

Structure:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	Type	Item referenced	Holder	Code[1]/ Status[2]	Date review completed	Comments
(b) (4)						
				dequate	2/26/10	Reviewed by Richard Chang
				4		
				4		
				4		
				4		

(b) (4)	
	4
	4
	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 REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Pending		
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Pending (Biowaiver requested)		
EA	Satisfactory (exclusion requested)		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

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

The Chemistry Review for ANDA 091306

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on approvability

This ANDA is presently non-approvable. The minor chemistry deficiencies listed in the review should be addressed before the application can be approved. Labeling, EES and Bioequivalence are pending.

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
Fluocinolone Acetonide Oil, 0.01% contains fluocinolone acetonide which is a synthetic, fluorinated corticosteroid. It is intended for topical dermatologic use for the relief of the inflammatory and pruritic manifestation of atopic dermatitis in patients 1 year or older. Each gram of Fluocinolone Acetonide Oil, 0.01% contains 0.11 (b) (4) mg fluocinolone acetonide in an oil consisting of isopropyl alcohol USP, refined peanut oil NF, isopropyl myristate NF, and light mineral oil NF.

Fluocinolone Acetonide Oil, 0.01% is a clear, colorless to light straw colored liquid. Fluocinolone acetonide oil will be marketed in the following package (b) (4) mL (1 oz) white round soft-shoulder bottle with a (b) (4) white, fine ribbed cap and a dropper.

It is to be stored in controlled room temperature and shipped at cool or refrigerated conditions. The proposed expiration dating for the drug product is 24 months.

Drug substance
The chemical name of fluocinolone acetonide is Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(6α,11β,16α)-6α,9-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with acetone. The drug substance is listed in the USP Monograph. It is a white to practically white crystalline powder. It is insoluble in water, freely soluble in acetone and glacial acetic acid, sparingly soluble in chloroform and methanol, and very slightly soluble in ether.

B. Description of How the Drug Product is Intended to be Used
Fluocinolone Acetonide Oil, 0.01%, should be applied five drops to the affected ear(s) twice daily for seven to fourteen days.

Maximum daily dose (MDD)

The MDD is calculated below based on the package insert information from DermOtic® Oil for Fluocinolone Acetonide Oil, 0.01%, which states that the product be applied to the affected ear(s) for maximum 14 days. In addition, the bottle for the firm's drug product is 20 mL fill.
MDD= (b) (4)
assuming 100% absorption

	IT	QT
DS	(b) (4)	
DP		

C. Basis for approvability or Not-approval Recommendation

The ANDA is non-approvable due to minor deficiencies. Labeling, bioequivalence reviews, and EES are pending.

31 pages have been withheld immediately following this page as b4

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

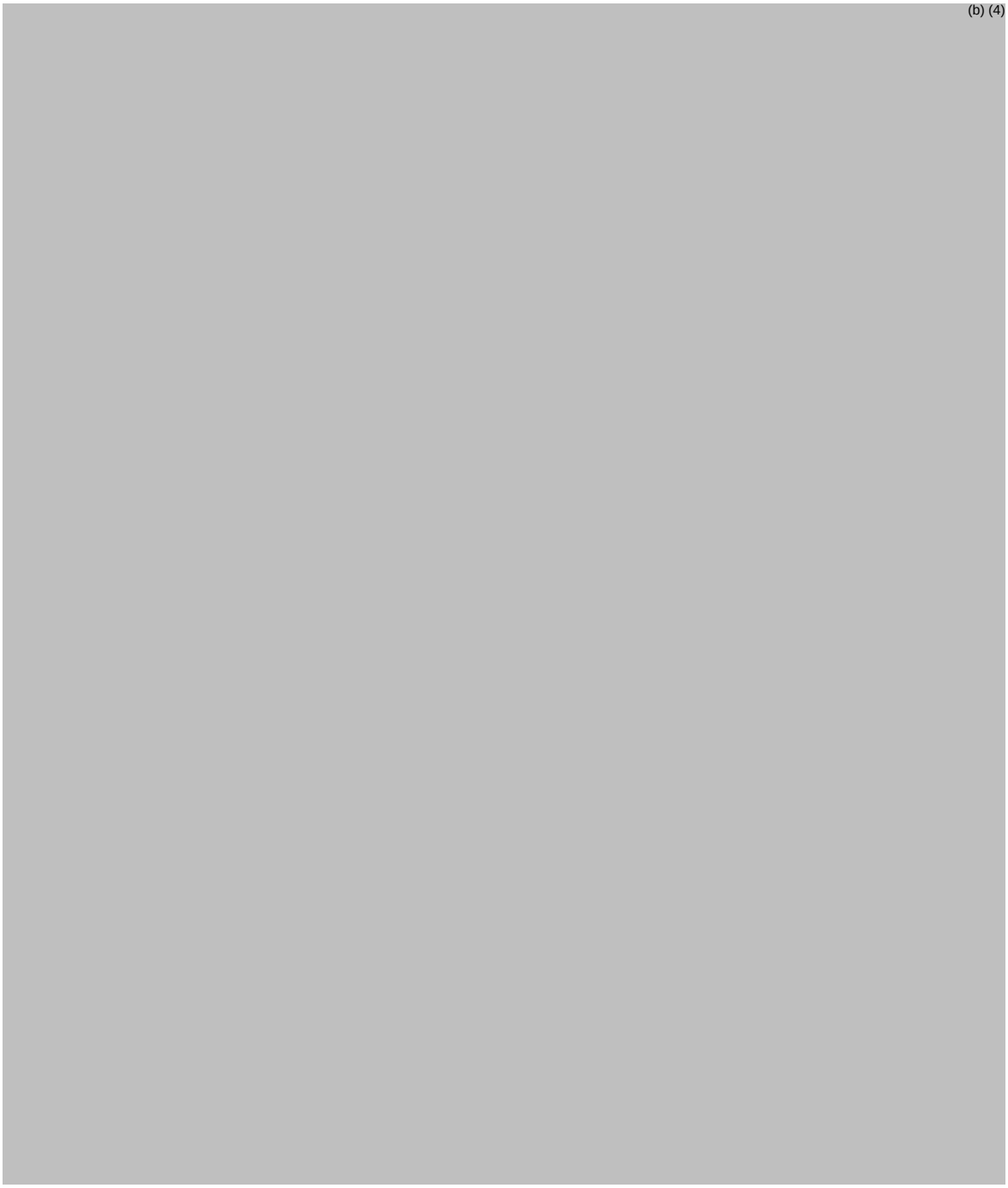
ANDA: 091306 APPLICANT: Identi Pharmaceuitcals Inc.

DRUG PRODUCT: Fluocinolone Acetonide Oil, 0.01% Ear Drops

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

(b) (4)



(b) (4)

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

1. Please provide all available drug product room temperature stability data.

2. Bioequivalency and labeling information you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you separately.

3. All facilities referenced in your ANDA should be in compliance with cGMP at the time of approval. We have requested an evaluation from the Office of Compliance.

Sincerely yours,

Paul Schwartz, Ph.D.
Acting Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 091306
ANDA DUP 091306
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-627/R. Chang/Review Chemist/November 17, 2009
HFD-627/J. Fan/ Team Leader/1/9/10
HFD-617/T. Tran/Project Manager/1/22/10;2/26/10

F/T by :TT

V:\Chemistry Division I\Team 3\FIRMSAM\Identi\LTRS&REV\091306.rev1.DOC

TYPE OF LETTER: NOT APPROVABLE - MINOR

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-91306	ORIG-1	IDENTI PHARMACEUTICALS	FLUOCINOLONE ACETONIDE

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/s/

RICHARD CHANG
03/10/2010

TRANG Q TRAN
03/11/2010

JAMES M FAN
03/11/2010

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 91-306

BIOEQUIVALENCE REVIEWS

Addendum to Review of a Request for a Waiver of an In Vivo Bioequivalence Study Requirement

ANDA No.	091306
Drug Product	Fluocinolone Acetonide Oil, 0.01%
Sponsor	Identi Pharmaceuticals Inc. (Identi)
Reference Listed Drug	DermOtic Oil (fluocinolone acetonide oil) 0.01% Ear Drops
Original Submission Date(s)	16 April 2009
Original Primary Reviewer	James L. Osterhout, PhD

ANDA 091306 when originally submitted contained the following Request for Waiver (In-Vivo BA/BE Study(ies)):

> Identi Pharmaceuticals LLC. contracted the manufacture of Fluocinolone Acetonide Oil 0.01% Ear Drops. Identi's Fluocinolone Acetonide Oil 0.01% Ear Drops, is qualitatively and quantitatively similar to Hill's DermOtic® Oil (fluocinolone acetonide oil) 0.01% Ear Drops. The compositional and test data support the equivalency of Identi's Fluocinolone Acetonide Oil 0.01% Ear Drops, to DermOtic® Oil (fluocinolone acetonide oil) 0.01% Ear Drops.
>
> Based upon these considerations, a waiver of *in-vivo* bioavailability/ bioequivalence study requirements for Identi's Fluocinolone Acetonide Oil, 0.01% Ear Drops, is requested.

In the review of Identi's request for waiver (finalized in DARRTS on August 31, 2010), the following statement was made:

> The sponsor's proposed formulation is acceptable for a waiver of the in vivo BE study requirements under 21 CFR § *320.22 (b) (1)*. A waiver is therefore granted. From a clinical bioequivalence perspective, this application is acceptable for approval. [emphasis added.]

The cited regulation, 21 CFR 320.22 (b) (1) requires that the proposed generic otic solution "[c]ontain[] the same active and inactive ingredients in the same concentration" as the reference listed drug. The formulation submitted by Identi is qualitatively (Q1), and quantitatively (Q2), the same as the reference listed drug (RLD) for all ingredients except two fragrance components in the RLD, which are omitted from Identi's formulation. Because Identi's formulation omits two inactive ingredients that are present in the RLD, this regulation does not apply.

The approval of ANDA 091306 without the submission of an in vivo BE study is nevertheless supported by the Division of Dermatology and Dental Products (DDDP). In its consult response dated August 20, 2009 (made in response to a request from the Office of Generic Drugs dated July 2, 2009), the DDDP determined that omission of the two fragrance components would not affect the safety and efficacy of the proposed generic product, and DDDP did not object to a

waiver of the in vivo BE study requirement. It is noted that the combined amounts of these fragrance ingredients is only (b) (4) % of the total % v/v of the RLD product.

It is therefore determined that, pursuant to 21 CFR 320.24(b)(6), under which "[a]ny other approach deemed adequate by FDA to measure bioavailability or establish bioequivalence" can be acceptable for determining bioavailability or bioequivalence of a drug product, bioequivalence of the Identi product and the RLD has been established.

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/s/

BRENDA S GIERHART
11/14/2011

DALE P CONNER
11/14/2011

Review of a Request for a Waiver of an In Vivo Bioequivalence Study Requirement

ANDA No.	091306
Drug Product	Fluocinolone Acetonide Oil, 0.01%
Sponsor	Identi Pharmaceuticals Inc.
Reference Listed Drug	DermOtic® Oil (fluocinolone acetonide oil) 0.01% Ear Drops
Original Submission Date(s)	16 April 2009
Submission Dates Under Review	16 April 2009
Reviewer	James L. Osterhout, PhD
Date of Review	15 October 2009

1 Executive Summary

Identi Pharmaceuticals Inc. requests a waiver of the in vivo bioequivalence study requirement for its generic fluocinolone acetonide oil 0.01% ear drops.

This product is a solution, and the sponsor's proposed formulation is qualitatively (Q1), and quantitatively (Q2), the same as the reference listed drug (RLD) for all components except for the two fragrance components, which were omitted from the sponsor's proposed formulation.

In a consult to The Division of Dermatology and Dental Products in the Office of New Drugs, it was determined that omission of the 2 fragrance components would not affect the safety and efficacy of the proposed generic product.

The sponsor's proposed formulation is acceptable for a waiver of the in vivo BE study requirements under 21 CFR § 320.22 (b) (1). A waiver is therefore granted. From a clinical bioequivalence perspective, this application is acceptable for approval.

2 Background

2.1 Summary of Drug Information

Drug Established Name	Fluocinolone Acetonide Oil, 0.01% (Ear Drops)
Reference Product	DermOtic® Oil (fluocinolone acetonide oil) 0.01% Ear Drops
RLD Manufacturer	Hill Dermaceuticals, Inc.
NDA Number	N019452
RLD Approval Date	09 November 2005

Indication(s)	Fluocinolone acetonide oil is a low to medium potency corticosteroid indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years and older.
Dose Regimen(s)	Apply 5 drops of fluocinolone acetonide oil into the affected ear. To apply, tilt head to one side so that the ear is facing up. Then gently pull the ear lobe backward and upward and apply 5 drops of oil into the ear. Keep head tilted for about a minute to allow oil to penetrate lower into the ear canal. Gently pat excess material dripping out of the ear using a clean cotton ball. Follow these instructions twice each day for 7 to 14 days.

2.2 Drug Formulations

USING % v/v of RLD Formulation calculated from batch record in NDA 19-452

	ANDA 091306 (mL)	RLD (L)	ANDA 091306 % v/v	RLD % v/v	Proportional Difference % v/v
Refined Peanut Oil, NF	48	(b) (4)	48.0	(b) (4)	(b) (4)
Light Mineral Oil, NF					
Oleth-2					
Isopropyl Myristate, NF					
Isopropyl Alcohol, NF					
Cream Fragrance					
Balsam Pine Fragrance					
Fluocinolone Acetonide, USP					
Total Volume					

USING % v/v of RLD Formulation found in Table 2 of NDA 19-452

	ANDA 091306 (mL)	ANDA 091306 % v/v	RLD % v/v	Proportional Difference % v/v
Refined Peanut Oil, NF	48	48.0	(b) (4)	(b) (4)
Light Mineral Oil, NF				
Oleth-2				
Isopropyl Myristate, NF				
Isopropyl Alcohol, NF				
Cream Fragrance				
Balsam Pine Fragrance				
Fluocinolone Acetonide, USP	0.01 g			

Other than the two fragrance components, none of the inactive ingredients in the Generic proposed formulation are greater then 5% proportionally different from the amounts found in the RLD formulation.

[1] This volume does not take into account the volume addition of the (b) (4) active ingredient.

3 Application History

The sponsor has removed the 2 fragrance components found in the RLD Formulation from their proposed formulation.

21CFR 314.94(a)(9)(iv) states that "Generally, a drug product intended for ophthalmic or otic use shall contain the same inactive ingredients and in the same concentration as the reference listed drug…". "However, an applicant may seek approval of a drug product that differs from the reference listed drug in preservative, buffer, substance to adjust tonicity, or thickening agent provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product,…"

Furthermore, the regulations in 21 CFR 320.22(b)(1)(i-ii) clearly specify that a waiver for an otic product is only appropriate for a product that; "Contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application."

Given the above regulations, it was unclear if adding or removing a fragrance is acceptable for an ANDA submission for an otic product. In a consult to the Division of Dermatology and Dental Products in the Office of New Drugs, it was determined that omission of the 2 fragrance components would not affect the safety and efficacy of the proposed generic product. The combined amounts of these fragrance ingredients is only (b) (4)% of the total % v/v of the RLD product.

The sponsor's proposed formulation is qualitatively and quantitatively the same as the reference listed drug, DermOtic® Oil (fluocinolone acetonide oil) 0.01% Ear Drops for all other components in the formulation.

4 Conclusion and Recommendation

The drug product is an otic solution and contains the same active drug in the same concentration and dosage form as the RLD. The proposed formulation is qualitatively and quantitatively the same as the reference listed drug, DermOtic® Oil (fluocinolone acetonide oil) 0.01% Ear Drops for all components in the formulation except omission of the fragrance, which amounts to only (b) (4)% v/v of the RLD product. The omission of the 2 fragrance components will not affect the safety or efficacy of the sponsor's proposed formulation.

A waiver of the in vivo bioequivalence study requirement is granted based on 21 CFR § 320.22 (b) (1). From a clinical bioequivalence perspective, this application is acceptable for approval.

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 091306

APPLICANT: Identi Pharmaceuticals Inc.

DRUG PRODUCT: Fluocinolone Acetonide Oil, 0.01% Ear Drops

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

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

Sincerely yours,

{See appended electronic signature page}

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-91306	ORIG-1	IDENTI PHARMACEUTICALS	FLUOCINOLONE ACETONIDE

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/s/

JAMES L OSTERHOUT
08/30/2010

DENA R HIXON
08/30/2010
I concur.

DALE P CONNER
08/31/2010

BIOEQUIVALENCE CHECKLIST for First Generic ANDA
FOR APPLICATION COMPLETENESS

ANDA# 91-306 **FIRM NAME** Identi Pharmaceuticals, LLC

DRUG NAME Fluocinolone Acetonide Oil, 0.01% Ear Drops
DOSAGE FORM Topical Oil (Ear Drops)
STRENGTHS 0.01%
SUBJ: The request for study submitted by Identi Pharmaceuticals, LLC on March 24, 2009 for its Fluocinolone product satisfies the statutory requirements of "completeness" so that the ANDA may be filed.

Requested by: _____ Date: _____
Chief, Regulatory Support Team, (HFD-615)

	Summary of Findings by Division of Bioequivalence
☐	**Study meets statutory requirements**
☐	**Study does NOT meet statutory requirements**
	Reason:
☒	**Waiver meets statutory requirements**
☐	**Waiver does NOT meet statutory requirements**

RECOMMENDATION: ☒ **COMPLETE** ☐ **INCOMPLETE**

Reviewed by:

_____ Date: _____
Deanah L. Mitchell, Ph.D.
Reviewer

_____ Date: _____
April C. Braddy, Ph.D.
Team Leader

_____ Date: _____
Hoainhon Nguyen-Caramenico
Acting Deputy Director

Item Verified:	YES	NO	Required Amount	Amount Sent	Comments[1]
Protocol	☐	☒			N/A
Assay Methodology	☐	☒			N/A
Procedure SOP	☐	☒			
Methods Validation	☒	☐			Found in Section 3.2.S.4.2
Study Results Ln/Lin	☐	☒			N/A
Adverse Events	☐	☒			N/A
IRB Approval	☐	☒			N/A
Dissolution Data	☐	☒			N/A
Pre-screening of Patients	☐	☒			N/A
Chromatograms	☐	☒			N/A
Consent Forms	☐	☒			N/A
Composition	☒	☐	1	1	Found in Volume 5 Section 5.3.1.2 of the electronic submission.
Summary of Study	☐	☒			N/A
Individual Data & Graphs, Linear & Ln	☐	☒			N/A
PK/PD Data Disk Submitted)	☐	☒			N/A
Randomization Schedule	☐	☒			N/A
Protocol Deviations	☐	☒			N/A
Clinical Site	☐	☒			N/A
Analytical Site	☐	☒			N/A

1 This is an electronic submission

Study Investigators	☐	☒			N/A
Medical Records	☐	☒			N/A
Clinical Raw Data	☐	☒			N/A
Test Article Inventory	☒	☐			Found in Volume 3 Section 3.2.R of the electronic submission. [(b) (4) kg]
BIO Batch Size	☒	☐			Found in Volume 3 Section 3.2.P.5.4 of the electronic submission. [Batch Size: (b) (4) kg]
Assay of Active Content Drug	☒	☐			Found in Volume 3 Section 3.2.S.4.4 of the electronic submission. [(b) (4)]
Content Uniformity	☐	☒			N/A
Date of Manufacture	☒	☐			Found in Volume 3 Section 3.2.S.4.4. of the electronic submission. [Lot No. 54345; Mfg. Date: 11/12/06]
Exp. Date of RLD	☐	☒			
BioStudy Lot Numbers	☐	☒			N/A
Statistics	☐	☒			N/A
Summary results provided by the firm indicate studies pass BE criteria	☐	☒			N/A
Waiver requests for other strengths / supporting data	☐	☒			N/A

I. Additional Comments regarding the ANDA:

1. This is a First Generic application for Fluocinolone Acetonide Oil/Drops (Otic), 0.01%. The Reference Listed Drug (RLD) is DermOtic® Oil (Fluocinolone Acetonide Oil), 0.01% Ear Drops by Hill Dermaceuticals (NDA# 019452 approved on November 09, 2005).

2. Currently, the Division of Bioequivalence recommends the following based on 21 CFR § 320.22(b)(1)(i-ii):

For certain drug products, the in vivo bioavailability of bioequivalence of the drug product may be self-evident. FDA shall waive the requirement for the submission of evidence obtained in vivo measuring the bioavailability or demonstrating the bioequivalence of these drug products. A drug products in vivo bioavailability or bioequivalence may be considered self-evident based on other data in the application if the product meets one of the following criteria:

(1) The drug product:

(i) Is a parental solution intended solely for administration by injection, or an ophthalmic or otic solution; and

(ii) Contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application.

3. The applicant of the current Abbreviated New Drug Application (ANDA), Identi Pharmaceuticals, LLC, is seeking an approval of a generic product to DermOtic® Oil (Fluocinolone Acetonide Oil), 0.01% Ear Drops. The drug is a low to medium potency corticosteroid indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years and older. The firm's test product only differs from the RLD product in that it does not contain fragrances whereas the RLD product contains less than (b) (4)% volume/volume of fragrances. All other qualitatively (Q1) and quantitatively (Q2) differences in the formulation are within ± 5% based on the % volume/volume comparison of each of the inactive ingredients. From the Division of Bioequivalence standpoint, this submission meets all of the statutory requirements, and is therefore considered **acceptable** for filing.

4. The differences in the formulation pertaining to the fragrances will be addressed at the time of the waiver request review. The DBE has also submitted a clinical consult to the Clinical Division in the Office of Generic Drugs to request the clinical opinion on the safety and efficacy effect, if any, of the lack of fragrances in the test formulation. The clinical consult response will be incorporated into the waiver request review.

II. Additional Attachment:

1) E-mail Communication #1:

From: Raghavachari, Ramesh
Sent: Friday, May 15, 2009 11:55 AM
To: Mitchell, Deanah
Subject: RE: Question about NDA 19452

Hi Deanah,
From my review the otic formulation is the same as that of the topical oil. It is just packaged differently or otic use with labeling.
Hope it helps,
Ramesh

From: Mitchell, Deanah
Sent: Friday, May 15, 2009 11:00 AM
To: Raghavachari, Ramesh
Cc: Mitchell, Deanah
Subject: Question about NDA 19452

Hello Ramesh,

I am a reviewer in The Office of Generic Drugs, Division of Bioequivalence. I am currently reviewing an application for Fluocinolone Acetonide, Oil Drops (Otic) 0.01%. The RLD is NDA 19452 by Hill Dermaceuticals (Approved Nov. 9, 2005). I am looking for the formulation for the Oil/Drops and have not been able to locate it. I contacted Jane Chang because I saw her as one of the most recent reviewers for a Chemistry supplement. Would you happen to know how to get the formulation for the Oil Drops (Otic)? Thanks for any help you may be able to provide.

Deanah L. Mitchell, Ph.D.
Pharmacologist
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation Research
Food and Drug Administration
7520 Standish Place, MPN1 HFD-650, Rm. 1344
Rockville, Maryland 20855
Tel: 240-276-8792
Fax: 240-276-8766
deanah.mitchell@fda.hhs.gov

2) Formulation Information:

A: NDA Formulation[2,3] (NDA # 19452): (NOT FOR RELEASE UNDER FOIA)

Ingredient	Percentage
Fluocinolone Acetonide, USP	0.010
Refined peanut Oil, NF[a]	(b) (4)
White Mineral Oil, USP	
Oleth-2	
Isopropyl Myristate, NF	
Isopropyl Alcohol, NF	
Cream Fragrance # (b) (4)	
Balsam Pine Fragrance (b) (4)	

Note: For the inactive ingredients, the "Percentage" in the RLD formulation is based on Volume/Volume (v/v) * 100 (See attachment)
For the active ingredient, the "Percentage" in the RLD formulation is based on weight/volume (w/v) * 100
a- Refined peanut oil, NF has been heated at 475 °F for 15 minutes to denature possible peanut allergens.
*****The RLD labeling states that Light Mineral Oil is an inactive ingredient in Fluocinolone Acetonide Oil. Therefore, in the table above, White Mineral Oil, USP is used interchangeably as Light Mineral Oil.

B: ANDA Formulation: Fluocinolone Acetonide Topical Oil, 0.01% (Ear Drops)[4]

RLD Unit Composition (maximum daily dose = 10 drops or 0.0228 mg Fluocinolone Acetonide)			
Ingredient	**Generic**		**RLD**
	v/v %	**w/w %**	**amount**
Fluocinolone Acetonide, USP	0.01 g	0.011	0.01% w/v ≈ 0.11 mg per gram
Isopropyl Alcohol, USP	(b) (4)		
Isopropyl Myristate, NF			
Oleth-2			
Mineral Oil, USP			
Peanut Oil, NF			
Cream Fragrance (b) (4)			
Balsam Pine fragrance (b) (4)			
Total	**100.00 mL**	(b) (4)	

2 Division of System Files v. 2.0; SE5-024: Pediatric effica, Pharmacologist; N 019452 SE5 024 12-Feb-2007. Review Sign off date: 06/13/2007.
3 Archival Copy of NDA 19452; Volume 1.1. Date: August 14, 1985. Page 167.
4 ANDA submission, Section 2.3.P.1: Formulation Composition

C: Formulation Differences between the Test and Reference Products

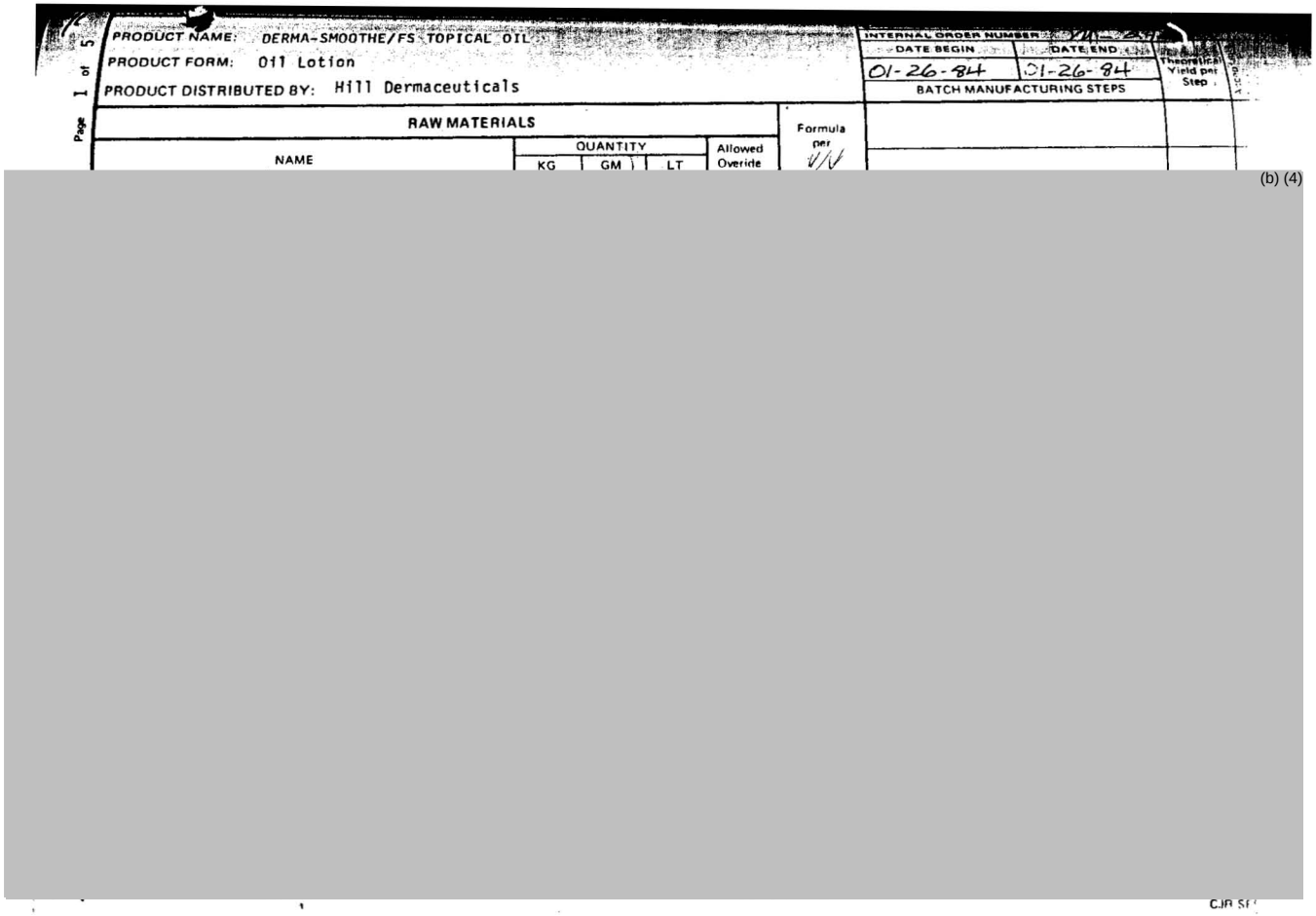
Ingredient	w/v of Test Product* per 100 mL	W/v of RLD Product per 100 mL	Q1/Q2 % Difference between RLD and Test Product**
Fluocinolone Acetonide	0.01 g	0.01 g	0.0%
Ingredient	**v/v of Test Product* per 100 mL**	**v/v of RLD Product per 100 mL**	**Q1/Q2 % Difference between RLD and Test Product****
Isopropyl Alcohol	(b) (4)		
Isopropyl Myristate			
Oleth-2			
Light Mineral Oil			
Refined Peanut Oil			
Cream Fragrance (b) (4)			
Balsam Pine Fragrance (b) (4)			
Total	100 mL	100 mL	

*As calculated by the firm, Identi Pharmaceuticals, LLC.
** Percent difference is calculated as: (Test – Reference)/ Reference * 100

ADDITIONAL ATTACHMENT #2:

Raw excipients of NDA 19452

(Archival Copy of NDA 19452; Volume 1.1. Date: August 14, 1985. Page 167).



Page 1 of 5

PRODUCT NAME: DERMA-SMOOTHE/FS TOPICAL OIL

PRODUCT FORM: Oil Lotion

PRODUCT DISTRIBUTED BY: Hill Dermaceuticals

INTERNAL ORDER NUMBER:

DATE BEGIN: 01-26-84 DATE END: 01-26-84

RAW MATERIALS

NAME	QUANTITY KG	GM	LT	Allowed Overide	Formula per

BATCH MANUFACTURING STEPS

Theoretical Yield per Step

(b) (4)

[redacted]

ADDITIONAL ATTACHMENT #3:

From: Nguyen, Hoainhon T
Sent: Thursday, June 25, 2009 3:55 PM
To: Braddy, April
Cc: Mitchell, Deanah; Nguyen, Hoainhon T
Subject: Checklist Review for ANDA 91306

April,
Per Dale's recommendation, since the test and RLD formulations are Q1Q2 match except for the fragrances, we will **accept** the application for filing and evaluate the effect of the fragrances later based on our clinical consult. Please go ahead and complete the checklist review, and prepare a consult request at the same time. And also, just in case another ANDA comes in with a similar issue.
Please let me know if you have other questions.
Thanks,
Hoai

OUTCOME PAGE

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
8276	3/24/2009	Paragraph 4	Paragraph 4 Checklist	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/

Hoainhon T. Nguyen
6/30/2009 02:36:23 PM
For Dale P. Conner, Pharm. D., Director, Division of Bioequivalence I

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 91-306

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

SCIREGS International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

November 15, 2011

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0020 Telephone Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a telephone amendment to our abbreviated new drug application (ANDA 091-306) for Fluocinolone Acetonide Oil 0.01% Ear Drops.

As requested by the agency, we have revised our submission to include a Waiver of the requirements to contain the same inactive ingredients in products for otic use pursuant to 21 CFR §314.94(a)(9)(iv) and have provided it in Module 1 Section 1.12.5 Request for Waiver.

This completes our submission. This submission is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

November 15, 2011

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0019 Correspondence

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 §314.60, SciRegs International Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits correspondence to our abbreviated new drug application (ANDA 091-306) for Fluocinolone Acetonide Oil 0.01% Ear Drops.

Please be advised that there was a typographical error made to the filing form for the Applicant Information section, name of applicant. Identi Pharmaceuticals is a limited liability company (LLC) but was inadvertently listed an incorporation (Inc). Please address all future correspondence in relation to this ANDA to Identi Pharmaceuticals LLC.

This completes our submission. This submission is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville, MD

November 14, 2011

RE: ANDA 091306

ADMINISTRATIVE RECONSIDERATION AND STAY OF ACTION

Pursuant to 21 C.F.R. § 10.33(a) and (h), the Commissioner has concluded that FDA must reconsider the approval of Identi Pharmaceuticals Inc.'s ("Identi") Abbreviated New Drug Application ("ANDA") 091306 for fluocinolone acetonide oil, 0.01% ear drops. The Commissioner has concluded that it is in the public interest to do so because there is an outstanding question regarding this approval that the Agency must consider. To permit this reconsideration, FDA will stay the approval of ANDA 091306 pursuant to 21 CFR 10.35(a) until November 18, 2011, at which time FDA expects to have completed its reconsideration of the application.

Accordingly, the approval of ANDA 091306 is hereby stayed until November 18, 2011. Marketing, sales, and shipment under ANDA 091306 are prohibited during the pendency of this administrative stay.

John M. Taylor III
Counselor to the Commissioner
Food and Drug Administration

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

/s/

BRENDA S GIERHART
11/14/2011

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

November 14, 2011

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0018 Telephone Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a telephone amendment to our abbreviated new drug application (ANDA 091-306) for Fluocinolone Acetonide Oil 0.01% Ear Drops.

As requested by the agency we have revised our bioequivalence waiver pursuant to *21 CFR* 314.90(a) Waivers and have provided it in Module 1 Section 1.12.15 Request for Waiver.

This completes our submission. This submission is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

ROUTING SHEET

APPROVAL TENTATIVE APPROVAL SUPPLEMENTAL APPROVAL (NEW STRENGTH) CGMP

Division: I	**Team: 13**	**PM: Trang Tran**

Electronic ANDA: Yes No

ANDA #:091306
Firm Name:Identi Pharmaceuticals Inc.
ANDA Name:Fluocinolone Acetonide Topical Oil, 0.01% (Ear Drops)
RLD Name:DermOtic Ear Drops, 0.01%

Electronic AP Routing Summary Located:
V:\Chemistry Division I\Team 13\Electronic AP Summary\91306.ARS.doc

AP/TA Letter Located:
V:\Chemistry Division I\Team 13\FIRMSAM\Identi\LTRS&RVS\91306.AP.DOC

Project Manager Evaluation: **Date: 4/14/11 Initials:** TT

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

Original Rec'd date 4/16/09 | Date of Application 4/16/09 | Date Acceptable for Filing 4/20/09

Patent Certification (type) II | 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 | Priority Approval (Top 100, PEPFAR, etc.)? Yes No Comment:

DMF#: (b) (4) (provide MF Jackets) | Prepared Draft Press Release sent to Cecelia Parise Yes No Date:

Suitability Petition/Pediatric Waiver | Pediatric Waiver Request: Accepted Rejected Pending

EER Status: Pending Acceptable OAI *EES Date Acceptable: 12/17/10* 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) 10/13/2011 Addendum Needed: Yes No Comment:
Date of Acceptable Bio 8/31/2010 Bio reviews in DARRTS: Yes No (Volume location:)
Date of Acceptable Labeling 10/12/11 Attached labeling to Letter: Yes No Comment:
Date of Acceptable Sterility Assurance (Micro) N/A

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: REMS Required: Yes No REMS Acceptable: Yes No

Regulatory Support

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

Division

1st Generic Review

Bob West / Peter Rickman
Keith Webber

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

OGD APPROVAL ROUTING SUMMARY

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

Martin Shimer **Date: 4/15/2011**

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	
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 4/20/2009, BOS=DermOtic Oil NDA 19452, PII cert provide. ANDA ack for filing on 4/20/2009(LO dated 10/15/2009). There are no remaining unexpired patents or exclusivities which protect the RLD. This ANDA is eligible for immediate Full Approval. Update 10/3/2011-there have been no changes in patent or legal status since this ANDA was evaluated in April. Application remains eligible for Full Approval.	

2. ***Labeling Endorsement***

Reviewer, : Labeling Team Leader, :

Date Date

Initials Initials

REMS required? REMS acceptable?

Yes No Yes No n/a

Comments:

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 10/13/11**

Chemistry Div. **I (Schwartz)** **InitialsASR**

Comments:CMC Approvable

5. ***First Generic Evaluation*** **First Generics Only**

Frank Holcombe **Date**

Assoc. Dir. For Chemistry **Initials**

Comments: (First generic drug review)

OGD Office Management Evaluation

Reference ID: 3030011

6. Peter Rickman **Date 10/17/2011**
Director, DLPS **Initials WPR**
Para.IV Patent Cert: Yes☐ No☒
Pending Legal Action: Yes ☐ No ☒
Petition: Yes☒ No☐
Comments: BOS=DermOtic Oil NDA 19452, applicant provided a PII patent cert. there are no remaining unexpired patents or exclusivities which protect the RLD. chemistry acceptable 10/13/2011. bio acceptable 8/31/2010 (waiver granted). labeling acceptable 10/12/2011. this ANDA is eligible for immediate Full Approval.

AND/OR

7. Robert L. West **Date _____**
Deputy Director, OGD **Initials _____**
Para.IV Patent Cert: Yes☐ No☐
Pending Legal Action: Yes☐ No☐
Petition: Yes☐ No☐
Press Release Acceptable ☐
Date PETS checked for first generic drug _____

Comments:

8. ***OGD Director Evaluation***
Keith Webber
Deputy Director, OPS
Comments:
First Generic Approval ☐
PD or Clinical for BE ☐
Special Scientific or Reg.Issue ☐
Press Release Acceptable ☐

Comments:

9. Project Manager
Date 10/17/11
Initials TT

Check Communication and Routing Summary into DARRTS

EER DATA:

APPEARS THIS WAY IN THE ORIGINAL

DARRTS Application History:

APPEARS THIS WAY IN THE ORIGINAL

Orange Book Report:

APPEARS THIS WAY IN THE ORIGINAL

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

/s/

TRANG Q TRAN
10/17/2011

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

October 4, 2011

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0017 Labeling Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a telephone amendment to our abbreviated new drug application (ANDA 091-306) for Fluocinolone Acetonide Oil 0.01% Ear Drops.

Labeling Deficiencies

1. *CONTAINER: Revise "Net Contents 20 mL (1 fl oz)" to read "Net Contents 20 mL."*

   As requested, the wording on the container label was revised to read *"Net Contents 20 mL."* The revised final printed bottle label is included in Section 1.14.2.1 Final Labels. Identi is also providing a revised bottle label side-by-side comparison in Section 1.14.2.3 Final Label Text.

2. *INSERT: CLINICAL STUDIES: Revise to include this section in its entirety except for the last sentence:*

   "importantly, the bulk peanut oil, NF, used in fluocinolone acetonide oil is heated at 475°F for at least 15 minutes, which should provide for adequate decomposition of allergenic proteins."

   This information is product specific and should not be included in your labeling if it does not pertain to your drug.

   As requested, this section of the insert has been revised in its entirety and includes the peanut oil statement. Please be advised that our source of peanut oil is heated by the manufacturer at 475°F for at least 15 minutes. The revised insert text is provided in Section 1.14.2.3 Final Label Text. The Final Printed Label version of the insert us provided in Section 1.14.2.2 Final Package Insert. The SPL labeling has also been revised and is provided in Section 1.14.2.3 Final Label Text. Additionally, Identi is providing a revised side-by-side comparison of the insert in Section 1.14.2.3 Final Label Text.

Labeling Comments:

1. *CARTON: (20 mL): Satisfactory in Final Print.*

The carton has been updated to reflect the change in revision date for the other labeling documents. The revised carton label is provided in Section 1.14.2.1 Final Labels.

Please submit the requested information as telephone amendments.

As instructed, this response is provided as a Telephone Amendment.

This completes our submission. This submission is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

September 29, 2011

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0016 Telephone Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a telephone amendment to our abbreviated new drug application (ANDA 091-306) for Fluocinolone Acetonide Oil 0.01% Ear Drops. On September 26, 2011, Identi received the following telephone deficiency (by e-mail) from Richard D. Chang Chemistry Reviewer, Office of Generic Drugs:

1. *Please submit a revised Refined Peanut Oil Specifications in compliance with the USP monograph and in line with ANDA 201759 and 201764.*

   As requested, the revised Refined Peanut Oil Specifications in compliance with the USP monograph and in line with ANDA 201759 and 201764 are provided in Section 3.2.P.4.1 Specifications.

2. *Please remove the following tests and specifications from your drug product release and stability specifications:* (b) (4)

   Please submit a revised drug product release and stability specifications.

   As requested, Identi removed the following tests and specifications from our drug product release and stability specifications: (b) (4)

   and submitted revised drug product release specifications in Section 3.2.P.5.1 Specifications and stability specifications in Section 3.2.P.8.1 Stability. The method for related compounds and assay has also been revised to reflect the changes to the impurities reporting. The revised method 701-AS-RC is provided herein.

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

Please submit the requested information as telephone amendments.

As instructed, this response is provided as a Telephone Amendment.

This completes our submission. This submission is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

Telephone Fax

ANDA 91-306

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
240-276-8984

TO: Identi Pharmaceuticals, LLC. TEL: 410 309-3145

ATTN: Jeanne Taborsky FAX: 410 309-6145

FROM: Beverly Weitzman

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 Fluocinonide Acetonide Oil (Ear Drops)

Pages (including cover): _3___

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/

REVIEW OF PROFESSIONAL LABELING #1
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 91-306
Date of Submission: April 16, 2009, July 8, 2010, March 16, 2011 and March 22, 2011
Applicant's Name: Identi Pharmaceuticals, LLC.
Established Name: Fluocinolone Acetonide Oil, 0.01% (Ear Drops)

Labeling Deficiencies:

1. **CONTAINER:** Revise "Net Contents 20 mL (1 fl oz)" to read as "Net Contents 20 mL"
2. **INSERT: CLINICAL STUDIES:** Revise to include this section in its entirety except for the last sentence **"Importantly, the bulk peanut oil NF, used in fluocinolone acetonide oil is heated at 475° F for at least 15 minutes, which should provide for adequate decomposition of allergenic proteins".** This information is product specific and should not be included in your labeling if it does not pertain to your drug product.

Labeling Comments:

1. **CARTON: (20 mL): Satisfactory in Final Print.**

Revise your labeling, as instructed above, and submit final printed 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 submission, with all differences annotated and explained.

{See appended electronic signature page}

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

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

/s/

JOHN F GRACE
09/27/2011
for Wm Peter Rickman

This memo memorializes the basis for the ANDA labeling carve-out of information relating to peanut protein in the labeling for fluocinolone products that reference Hill Dermaceutical's Dema-Smoothe (NDA 19-452).

Background:

The package insert for the reference listed drug (RLD) Derma-Smoothe, (NDA 19-452) includes a statement describing the amino acid analysis or S-ELISA testing methodology for peanut proteins. The statement for the body oil reads, "The peanut oil used in Derma-Smooth/FS is tested for peanut proteins through amino acid analysis which can detect the quantity of amino acids to below 0.5 parts per million," and the statement for the scalp oil and ear drops reads, "Peanut oil used in this product is routinely tested for peanut proteins using a sandwich enzyme-linked immunosorbent assay test (S-ELISA) kit, which can detect peanut proteins to as low as 2.5 parts per million (ppm)."

As described in FDA's Citizen Petition response dated March 25, 2009 (Docket No. 2004-P-0215), the agency has determined that, at this time, there does not appear to be any test (including S-ELISA and amino acid analysis) that has been validated for the purpose of reliably quantifying residual protein in peanut oil. (CP response at 26). The Agency stated that a topical drug formulated with fully refined peanut oil that meets the USP NF standard is "adequately safe to permit approval." The agency further concluded that if manufacturers formulate their products with fully refined peanut oil that meets the USP NF standard, then the "addition of a test to *quantitate protein* in refined peanut oil would not improve the safety of products formulated with this excipient and will not be required." Id. at 30 (emphasis in original).

(b) (4)

(b) (4)

Several ANDAs are ready for approval. The generic firms included in their labeling the same statements describing the testing methodology for peanut proteins as the RLD. However, the generic firms, like Hill, (b) (4) The Office of Generic Drugs recommends the statements regarding the amount of residual peanut protein and test method be removed from the insert labeling as follows:

Remove:

Body Oil: The peanut oil used in Derma-Smooth/FS is tested for peanut proteins through amino acid analysis which can detect the quantity of amino acids to below 0.5 parts per million

and

Scalp Oil or Ear Drops: "Peanut oil used in this product is routinely tested for peanut proteins using a sandwich enzyme-linked immunosorbent assay test(S-ELISA) kit, which can detect peanut proteins to as low as 2.5 parts per million (ppm)"

Legal/Regulatory Context and Conclusions

ANDAs are required by statute and regulation to have the same labeling as the listed drug they reference except for differences required because of differences approved under a suitability petition or because the drug product and the RLD "are produced or distributed by different manufacturers." 505(j)(2)(A)(v); 21 C.F.R. 314.94(a)(8)(iv); see also 505(j)(4)(G). The use of the term "same" in the statute and regulations does not mean that the labeling for the ANDA must be identical to that for the RLD. Permissible differences due to difference in manufacturer may include, for example, "differences in expiration date, formulation, bioavailability or pharmacokinetics, labeling revisions made to comply with current FDA labeling guidelines or other guidance, or omission of an indication or other aspect of labeling protected by patent or accorded exclusivity under section 505(j)(5)(F) of the act." 21 C.F.R. 314.94(a)(8)(iv).

FDA has determined that there is no validated assay for residual peanut protein. FDA has further determined that any peanut oil that is fully refined in accordance with the USP NF process is sufficiently safe for use in topical fluocinolone products and cannot be reliably determined to be safer for peanut allergic individuals than any other peanut oil refined in accordance with the USP NF process. As a result, when manufacturers

use peanut oil that is fully refined in accordance with the USP NF process, FDA has determined that the addition of a test to quantitate protein in refined peanut oil would not improve the safety of products formulated with this excipient and will not be required. (CP response at 30.) Accordingly, FDA has determined that no product, NDA or ANDA, should reference in its labeling an unvalidated assay for peanut protein (such as the S-ELISA test or the amino acid test) that implies an additional safety benefit that has not been shown to exist.

In this case, the Hill fluocinolone labeling includes information about assays for peanut protein that have not been validated and FDA has asked Hill to remove references to these assays from the Derma-Smoothe labeling. Although Hill has not yet complied with FDA's request, FDA stands by its conclusion that, based on the information before it, the references to unvalidated assays in the Derma-Smoothe labeling are misleading and should be removed. Given FDA's conclusions about peanut oil in general and the unvalidated nature of the S-ELISA and amino acid assays as described in the Hill CP response (b) (4) FDA believes that ANDA applicants referencing Derma-Smoothe should not be required to include this unnecessary and misleading information in their labeling. Accordingly, FDA concludes that ANDA applicants can remove references to assays for residual peanut protein from their labeling to comply with the labeling guidelines that FDA has provided to Hill. The resulting difference between ANDA and RLD labeling is a permitted difference due to difference in manufacturer within the meaning of the statute and regulations.

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

/s/

CARRIE L LEMLEY
09/21/2011

WILLIAM P RICKMAN
09/22/2011

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

August 19, 2011

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0015 Telephone Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a gratuitous amendment to our abbreviated new drug application (ANDA 091-306) for Fluocinolone Acetonide Oil 0.01% Ear Drops.

On August 9, 2011, Identi received the following telephone deficiency (by e-mail) from Richard Chang Chemistry Reviewer, Office of Generic Drugs:

> "*This is in reference to your ANDA 091306 Gratuitous Amendment dated June 08, 2011. Please submit a test method verification report by Amneal for API impurities determination using the supplier's test method.*"

As requested, Identi is herein providing a copy of the method verification report and the respective test method.

This completes our submission. This submission is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

Record of Telephone Conversation

On June 08, 2011, the firm submitted a gratuitous amendment to change the testing laboratory from (b) (4) to Amneal Pharmaceuticals for API testing. No test method verification report was submitted in the amendment. On August 09, 2011, the following deficiency was communicated with the firm:

Please submit a test method verification report by Amneal for API impurities determination using the supplier's test method.

Date:
August 09, 2011

ANDA Number:
091306

Product Name:
Fluocinolone acetonide oil 0.01% ear drops

Firm Name:
Identi

Firm Representative:
Jeanne Taborsky

Phone Number:
410-309-3145
Jeanne.taborsky@scireg.com

FDA Representative:
Richard Chang

Signatures:
Rc

CC: ANDA
V:\FIRMSAM\Identi\TELECONS\091306.doc

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

/s/

RICHARD CHANG
08/09/2011

SciREGS International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

June 8, 2011

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0014 Gratuitous Amendment – Change in Testing Lab Responsibilities

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a gratuitous amendment to our abbreviated new drug application (ANDA 091-306) for Fluocinolone Acetonide Oil 0.01% Ear Drops.

Identi is transferring the testing of the active pharmaceutical ingredient from (b) (4) (b) (4) to Amneal Pharmaceuticals. Amneal will not be transferring the method for assay or impurities, but rather using the USP regulatory method to test assay, and the FDA reviewed API supplier method to test impurities. Amneal is already approved as the manufacturer, and as the testing lab for inactive ingredients and the finished product. Amneal was satisfactorily inspected in July 2010. The CGMP and Debarment Certifications are already on file in the ANDA.

This completes our submission. This submission is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

March 22, 2011

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0013 Labeling Amendment - FPL

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a labeling amendment to our abbreviated new drug application (ANDA) for Fluocinolone Acetonide Oil 0.01% Ear Drops. Reference is made to the labeling documents submitted in the amendment eCTD 0012 filed, March 16th 2011.

Identi has revised the insert to update the peanut oil statement as per guidance from FDA's labeling division. The revised final printed labeling insert is provided in Module 1 Section 1.14.2.2 Final Printed Labeling. The revised SPL and labeling insert texts and side-by-side comparisons were previously submitted to the Agency under separate cover dated, March 16th, 2011. Identi notes and acknowledges that the Labeling review is still pending with the labeling division.

This completes our submission. This ANDA is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

March 16, 2011

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0012 Chemistry Minor Amendment Response to Deficiency Letter and revised labeling

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a chemistry minor amendment to our abbreviated new drug application (ANDA) for Fluocinolone Acetonide Oil 0.01% Ear Drops. Reference is made to the Agency deficiency letter, dated January 24, 2011 and our previous submissions to this ANDA.

The agency deficiency and our responses are listed below:

(b) (4)

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

(b) (4)

warning on Peanut content was already part of the insert, and Peanut Oil is clearly listed on the carton as an ingredient, as it is on the innovator carton.

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

1. *Please provide all available drug product room temperature stability data.*

   As requested, Identi provided all available stability data to date in Module 3 Section 3.2.P.8.3 Stability Data.

2. *Labeling information you have provided is pending review. After the review is completed, any deficiencies found will be communicated to you separately.*

   Identi notes and acknowledges that the Labeling review is still pending with the labeling division, and Identi had provided revised insert herein.

3. *All facilities referenced in your ANDA should be in compliance with cGMPs at the time of approval. We have requested an evaluation from the Office of Compliance.*

   The facilities referenced in ANDA 091-306 Fluocinolone Acetonide Oil 0.01% (Ear Drops) that are subject to inspection have been inspected and are in compliance with cGMPs.

This completes our submission. This ANDA is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

Record of Telephone Conversation

A teleconference was held on February 07, 2011 for ANDA 091306 and the participants include the following: Jeanne Taborsky (Regulatory Affairs), Doug Taylor (Test Laboratory), Upen Shah, Srinivas Kone, and Jiten Parikh (Manufacturer), Roger Allen (Representing ANDA holder), Richard Chang, James Fan, Trang Tran (OGD), and James Allgire, B. Westenberger, Hongping Ye (FDA Division of Pharmaceutical Analysis (DPA) Laboratory). The key points discussed in the meeting is summarized as follows:

(b) (4)

Date:
February 07, 2010

ANDA Number:
091306

Product Name:
Fluocinolone Acetonide Oil, 0.01% Ear Drops

Firm Name:
Identi

Firm Representative:
See summary

Phone Number:
1-410-309-3145

FDA Representative:
See summary

Signatures:
Richard Chang

CC: ANDA

V:\Chemistry Division I\Team 13\T-CONS\091306 .doc

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

/s/

RICHARD CHANG
02/09/2011

TRANG Q TRAN
02/09/2011

JAMES M FAN
02/10/2011

QUALITY DEFICIENCY - MINOR

ANDA 091306

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

APPLICANT: SciRegs International, Inc.
U.S. Agent for: Identi Pharmaceuticals Inc.
ATTN: Jeanne Taborsky

TEL: (410) 309-3145

FAX: (410) 309-6145

FROM: Trang Q. Tran

FDA CONTACT PHONE: (240) 276-8518

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated April 16, 2009, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Fluocinolone Acetonide Oil, 0.01% Ear Drops.

Reference is also made to your amendments dated December 15 and December 17, 2010.

The Division of Chemistry 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.

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

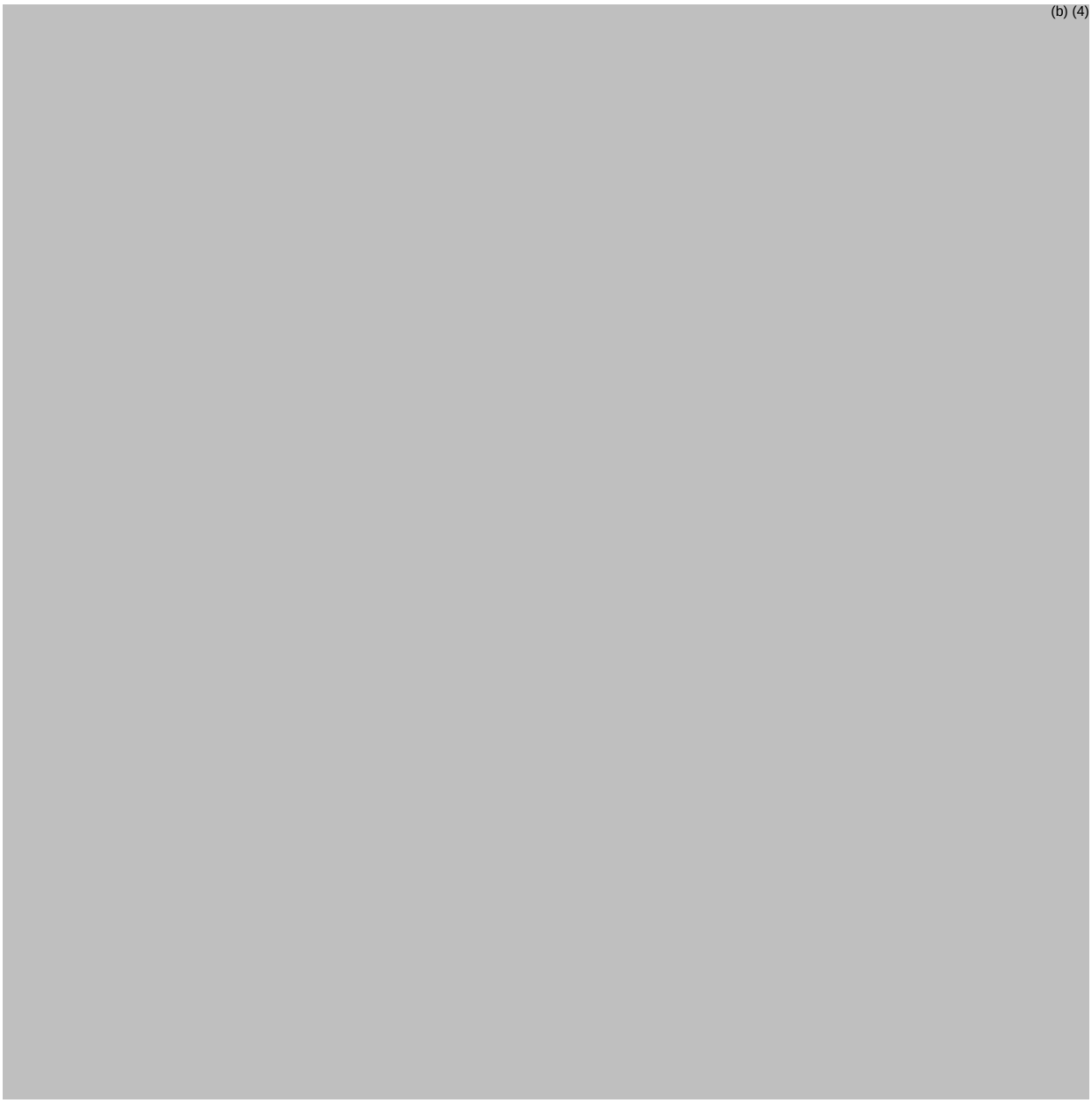
ANDA: 091306 APPLICANT: Identi Pharmaceuitcals Inc.

DRUG PRODUCT: Fluocinolone Acetonide Oil, 0.01% Ear Drops

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

(b) (4)



(b) (4)

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

1. Please provide all available drug product room temperature stability data.

2. Labeling information you have provided is pending review. After the review is completed, any deficiencies found will be communicated to you separately.

3. All facilities referenced in your ANDA should be in compliance with cGMP at the time of approval. We have requested an evaluation from the Office of Compliance.

Sincerely yours,

{See appended electronic signature page}

Paul Schwartz, Ph.D.
Acting Director
Division of Chemistry I
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/

JAMES M FAN
01/22/2011
for Paul Schwartz

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

December 17, 2010

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0011 Gratuitous Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a gratuitous amendment to our abbreviated new drug application (ANDA) for Fluocinolone Acetonide Oil 0.01% Ear Drops. Reference is made to Identi's Minor Amendment eCTD 0007, dated September 20, 2010.

(b) (4) was provided as a testing facility for the drug substance and drug product release and stability for the test batch in the original submission. (b) (4) was approved for this testing in the ANDA. (b) (4) was withdrawn in eCTD 0007 because the testing was being transferred to an alternate facility, Amneal Pharmaceuticals. Amneal is in the process of completing the methods transfer validation. Identi is requesting that (b) (4) be re-instated in the ANDA for drug substance and drug product testing.

Please refer to Section 1.3.3 Debarment for the debarment certification and to Section 3.2.P.3.1 for the CGMP certification. These certifications were submitted in the original ANDA application eCTD 0000 dated, April 16, 2009. We note and acknowledge that all facilities referenced in our ANDA should be in compliance with cGMP at the time of approval. (b) (4) has already been inspected in conjunction with ANDA 91-306 Fluocinolone Acetonide Oil (Ear Drops) in (b) (4) The inspection result was satisfactory.

This completes our submission. This ANDA is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

December 15, 2010

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0010 Gratuitous Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a gratuitous amendment to our abbreviated new drug application (ANDA) for Fluocinolone Acetonide Oil 0.01% Ear Drops.

Identi requests to withdrawal without prejudice Amneal Pharmaceuticals as a testing laboratory for the active pharmaceutical ingredient (API). Post approval, once the method transfer protocol is executed/, Identi will submit a post approval supplement to add Amneal Pharmaceutical as a testing facility for the API.

This completes our submission. This submission is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Division of Pharmaceutical Analysis, HFD-920
Attn: James Allgire, Team Leader
Office of Testing and Research
Office of Pharmaceutical Science
Center for Drug Evaluation and Research
114 Market Street
St. Louis, MO 63101

December 6, 2010

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
ANDA holder – Identi Pharmaceuticals, Inc.
Contract Manufacturer- Amneal Pharmaceuticals

Dear Sir:

Pursuant to your request of November 24, 2010, we are hereby providing you with the necessary items to conduct an evaluation of the (b) (4)

Phone 410-409-3145
FAX 410-409-6145

Secure e-mail: Jeanne.Taborsky@SciRegs.com
web: www.SciRegs.com

The materials sent to you include the following:

(b) (4)

Please contact C. Jeanne Taborsky, SciRegs International, Inc. at Phone (410) 309-3145; Fax (410) 309-6145 if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky
US Regulatory Agent
SciRegs International, Inc.
Regulatory Affairs

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

October 1, 2010

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0008 Telephone Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a minor amendment to our abbreviated new drug application (ANDA) for Fluocinolone Acetonide Oil 0.01% Ear Drops. Reference is made to the Agency e-mail deficiency letter, dated September 30, 2010 and our previous submissions to this ANDA. The agency deficiency and our responses are listed below:

Deficiencies:

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

(b) (4)

This completes our submission. This ANDA is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

From: Tran, Trang [mailto:Trang.Tran@fda.hhs.gov]
Sent: Thursday, September 30, 2010 2:30 PM
To: 'Elizabeth Deiss'
Subject: RE: Fluocinolone

Hi Elizabeth,

We have received your response to the latest deficiency letter dated September 20, 2010. Below is the comments from our chemistry team. Please submit a telephone amendment with the appropriate revisions.

Regards,

Trang

Deficiencies:

(b) (4)

[redacted]

From: Elizabeth Deiss [mailto:elizabeth.deiss@sciregs.com]
Sent: Wednesday, September 29, 2010 10:04 AM
To: Tran, Trang
Subject: RE: Fluocinolone

Dear Trang,

We just wanted to check in with your and make sure that you had received our response from the 20th of September for the latest deficiency letter. We were wondering if you had been able to review our finished product and stability limits. We are getting ready to submit two sister ANDA's that will have the same specifications and wanted to be sure we didn't require further revisions.

Thank you very much.

Regards,

Elizabeth Deiss
AVP Quality Assurance
SciRegs International Inc.

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

/s/

RICHARD CHANG
09/30/2010

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

September 20, 2010

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0007 Minor Amendment Response to Deficiency Letter

Request to Reclassify as Telephone Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a minor amendment to our abbreviated new drug application (ANDA) for Fluocinolone Acetonide Oil 0.01% Ear Drops. Reference is made to the Agency deficiency letter, dated September 3, 2010 and our previous submissions to this ANDA. Since this deficiency letter contains essentially only a request to revise specifications and the response was made quickly, Identi is requesting that the deficiency be changed to a telephone amendment to expedite the review process.

The agency deficiency and our responses are listed below:

(b) (4)

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

(b) (4)

Please note that in response to the deficiencies listed below, revised specifications are provided in Section 3.2.P.3.4 Controls for Critical Steps and Intermediates, Section 3.2.P.5.1 Drug Product Specifications, Section 3.2.P.5.6 Justification of Specifications.

(b) (4)

(b) (4)

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

1. *Information related to labeling is under review. After the review is completed, any deficiencies found will be communicated to you separately.*

   We note and acknowledge that the labeling is under review. After the review is completed, any deficiencies found will be communicated to you separately.

2. *All facilities referenced in your ANDA should be in compliance with cGMP at the time of approval.*

   We note and acknowledge that all facilities referenced in our ANDA should be in compliance with cGMP at the time of approval. The facilities are ready for inspection.

   Identi Pharmaceuticals LLC contracted (b) (4) to perform drug product Release and Stability up to 6 months. Since the product is being manufactured at Amneal and the method transferred, Identi determined that it is more efficient to store and test the samples at the manufacturing site. Identi is no longer requesting approval of (b) (4) for commercial manufacturing. We will be using Amneal Pharmaceuticals for drug substance release and finished product release and stability testing.

3. (b) (4)

This completes our submission. This ANDA is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

QUALITY DEFICIENCY - MINOR

ANDA 091306

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

APPLICANT: SciRegs International, Inc.
US Agent for: Identi Pharmaceuticals Inc.
ATTN: C. Jeanne Taborsky

TEL: 410-309-3145

FAX: 410-309-6145

FROM: Trang Q. Tran

FDA CONTACT PHONE: (240) 276-8518

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated April 16, 2009, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Fluocinolone Acetonide Oil, 0.01% Ear Drops.

Reference is also made to your amendments dated July 8, August 12, and August 17, 2010.

The Division of Chemistry has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached __**1**__ page. 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: 091306 APPLICANT: Identi Pharmaceuticals Inc.

DRUG PRODUCT: Fluocinolone Acetonide Oil, 0.01% Ear Drops

The deficiencies presented below represent MINOR deficiencies.

Deficiencies:

(b) (4)

5. We noticed that the stability data generated for the test batch from (b) (4) and Amneal Pharmaceuticals are quite different. Please explain.

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

1. Information related to labeling is under review. After the review is completed, any deficiencies found will be communicated to you separately.

2. All facilities referenced in your ANDA should be in compliance with cGMP at the time of approval.

3. (b) (4)

Sincerely yours,

{See appended electronic signature page}

Paul Schwartz, Ph.D.
Acting Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-91306	ORIG-1	IDENTI PHARMACEUTICALS	FLUOCINOLONE ACETONIDE

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

/s/

JAMES M FAN
09/03/2010

BIOEQUIVALENCY COMMENTS

ANDA 091306

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

APPLICANT: Identi Pharmaceuticals Inc. TEL: 410-309-3145
U.S. Agent: SciRegs International, Inc.
ATTN: C. Jeanne Taborsky FAX: 410-309-6145
President & CEO

FROM: Nitin K. Patel PROJECT MANAGER: (240) 276-8887
(240) 276-8966 (fax)

Dear Madam:

This facsimile is in reference to the bioequivalency data submitted on April 16, 2009, pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Fluocinolone Acetonide Oil, 0.01% Ear Drops.

The Division of Bioequivalence has completed its review of the submission(s) referenced above and has provided comments which are presented on the attached __1__ page. This facsimile is to be regarded as an official FDA communication and unless requested, a hard-copy will not be mailed.

Please direct any questions concerning this communication to the Project Manager identified above.

SPECIAL INSTRUCTIONS:

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BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 091306 APPLICANT: Identi Pharmaceuticals Inc.

DRUG PRODUCT: Fluocinolone Acetonide Oil, 0.01% Ear Drops

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

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

Sincerely yours,

{See appended electronic signature page}

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-91306	ORIG-1	IDENTI PHARMACEUTICALS	FLUOCINOLONE ACETONIDE

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/s/

NITIN K PATEL
08/31/2010

DALE P CONNER
09/01/2010

QUALITY DEFICIENCY - MINOR

ANDA 091306

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

APPLICANT: SciRegs International, Inc.
US Agent for: Identi Pharmaceuticals Inc.
ATTN: C. Jeanne Taborsky

TEL: (410) 309-3145

FAX: (410) 309-6145

FROM: Trang Q. Tran

FDA CONTACT PHONE: (240) 276-8518

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated April 16, 2009, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Fluocinolone Acetonide Oil 0.01% Ear Drops.

The Division of Chemistry 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.

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
Document Control Room
7620 Standish Place
Rockville, Maryland 20857

*After the effective date, **01-Aug-2010**, ANDAs will only be accepted at the new mailing address listed above. **DO NOT submit your ANDA Regulatory documents to this address prior to 01-Aug-2010.** 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

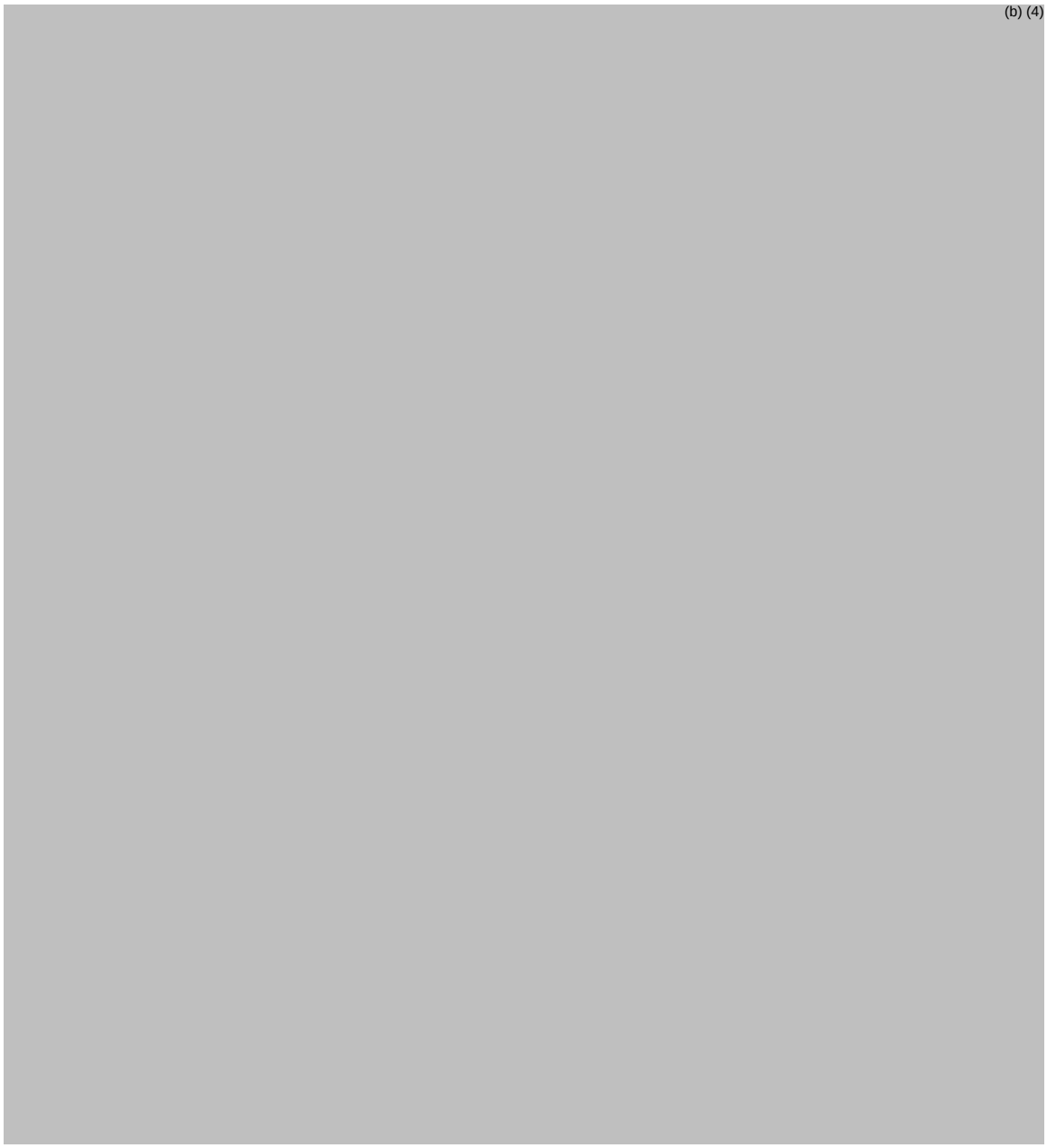
ANDA: 091306 APPLICANT: Identi Pharmaceuitcals Inc.

DRUG PRODUCT: Fluocinolone Acetonide Oil, 0.01% Ear Drops

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

(b) (4)



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

1. Please provide all available drug product room temperature stability data.

2. Bioequivalency and labeling information you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you separately.

3. All facilities referenced in your ANDA should be in compliance with cGMP at the time of approval. We have requested an evaluation from the Office of Compliance.

Sincerely yours,

{See appended electronic signature page}

Paul Schwartz, Ph.D.
Acting Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-91306	ORIG-1	IDENTI PHARMACEUTICALS	FLUOCINOLONE ACETONIDE

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/s/

JAMES M FAN
03/11/2010
James Fan for Paul Schwartz

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

August 27, 2009

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0002 Gratuitous Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.60, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a gratuitous amendment to our abbreviated new drug application (ANDA) for Fluocinolone Acetonide Oil 0.01% Ear Drops. Reference is made to the original submission eCTD 0000, on April 16, 2009 and the gratuitous amendment eCTD 0001 submitted August 26, 2009.

(b) (4)

This completes our submission. This ANDA is filed in eCTD format. Letters of Non-Repudiation have been submitted to the Agency under separate cover. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky
US Regulatory Agent
SciRegs International Inc.

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
7620 Standish Place
Rockville, MD 20855-2773

August 17, 2010

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0006 Gratuitous Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a gratuitous amendment to our abbreviated new drug application (ANDA) for Fluocinolone Acetonide Oil 0.01% Ear Drops.

Please note that there was a typographical error the 356h filing form for the concentration for the finished product. It was listed as 0.1% when it should have been listed as **0.01%**. A corrected filing form is provided with this submission.

This completes our submission. This ANDA is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky,
US Regulatory Agent
SciRegs International Inc.

Phone: (410) 309-3145
Fax: (410) 309-6145

Website: www.SciRegs.com
E-mail: Jeanne.Taborsky@sciregs.com

SciRegs International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

August 12, 2010

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0005 Gratuitous Minor Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a Minor Amendment to our abbreviated new drug application (ANDA) for Fluocinolone Acetonide Oil 0.01% Ear Drops. Reference is made to the following submissions:

eCTD	Date	Submission	Content
0000	April 16, 2009	Original	Complete original submission of batch manufactured at (b) (4)
0001	August 26, 2009	Gratuitous amendment	Additional testing laboratories Revised specifications and methods, validation Justification of specifications Additional stability (b) (4)
0003	October 6, 2009	Telephone amendment	Revised debarment cert Revised patent cert due to collapse of NDAs
0004	July 8, 2010	Minor Amendment	Response to deficiency letter Change in site change Revised bio waiver request Revised specifications Stability data to date for both test batches

In this amendment, Identi is providing the following information and documents:

Update facility information as provided in Section 1.1.2 Attachment 1 to FDA form 356h.

Amneal's Branchburg, NJ facility was re-inspected from July 19 to July 22 and 29th, 2010 and determined to be satisfactory.

Section 3.2.P.3.3 Description of Manufacturing Process and Process Controls

The Amneal executed test batch packaging record was provided in eCTD 0004. The Amneal unexecuted test batch packaging record is submitted herein.

Section 3.2.P.5. Controls for Finished Product

In eCTD 0004, we listed the impurity limits as specified unidentified a (b) (4) based upon a preliminary evaluation of the results for the intermediate stability samples. Upon further evaluation and (b) (4) is not related to the drug product. The specified degradant will remain as specified unidentified at (b) (4) See Section 3.2.P.8.1 Stability Summary. We have also reduced the unspecified impurities limits from (b) (4) to be consistent with ICH. The revised specifications are provided herein.

Section 3.2.P.7 Container Closure

Identi is providing a revised summary of container closure information to include Identi's and Amneal's part numbers for the components and reflect two vendor changes in ownership. Since our last submission, we were informed of the change in ownership of (b) (4) for the manufacturer of the closure. Please note that this is a change in ownership only. Documentation on the changes is provided. Identi commits to provide copies of revised Drug Master File Letters of Authorization as soon as they are available. The specification for the closure was revised to list the name change for the approved vendor.

The dropper assembly specifications were originally generated by (b) (4) the manufacturer withdrawn from our ANDA. The revised specifications more closely represent the commercial dropper assembly and the format is revised to match Identi documents and Amneal requirements.

Section 3.2.P.8 Stability

(b) (4)

reports are provided. Based upon these reports, we have revised our stability specifications.

The product passed test requirements under three months accelerated and long term testing to date. Identi is requesting approval with 24 months expiration dating.

This completes our submission. This ANDA is filed in eCTD format. A Letter of Non-Repudiation for SciRegs International Inc. has been submitted to the Agency under separate cover dated, February 1, 2008. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky
US Regulatory Agent
SciRegs International Inc.

OFFICE OF GENERIC DRUGS EXPEDITED REVIEW REQUESTED

ANDA/SUPPLEMENT #: 091306
DRUG: Fluocinolone Acetonide Oil, 0.01% Ear Drops

APPLICANT: Identi Pharmaceuticals Inc.
DATE OF SUBMISSION: April 16, 2009

The Office of Generic Drugs MaPP # 5240.1 lists the following criteria for granting expedited review status to a supplemental abbreviated new drug application. At least one of the criteria must be met.

1. PUBLIC HEALTH NEED. Events that affect the availability of a drug for which there is no alternative

2. EXTRAORDINARY HARDSHIP ON THE APPLICANT.

   a) Catastrophic events such as explosion, fire storms damage.

   b) Events that could not have been reasonably foreseen and for which the applicant could not plan. Examples include:

      - Abrupt discontinuation of supply of active ingredient, packaging material, or container closure; and
      - Relocation of a facility or change in an existing facility because of a catastrophic event (see item 2.a)

3. AGENCY NEED.
   a) Matters regarding the government's drug purchase program, upon request from the appropriate FDA office.
   b) Federal or state legal/regulatory actions, including mandated formation changes or labeling changes if it is in the Agency's best interest.
   c) Expiration-date extension or packaging change when the drug product is the subject of a government contract award.
   d) Request for approval of a strength that was previously tentatively approved (To be used in those cases where 180-day generic drug exclusivity prevented full approval of all strengths).

From: West, Robert L
Sent: Friday, August 06, 2010 11:42 AM
To: Tran, Trang
Cc: Fan, James M; Ames, Timothy W; Weitzman, Beverly; Chang, Richard; Solana-Sodeinde, Diana A; Hinchliffe, Thomas
Subject: RE: Expedited Request for ANDA-091306 Product Name: FLUOCINOLONE ACETONIDE Dosage Form: OIL Applicant: IDENTI PHARMACEUTICALS

To the Record:

I agree that Identi Pharmaceuticals ANDA 91-306 for Fluocinolone Acetonide Oil (for Otic Use) meets the criteria specified in CDER MaPP 5240.3 for "expedited review" status.

Thus, "expedited review" is granted to this ANDA.

Please adjust the review queues accordingly.

Thank you,

Bob

From: Tran, Trang

Sent: Wednesday, July 28, 2010 12:41 PM
To: West, Robert L
Subject: FW: Expedited Request for ANDA-091306 Product Name: FLUOCINOLONE ACETONIDE Dosage Form: OIL Applicant: IDENTI PHARMACEUTICALS

From: Tran, Trang
Sent: Thursday, July 22, 2010 1:35 PM
To: West, Robert L
Subject: RE: Expedited Request for ANDA-091306 Product Name: FLUOCINOLONE ACETONIDE Dosage Form: OIL Applicant: IDENTI PHARMACEUTICALS

Bob,

I've checked on the other Fluocinolone Acetonide Oil applications but they are either topical oil or withdrawn by firm. This is the only application intended for Otic use.

Thanks.

Trang

From: West, Robert L [mailto:Robert.West@fda.hhs.gov]
Sent: Thursday, July 22, 2010 1:18 PM
To: Tran, Trang
Subject: RE: Expedited Request for ANDA-091306 Product Name: FLUOCINOLONE ACETONIDE Dosage Form: OIL Applicant: IDENTI PHARMACEUTICALS

Trang:

It appears from DARRTs that there are additional ANDAs pending for Fluocinolone Acetonide Oil. Please determine which of those are also intended for otic use and let me know. We'll need to expedite all of them.

Thanks,

Bob

From: Tran, Trang
Sent: Tuesday, July 20, 2010 5:37 PM
To: West, Robert L
Cc: Ames, Timothy W; Fan, James M; Chang, Richard
Subject: Expedited Request for ANDA-091306 Product Name: FLUOCINOLONE ACETONIDE Dosage Form: OIL Applicant: IDENTI PHARMACEUTICALS

Hi Bob,

Identi Pharmaceuticals is requesting for expedited review for ANDA 091306 (Fluocinolone Acetonide Oil 0.01% Ear Drops) in the submission dated 7/8/2010. This request is based upon the fact that this is the first generic product for which there is no blocking patents or exclusivity on the RLD. The RLD NDA number is 19452.
Please let me know if this request can be granted.

Thanks.

Trang

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-91306	ORIG-1	IDENTI PHARMACEUTICALS	FLUOCINOLONE ACETONIDE

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/s/

TRANG Q TRAN
08/09/2010

SCIREGS International Inc
Scientific and Regulatory Affairs Consulting

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

July 8, 2010

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0004 Minor Amendment
Response to Deficiency, Site Change and Revised Labeling
Expedited Review Requested

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.96, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a Minor Amendment to our abbreviated new drug application (ANDA) for Fluocinolone Acetonide Oil 0.01% Ear Drops. Reference is made to the deficiency letter, dated March 11, 2010 and the following amendments:

eCTD	Date	Submission	Content
0000	April 16, 2009	Original	Complete original submission of batch manufactured at (b) (4)
0001	August 26, 2009	Gratuitous amendment	Additional testing laboratories Revised specifications and methods, validation Justification of specifications Additional stability (b) (4)
0003	October 6, 2009	Telephone amendment	Revised debarment cert Revised patent cert due to collapse of NDAs
0004	October 6, 2009	Minor Amendment	Response to deficiency letter Change in site change Revised bio waiver request Revised specifications Stability data to date for both test batches

Reference is made to MAPP 5240.3 *Review Order of Original ANDAs, Amendments and Supplements.* At this time there are no approved generic versions of Fluocinolone Acetonide Oil 0.01% Ear Drops on the market at this time. Additionally, the innovator has had regulatory issues which may have impacted distribution. We are requesting the FDA consider Expedited Review of our amendment to our original drug application based upon the fact that this is the first generic product for which there is no blocking patents or exclusivity on the reference listed drug.

In addition to responding to the deficiency letter, Identi is also submitting

- Revised labeling listing new manufacturer and distributor,
- Revised bioequivalence waiver request,
- Manufacturing site change to Amneal Pharmaceuticals, in Branchburg, New Jersey for the manufacture of the drug product and as an alternate testing laboratory for all tests,
- Adding (b) (4) as a testing laboratory for some of the raw materials,
- Adding (b) (4) for the testing of containers,
- Deleting (b) (4) as a manufacturing site, and
- Deleting (b) (4) as a testing laboratory for excipient residual solvents.

The debarment and cGMP certifications for Amneal and the testing laboratories are filed herein. Attachment 1 to filing form 356h and Section 3.2.P.3.1 Manufacturer have been updated to reflect these changes. In support of the site change, Identi manufactured a second test batch at Amneal using the same components sources as used for the first test batch.

Revised labeling listing Amneal as the manufacturer and distributor is provided in Section 1.14 Labeling. Identi will be submitting, under separate cover, revised labeling to add the statement "store upright" to the label. The executed batch records for the new test batch manufactured at Amneal are provided in Section 3.2.R.1.P.1 Executed Batch Records. In support of the site change, release testing of the drug substance, excipients, containers, and drug product are included in this submission along with the bulk hold study, proposed commercial batch records, and side-by-side comparisons of the processes, and stability data to date. Identi is continuing to investigate the nature of the peaks observed in the stability analysis and commits to resolve any outstanding analytical issues post approval.

With the site transfer, Identi made several process improvements in the manufacturing. (b) (4)

The agency's comments in the deficiency letter and our responses are as follows;

1. *Please clarify the discrepancy between your drug substance specification of NMT* (b) (4) *% for unspecified impurities and the limit of* (b) (4) *% for unidentified degradants in* (b) (4) *Identi COA and please revise the specs of un-specified impurities to NMT* (b) (4) *%.*

   There is no real discrepancy between the specifications of Identi and those on the certificate of analysis from (b) (4) but we do understand and share your concern about the reporting. Prior to submission, we requested that (b) (4) change the reporting form to be identical to the wording of the Identi specifications. We were informed by (b) (4) that their program required a *range* for the results and the only option was to list the range as " (b) (4) %." We are no longer using (b) (4) as a testing laboratory. The specifications for the second test batch are provided.

Our drug substance specifications were written to match the drug substance manufacturer specifications. As requested, the drug substance specifications authored by Identi have been revised to include the additional significant figure, changed from "(b) (4)%." To be consistent, we also added an additional significant figure to the Identi specifications for *specified impurities*. For a copy of the drug substance specifications please refer to Section 3.2.S.4.1 Specifications.

2. *Please clarify the statement that individual impurities test results of (b) (4)%' from (b) (4)) meet your drug substance specification for specified impurities (i.e. NMT (b) (4)%).*

This data from (b) (4) Report No, (b) (4), was not used to support the release of the drug substance. Report (b) (4) provides a comparison between the USP method for the analysis of fluocinolone acetonide drug substance and the (b) (4) method (b) (4) When the method comparison was performed, the limit of quantitation for impurities using the (b) (4) method was (b) (4)%.

After the original report was issued, the (b) (4) method was revised ((b) (4)), and the method validation study was extended to include assay and impurity evaluations of the drug substance. The method revision for the drug substance assessments includes a larger load on the column, resulting in a significant lowering of the LOQ for drug substance assessments. The current revision of the method (b) (4), located in Section 3.2.P.5.2 Analytical Procedures) yields an LOQ of approximately (b) (4)% of the drug substance assay concentration. The drug substance assay concentration is 10-fold higher than that for the product, thus supporting the drug substance specifications for specified impurities. The LOQ for drug product assay has been lowered to (b) (4)% of the nominal concentration. The LOQ is verified every time the method is conducted so no changes were made to the method validation.

3. *Please provide a process description, including the processing temperature for the refined peanut oil, NF. Also, please provide a commitment statement to pledge that a supplemental application is required to change peanut oil suppliers.*

While conducting our search for raw material suppliers, we discovered a patent held by Hill Dermaceuticals for fluorouracil in topical cream containing peanut oil. A copy of the patent is provided in Module 3.3 Literature. On page 2, item number 10, this patent lists Peanut Oil from Welch, Holme and Clark as one of interest that is suitable for use. Since Hill is the manufacturer of the RLD, we concluded that they are most likely using this (b) (4) Peanut Oil, NF is heated at 475° F for at least 15 minutes.

Identi commits to file a supplemental application in the event that we need to change the Peanut Oil, NF vendor.

4. *Please correct typographical errors in the Oleth-2 specifications for Microbiological Limit from* (b) (4)

As requested, we have corrected the typographical errors in the Oleth-2 specifications for Microbiological Limit from (b) (4) Copies of the revised specifications are provided in Control of Excipients Section 3.2.P.4.1 Specifications.

5. (b) (4)

2005 Insert

"Peanut oil used in this product is routinely tested for peanut proteins using a sandwich enzyme-linked immunosorbent assay test (S-ELISA) kit, which can detect peanut proteins to as low as 2.5 parts per million (ppm)."

2007 Insert

"Peanut oil used in this product is routinely tested for peanut proteins through amino acid analysis; the quantity of amino acids is below 0.5 parts per million (ppm)."

(b) (4)

6. (b) (4)

7. *Please revise your drug product release and stability spec for Specified Impurities from impurity limited in API' to `NMT(b) (4)%.'*

   According to the ICH guidelines, drug substance manufacturing impurites are limited in the drug substance, and degradants are limited in the finished product. As discussed with the review team, we removed the drug substance manufacturing impurities from our release and stability specifications rather than listing them as NMT(b) (4)%. The specifications for release and stability have been updated and are provided in Module 3 Section 3.2.P.5.1 Specifications and Module 3 Section 3.2.P.8.1 Stability Summary respectively.

8. *Please explain the out of specification results for Total Impurities and specified impurity of (b) (4) in your drug product stability studies.*

   Please refer to eCTD 0001 Revised Stability Results forms. The original report filed in eCTD 0000 for the one- and two-month accelerated storage data listing the (b) (4) impurity was incorrect and was corrected in the subsequent report. Please see the asterisk *b* on the eCTD 0001 Revised Stability Results forms. The chemical at this retention time was identified by HPLC – MS as a chemical unrelated to the active. A copy of the HPLC-MS report was provided in our submission eCTD 0001, dated August 26, 2009 in Section 3.2.P.5.3 Validation of Analytical Procedures. Our current test method provides for an ID solution containing (b) (4) impurity which is used to confirm the presence or absence of this related impurity.

9. *Please explain the discrepancy of the results for Container Evaluation between stability summary table results for Lot 04AX02A (i.e. "Conforms") and out of specification results in your drug product stability data sheets. Please explain the out of specification results for Container Evaluation (e .g. fading of lettering on label and pitting in interior) in your drug product stability studies.*

   Identi concurs that for the test batch Lot 04AX02A, the stability testing laboratory listed results *Conforms* and at the same time lists out-of-specification *fading of lettering on label* and *pitting interior of the bottle.*

   Identi conducted an investigation which indicates that the container did not fail stability. Samples of the bottle that were reported to have “pitting” were sent to SciRegs and forwarded to the manufacturer for evaluation. Unused bottles were also evaluated, and it was determined that the interior was not pitted, but rather random bottles contained what appeared to be minor manufacturing flaws- (b) (4) . These minor interior imperfections in the (b) (4) process were not the result of a failure on stability, but were inherent in the (b) (4) bottles and did not impact on the product. The manufacturer has taken action to eliminate the minor cosmetic flaw in future lots.

   The “labels” on the test batch bottles are R&D computer-generated stickers not production labels. SciRegs was informed by the laboratory that some of the R&D test batch stability sample “labels” failed our commercial stability attributes which was *letter and decoration*

(smearing, adhesion, etc.). In some cases, it was reported by the laboratory that the "labels" were compromised either by product prior to being placed on stability or possibly by the humidity in the stability chamber. At the time that the samples were placed on stability, it was observed that some of the labels were already compromised, but the sample IDs were not recorded. The defect of *fading* of the labels was documented at some of the time points. There is no indication that the *fading* was due to product interaction or exposure to light. The commercial printed label should not *fade*. Since the performance of the paper computer-generated stickers are not indicative of the performance of commercial printed labels, and the quality of the stickers was not documented at the onset of the study, this is not being considered a stability failure.

10. *Please correct the limit of Total Impurities in the stability data sheets to NMT(b) (4)% from NMT(b) (4)%.*

    Based upon an evaluation of the stability, compendial requirements and ICH requirements, Identi changed the total specified impurities (degradants) limit tc (b) (4)% on both the specifications and the test results forms. Please see Section 3.2.P.5.6 Justification of Specifications and Section 3.2.P.8.1 Stability Summary.

11. *Please include the time zero data to the stability data sheets.*

    Please be advised that while Identi would like to comply with this request for the first test batch, the T_0 data for this test batch was not listed on the (b) (4) form because the testing was conducted at (b) (4) and not (b) (4) For the second test batch, all testing is being performed at (b) (4) and all accelerated and long term data were listed on the results forms.

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

1. *Please provide all available drug product room temperature stability data.*

   As requested, we have provided all available drug product room temperature stability data to date for this test batch in Section 3.2.P.8.3 Stability Data. Please be advised that the new test batch produced at Amneal was also been placed on stability and the additional data for the second batch is provided.

2. *Bioequivalence and labeling information you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you separately.*

   Identi notes and acknowledges that the bioequivalence and labeling information we have provided is pending review and that after the reviews are completed, any deficiencies found will be communicated to us separately. Please note that a gratuitous labeling amendment has been filed herein listing the new manufacturing site and distributor change. Also a revised bioequivalence waiver request if provided incorporating comments issued by the agency to a control document letter from the RLD firm, Hill Dermaceuticals.

3. *All facilities referenced in your ANDA should be in compliance with cGMP at the time of approval. We have requested an evaluation from the Office of Compliance.*

   Identi notes and acknowledges that all facilities referenced in our ANDA should be in compliance with cGMP at the time of approval. Please be advised that the changes to the testing and manufacturing facilities are provided in this submission. The debarment certifications are provided in Module 1 Section 1.3.3 Debarment and the cGMP certifications are provided in Module 3 Section 3.2.P.3.1 Manufacture.

This completes our submission. This ANDA is filed in eCTD format with a word version of Module 2 and the labeling. Letters of Non-Repudiation have been submitted to the Agency under separate cover. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky
US Regulatory Agent
SciRegs International Inc.

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 #: 91-306 **FIRM NAME**: IDENTI PHARMS

PIV: NO **Electronic or Paper Submission:** ECTD FORMAT (ELECTRONIC DATA)

RELATED APPLICATION(S): NA

First Generic Product Received? YES

PER LISA TAN 5/11/09

Bio Assignments:		**Micro Review (No)**
☒ **BPH**	☐ **BCE**	
☐ **BST**	☐ **BDI**	

DRUG NAME: FLUOCINOLONE ACETONIDE

DOSAGE FORM: OIL, 0.01% (EAR DROPS)

Random Queue: 3

Chem Team Leader: Fan, Jim Chem PM: Rosalyn Adigun Labeling Reviewer: Beverely Weitzman
Bio PM: Diana Solana

Letter Date: APRIL 16, 2009 **Received Date**: APRIL 20, 2009

Comments: EC- 1 YES **On Cards:** YES
Therapeutic Code: 4025010 CORTICOSTEROIDS

Archival copy: ECTD FORMAT ELECTRONIC DATA **Sections** I
Review copy: NA E-Media Disposition: YES SENT TO EDR
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 Iain Margand	**Recommendation:**
Date 10/9/2009	☒ **FILE** ☐ **REFUSE to RECEIVE**
Supervisory Concurrence/Date: _____	**Date:** _____

ADDITIONAL COMMENTS REGARDING THE ANDA:
See e-mail comments from Dr. Hixon and Consult below.
Proposed product is Q1/Q2 to the RLD with the exception of the removal of the fragrances from the generic.
9/29/09:
Requested a revised Debarment Certification to remove the qualifying statement, "To the best of our knowledge.."
Requested a revised section 1.3.5.1, "Patent Information", to state correct RLD number listed in the OB, 19-452.
Requested a revised Bio Waiver Request to reflect full regulation for the product.
Requested the QOS in Word format in addition to PDF.
Requested the clarification of the COA for the drug substance as the COA has Indenti Pharmaceuticals as the DP manufacturer whereas the DP section states the DP manufacturer is (b) (4)
Requested a revised cGMP from (b) (4) **that states compliance with 21 CFR parts 210 and/or 211.**
10/9/09:
Requested information received via Gateway 10/6/09. Application is acceptable for filing.

Contact: Jeanne Taborsky 410-309-3145

From: Shimer, Martin
Sent: Monday, September 28, 2009 11:47 AM
To: Hixon, Dena R
Cc: Catterson, Debra M; Margand, Iain
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

Dena,

Thanks. We will proceed with filing the ANDA.

Marty

Iain-this looks like it is one that you were working on. Go ahead and put together the filing letter. Please append the filing checklist with a copy of this e-mail. Also verify that the checklist instructs the DR to assign this ANDA to the clinical team for the review of the waiver request.

From: Hixon, Dena R
Sent: Monday, September 28, 2009 11:30 AM
To: Shimer, Martin
Cc: Hixon, Dena R; Catterson, Debra M
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

Marty,
Thanks. I agree that it appears to have the appropriate sign-off. I dont'know why I was not able to download it from DARRTS last night. I agree that this supports filing the application. I believe that this waiver review should come to our team. I see that the consultant reviewer stated that there are errors in the list of ingredient amounts, so it will be important for a reviewer to take a new look to ensure that the differences are within +/- 5% except for the deletion of the fragrances.
Dena

From: Shimer, Martin
Sent: Monday, September 28, 2009 8:04 AM
To: Hixon, Dena R
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

Dena,

Here is the consult that appears in DARRTs. It appears to have been endorsed by Dr. Walker.

<< File: 91306Consult.pdf >>
Tx,

Marty

From: Hixon, Dena R
Sent: Sunday, September 27, 2009 11:48 PM
To: Shimer, Martin
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

Marty,
I tried to look up this consult response, and it appears to not be available. Was it a final signed off consult, or was it waiting for final sign-off? Is it possible that it was never signed off?
Dena

From: Shimer, Martin
Sent: Friday, September 25, 2009 11:16 AM
To: Hixon, Dena R
Cc: Nguyen, Hoainhon T; Conner, Dale P; Braddy, April; Mitchell, Deanah; Read, David T; Catterson, Debra M; Chang, Nancy
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

All,

I saw that the Division finished a consult that is uploaded into DARRTs which appears to be O.K. with permitting an in-vivo waiver. Can we go ahead and move forward with filing this ANDA with an in-vivo waiver request?

Tx,

Marty

From: Hixon, Dena R
Sent: Wednesday, July 29, 2009 5:21 PM
To: Shimer, Martin
Cc: Hixon, Dena R; Nguyen, Hoainhon T; Conner, Dale P; Braddy, April; Mitchell, Deanah; Read, David T; Catterson, Debra M; Chang, Nancy
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

Marty,
I have a slightly different perspective on the interpretation of 312.94(a)(9)(iv) for ophthalmics. (b) (5) [redacted] So we are at an impasse that will take some time to resolve.
Dena

From: Shimer, Martin
Sent: Wednesday, July 29, 2009 3:02 PM
To: Nguyen, Hoainhon T; Hixon, Dena R
Cc: Conner, Dale P; Braddy, April; Mitchell, Deanah; Read, David T; Catterson, Debra M; Chang, Nancy
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

(b) (5) [redacted]

(b) (5)

[redacted]

.

Marty

From: Nguyen, Hoainhon T
Sent: Wednesday, July 29, 2009 2:14 PM
To: Hixon, Dena R; Shimer, Martin
Cc: Conner, Dale P; Braddy, April; Mitchell, Deanah; Read, David T; Nguyen, Hoainhon T; Catterson, Debra M; Chang, Nancy
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

Thanks, Dena, for your input. I am also forwarding the emails below to Marty.
Hoai

From: Hixon, Dena R
Sent: Tuesday, July 28, 2009 5:06 PM
To: Nguyen, Hoainhon T; Chang, Nancy; Catterson, Debra M
Cc: Conner, Dale P; Braddy, April; Mitchell, Deanah; Hixon, Dena R; Read, David T
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

Hoai and others,
As I am going through some emails that have been stuck in my inbox, I have come across this, and I want to add another regulatory wrinkle here.

(b) (5)

[redacted]

[redacted] I am copying Dave Read for his input on this.
Dena

From: Nguyen, Hoainhon T
Sent: Monday, July 06, 2009 8:44 AM
To: Chang, Nancy; Hixon, Dena R; Catterson, Debra M
Cc: Conner, Dale P; Braddy, April; Mitchell, Deanah; Nguyen, Hoainhon T
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

Hello Nancy,
We will send this consult directly to DDDP. Thanks very much for

your input.
Hoai

From: Chang, Nancy
Sent: Wednesday, July 01, 2009 4:17 PM
To: Nguyen, Hoainhon T; Hixon, Dena R; Catterson, Debra M
Cc: Conner, Dale P; Braddy, April; Mitchell, Deanah
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

Hi Hoai,

Thanks for running this by us first: the concern I'd have about lack of fragrance is, if anything, less than the concern I have about generics that have a different size, shape, color or taste compared to the RLD, or with generic containers/vials/packaging that differ from the RLD. I don't have any reason to believe that the lack of fragrance will contribute to misuse or to medical mixups, although, as with some of the factors listed above, it is certainly possible it could affect patient acceptance and subjective perception of the product. There certainly is an argument to be made (b) (5) If you'd like to also get an official opinion from OND, then it would probably be best for you to send this to them directly.

Nancy

From: Nguyen, Hoainhon T
Sent: Wednesday, July 01, 2009 3:50 PM
To: Chang, Nancy; Hixon, Dena R; Catterson, Debra M
Cc: Conner, Dale P; Braddy, April; Mitchell, Deanah; Nguyen, Hoainhon T
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

Hi Nancy,

We are considering granting a waiver for this test product, because other ingredients are Q1/Q2 match compared with the RLD except for the lack of fragrances in the test formulation, which we think should be acceptable. However, we just want to make sure that there is no clinical concern for such formulation. Therefore, we would like your opinion and/or concurrence.
Thanks,
Hoai

From: Chang, Nancy
Sent: Wednesday, July 01, 2009 3:39 PM
To: Nguyen, Hoainhon T; Hixon, Dena R; Catterson, Debra M
Cc: Conner, Dale P; Braddy, April; Mitchell, Deanah
Subject: RE: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

Hi Hoai,

Could you please clarify what your concern is here? The labeling I found doesn't seem to mention fragrance at all except in the description section. Is the concern that the lack of fragrance could somehow cause patients to use the product incorrectly? Or is the question whether or not this is appropriate for a waiver under CFR 320.22 given that the formulations differ in the presence of fragrance?

Thanks,
Nancy

From: Nguyen, Hoainhon T
Sent: Wednesday, July 01, 2009 1:40 PM
To: Hixon, Dena R; Catterson, Debra M; Chang, Nancy
Cc: Conner, Dale P; Nguyen, Hoainhon T; Braddy, April; Mitchell, Deanah
Subject: Clinical Consult for ANDA 91306 Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01%, Ear Drops

Hello Dena, Debbie and Nancy,
Since Dena is on leave, and I have been informed that Debbie triages the clinical consults for your Clinical Team, I am sending this consult request to all three of you. Please let us know if this is the appropriate consult to be sent to your team presently, or if you would like us to send it to the new drug division directly.
We are requesting your clinical recommendation with respect to the acceptability of the test formulation in comparison with the RLD. The test formulation only differs from the RLD in the fragrances, which it lacks, and which only the RLD contains (less than (b) (4) v/v). All other ingredients of the test formulation are within 5% difference compared with those of the RLD product.
Please see our consult request memo attached for additional details.
Thanks very much in advance for your consideration and input.
Hoai

<< File: Clinical Consult Request 91306.doc >>

Release Testing and In Vivo Bioequivalence Documentation ("SUPAC-SS Guidance," May 1997)

Review:

Background

Identi Pharmaceutical's ANDA 91-306 for Fluocinolone Acetonide Oil, 0.01% Ear Drops (the Test Product) is the first generic drug application for Fluocinolone Acetonide Oil/Drops (Otic), 0.01%. The drug is a low-to-medium potency topical corticosteroid indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years and older. The Reference Listed Drug (RLD) product is DermOtic® Oil (Fluocinolone Acetonide Oil, 0.01% Ear Drops), which is marketed by Hill Dermaceuticals, approved under NDA 19-452 in 2005. DermOtic® Oil is also marketed as Derma-Smoothe/FS Body Oil® for the treatment of atopic dermatitis, and as Derma-Smoothe/FS Scalp Oil® for the treatment of psoriasis of the scalp. Fluocinolone Acetonide in DermOtic® Oil has a molecular weight of 452.50. It is a white crystalline powder that is odorless, stable in light, and melts at 270°C with decomposition. It is soluble in alcohol, acetone and methanol, slightly soluble in chloroform, and insoluble in water. Each gram of DermOtic® Oil contains approximately 0.11 mg of Fluocinolone Acetonide in a blend of oils, which contains isopropyl alcohol, isopropyl myristate, light mineral oil, oleth-2, refined peanut oil NF and fragrances.

OGD finds that the Sponsor's Test Product appears to be qualitatively (Q1) and quantitatively (Q2) "equivalent" to the RLD product, except for the lack of fragrances, which are present in the RLD product only. Specifically, the Q1 and Q2 differences in the formulation are within + 5% based on the % volume/volume comparison of each of the inactive ingredients, and the differences in the formulation pertain to the two fragrances, Cream Fragrance (b) (4) and Balsam Pine Fragrance (b) (4). The Test Product does not contain these or any other fragrances, and the deletion of fragrance is viewed by the Sponsor as a "product improvement." With the assertion that the two products are otherwise qualitatively and quantitatively equivalent, i.e., containing the same active and inactive ingredients in the same concentration as the RLD product,[1] the Sponsor submitted a waiver request of *in vivo* bioequivalence (BE) requirements for its Fluocinolone Acetonide Oil, 0.01% Ear Drops, based on 21 CFR § 320.22(b)(1)(i-ii):

> 320.22 - Criteria for waiver of evidence of in vivo bioavailability or bioequivalence.
>
> (b) For certain drug products, the in vivo bioavailability or bioequivalence of the drug product may be self-evident. FDA shall waive the requirement for the submission of evidence obtained in vivo measuring the bioavailability or demonstrating the bioequivalence of these drug products. A drug product's in vivo bioavailability or bioequivalence may be considered self-evident based on other data in the application if the product meets one of the following criteria: (1) The drug product: (i) Is a parenteral

[1] The Sponsor also believes that they are (b) (4), as disclosed in a patent for another product.

> solution intended solely for administration by injection, or an ophthalmic or otic solution; and (ii) Contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application.

OGD requests DDDP to review the formulations of the Test Product and the RLD product in order to determine whether the difference in formulation as it pertains to fragrances is acceptable, and whether it will have an impact on the safety and/or efficacy of the proposed Test Product.

Review of Formulation Differences

FDA's NDA review for the RLD product and its formulation composition is summarized as follow (Tables 1 and 2):

Table 1 Excipients data for the RLD, submitted in the original NDA

D: Raw Excipients of NDA 19452[4]

PRODUCT NAME: DERMA-SMOOTHE/FS TOPICAL OIL
PRODUCT FORM: Oil Lotion
PRODUCT DISTRIBUTED BY: Hill Dermaceuticals
DATE BEGIN: 01-26-84 DATE END: 01-26-84
RAW MATERIALS | QUANTITY | BATCH MANUFACTURING STEPS

(b) (4)

[redacted]

Table 2 Active ingredient and excipients composition data for the RLD, submitted in the original NDA

A: NDA Formulation[1,2] (NDA # 19452): (NOT FOR RELEASE UNDER FOIA)

Ingredient	Percentage
Fluocinolone Acetonide, USP	0.010
Refined peanut Oil, NF[a]	(b) (4)
White Mineral Oil, USP	
Oleth-2	
Isopropyl Myristate, NF	
Isopropyl Alcohol, NF	
Cream Fragrance # (b) (4)	
Balsam Pine Fragrance (b) (4)	

Note: For the inactive ingredients, the "Percentage" in the RLD formulation is based on Volume/Volume (v/v) * 100
For the active ingredient, the "Percentage" in the RLD formulation is based on weight/volume (w/v) * 100
a- Refined peanut oil, NF has been heated at 475 °F for 15 minutes to denature possible peanut allergens.
*The RLD labeling states that Light Mineral Oil is an inactive ingredient in Fluocinolone Acetonide Oil. Therefore, in the table above, White Mineral Oil, USP is used interchangeably as Light Mineral Oil.

In Table 3, the Test Product formulation is summarized (copied electronically from the Sponsor's ANDA submission, as Table 1 Unit Composition, Section 2.3.P.1 Description and Composition of the Drug Product):

Table 3 Active ingredient and excipients data for the Test Product, submitted in the current ANDA

Table 1: Unit Composition (maximum daily dose = 10 drops, 0.0228 mL)				
Ingredient	**w/v**	**w/w%**	**IIG limits**	**Purpose**
Fluocinolone Acetonide, USP	0.01 g	0.011 (	NA	Active ingredient
Isopropyl Alcohol, USP	(b) (4)			
Isopropyl Myristate, NF				
Oleth-2				
Light Mineral Oil, NF				
Refined Peanut Oil, NF				
Total	100.00 mL	(b) (4)	NA	NA

Reviewers Comment:
Please note that in Table 3, the first row is for the active ingredient, Fluocinolone, which is listed as 0.01g (weight); the other ingredients from the rows below are excipients, which are listed as ml (volume). Therefore, the column heading for column 2, w/v (which denotes weight by volume) is accurate only for the first row, Fluocinolone, 0.01 g/100 mL. For the rest of the cells in that column, which contain values for the excipients, the heading should be v.

Note to other reviewers: Table 4 RLD Unit Composition, in Module 2 Section 2.3.P.1 Drug Product (page 2/38) contains multiple errors, and was not used for this consult. This reviewer understands the above referenced table to be the correct version.

Using data from the above tables (Tables 1, 2, and 3), the OGD Pharmacology Reviewer (Dr. D. Mitchell) in DBE_1/OGD compiled the following comparisons between the Test Product and the RLD Product:

Table 4 Formulation differences between Test and the RLD products[2]

C: Formulation Differences between the Test and Reference Products

Ingredient	w/v of Test Product* per 100 mL	v/v of RLD Product per 100 mL	Q1/Q2 % Difference between RLD and Test Product**
Fluocinolone Acetonide	0.01 g	0.01 g	0.0%
Ingredient	**v/v of Test Product* per 100 mL**	**v/v of RLD Product per 100 mL**	**Q1/Q2 % Difference between RLD and Test Product****
Isopropyl Alcohol	(b) (4)		
Isopropyl Myristate			
Oleth-2			
Light Mineral Oil			
Refined Peanut Oil			
Cream Fragrance (b) (4)			
Balsam Pine Fragrance (b) (4)			
Total	100 mL	100 mL	

*As calculated by the firm, Identi Pharmaceuticals, LLC.
** Percent difference is calculated as: (Test – Reference)/ Reference * 100

Conclusion/Recommendation:
We understand that OGD concludes that the Q1/Q2 differences in the excipients (other than fragrances) between the RLD and the Test Product do not exceed 5%. Based on OGD's analysis, it appears that the only other difference between the Test Product and the RLD is the *lack of,* or deletion of fragrances in the Test Product. We understand that these differences are considered by the OGD to be unlikely to have any detectable impact on formulation quality and performance, and that OGD is currently recommending waiving the requirement for the submission of evidence obtained *in vivo* measuring the bioavailability or demonstrating the bioequivalence of the drug products.

If this product were a semi-solid dosage form, the SUPAC-SS Guidance would apply, which states that deletion of an ingredient intended to affect fragrance is unlikely to have any detectable impact on formulation quality and performance, and that it would be considered a Level 1 change and no bioequivalence testing would be necessary. The

[2] The OGD reviewer confirmed that refined peanut oil v/v % (column 3) for the RLD should be (b) (4), consistent with the number in Tables 1 and 2. The number (b) (4) is a typo.

Guidance also states that any change in an excipient up to 5% of approved amount of that excipient is also unlikely to have any detectable impact on formulation quality and performance (however, please note the total additive effect of all excipient changes should not be more than 5%). Though the Test Product is not a semi-solid dosage form, the SUPAC-SS Guidance nevertheless provides a useful regulatory framework for evaluation. For this instance with the available information that has been provided, we would not object to waiver for bioequivalence testing if the present excipients are within +/- 5% of the RLD, and are not structure forming agents that might impact bioavailability. With regards to the deletion of the fragrances, given that the two fragrances in question are present in the RLD at an extent of (b) (4) % of the total amount (v/v), and that such "minor" changes are explicitly allowed under SUPAC-SS in such situations, we would not object to an in vivo bioavailability waiver on these grounds for this product.

Thank you for this consult; please let us know if we could be of further assistance.

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: APRIL 16, 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 10/6/09 amendment 2. List of Convictions statement (original signature) YES	☒
1.3.4	**Financial Certifications** Bioavailability/Bioequivalence Financial Certification (Form FDA 3454) NO Disclosure Statement (Form FDA 3455, submit copy to Regulatory Branch Chief) NO	☐
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) no patents 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 exclusivities	☒
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 Y b. Type III DMF authorization letter(s) for container closure Y 2. US Agent Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) Y	☒
1.12.11	**Basis for Submission** NDA# : 21-930 PLEASE CALL FIRM AND CHANGE BOS TO 19-452 (see 10/6/09 amendment) Ref Listed Drug: DEM OTIC Firm: HILL DERMACEUTICS INC. 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 Fluocinolone Acetonide 3. Inactive ingredients 4. Route of administration Topical (Otic) 5. Dosage Form Solution/Oil 6. Strength 0.01%	☒
1.12.14	**Environmental Impact Analysis Statement** YES	☒
1.12.15	**Request for Waiver 21 CFR 320.22(b)(1) - see 10/6/09 amendment** Request for Waiver of In-Vivo BA/BE Study(ies): YES	☒
1.14.1	**Draft Labeling (Mult Copies N/A for E-Submissions)** **1.14.1.1** 4 copies of draft (each strength and container) Y **1.14.1.2** 1 side by side labeling comparison of containers and carton with all differences annotated and explained Y **1.14.1.3** 1 package insert (content of labeling) submitted electronically Y ***Was a proprietary name request submitted? No (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 Y **1.14.3.3** 1 RLD label and 1 RLD container label Y	☒

MODULE 2
SUMMARIES ACCEPTABLE

2.3	**Quality Overall Summary (QOS)** **E-Submission: PDF Y** **Word Processed e.g., MS Word** Y – see 10/6/09 amendment 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)** Y **2.3.S** **Drug Substance (Active Pharmaceutical Ingredient)** **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** **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) N/A** **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 **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) Y 2. Function or Responsibility Y 3. Type II DMF number for API DMF# (b) (4) 4. CFN or FEI numbers	☒
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) Y **3.2.S.4.2 Analytical Procedures** Y **3.2.S.4.3 Validation of Analytical Procedures** Y 1. Spectra and chromatograms for reference standards and test samples see 3.2.S.4.4 2. Samples-Statement of Availability and Identification of: a. Drug Substance Y b. Same lot number(s) Y **3.2.S.4.4 Batch Analysis** 1. COA(s) specifications and test results from drug substance mfgr(s) Y 2. Applicant certificate of analysis Y **3.2.S.4.5 Justification of Specification** Y	☒
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 Y 2. Inactive ingredients and amounts are appropriate per IIG Q1/Q2 with the exception of the removal of the fragrances from the proposed generic product. (see below)	☒
3.2.P.2	**Pharmaceutical Development** Pharmaceutical Development Report	☒
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) YES 2. CGMP Certification: YES 3. Function or Responsibility YES 4. CFN or FEI numbers **3.2.P.3.2 Batch Formula** Y **3.2.P.3.3 Description of Manufacturing Process and Process Controls** 1. Description of the Manufacturing Process Y 2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified (b) (4) kg 3. If sterile product: Aseptic fill / Terminal sterilization N/A 4. Reprocessing Statement Y **3.2.P.3.4 Controls of Critical Steps and Intermediates** Y **3.2.P.3.5 Process Validation and/or Evaluation** Y 1. Microbiological sterilization validation 2. Filter validation (if aseptic fill) N/A	☒
3.2.P.4	**Controls of Excipients (Inactive Ingredients)** Source of inactive ingredients identified Y **3.2.P.4.1 Specifications** 1. Testing specifications (including identification and characterization) Y 2. Suppliers' COA (specifications and test results) Y **3.2.P.4.2 Analytical Procedures** Y **3.2.P.4.3 Validation of Analytical Procedures** Y **3.2.P.4.4 Justification of Specifications** Applicant COA Y	☒

MODULE 3

3.2.P DRUG PRODUCT

ACCEPTABLE

3.2.P.5	**Controls of Drug Product** **3.2.P.5.1 Specification(s)** Y **3.2.P.5.2 Analytical Procedures** Y **3.2.P.5.3 Validation of Analytical Procedures** Y Samples - Statement of Availability and Identification of: 1. Finished Dosage Form Y 2. Same lot numbers y **3.2.P.5.4 Batch Analysis** 04AX02A Certificate of Analysis for Finished Dosage Form 04AX02B **3.2.P.5.5 Characterization of Impurities** Y **3.2.P.5.6 Justification of Specifications** Y	☒
3.2.P.7	**Container Closure System** 1. Summary of Container/Closure System (if new resin, provide data) Y 2. Components Specification and Test Data Y 3. Packaging Configuration and Sizes (b) (4) mL plastic bottles and dropper 4. Container/Closure Testing Y 5. Source of supply and suppliers address Y	☒
3.2.P.8	**3.2.P.8.1 Stability (Finished Dosage Form)** 1. Stability Protocol submitted Y 2. Expiration Dating Period 24 months **3.2.P.8.2 Post-approval Stability and Conclusion** Post Approval Stability Protocol and Commitments Y **3.2.P.8.3 Stability Data** 1. 3 month accelerated stability data Y – upright and inverted 04AX02A 2. Batch numbers on stability records the same as the test batch 04AX02B	☒

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)** **3.2.R.2.S Comparability Protocols** **3.2.R.3.S Methods Validation Package NA** 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 see attached Theoretical Yield Actual Yield Packaged Yield **3.2.R.1.P.2 Information on Components** Y **3.2.R.2.P Comparability Protocols** Y **3.2.R.3.P Methods Validation Package** Y Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☒

MODULE 5

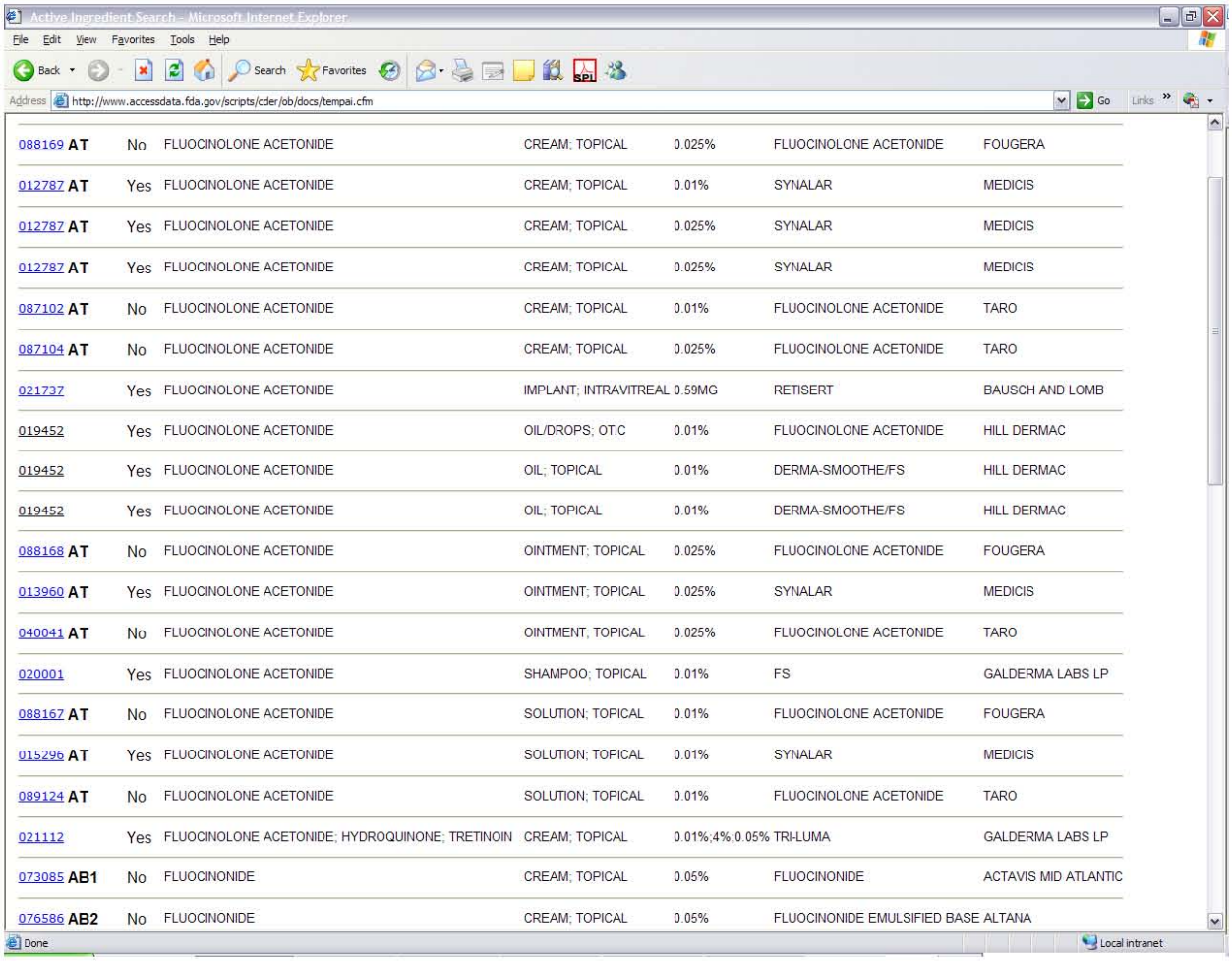
CLINICAL STUDY REPORTS

ACCEPTABLE

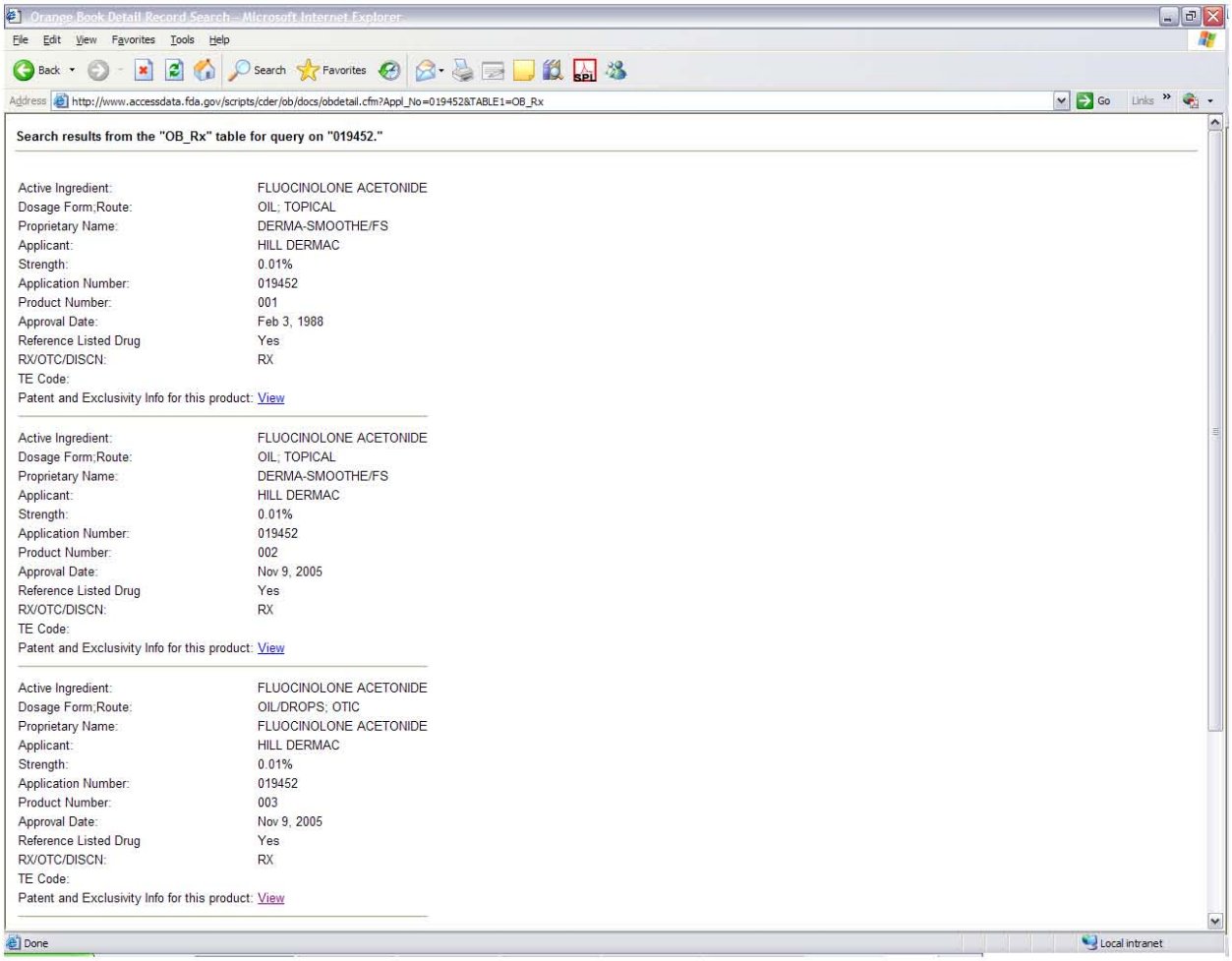
5.2	**Tabular Listing of Clinical Studies**	☐
5.3.1 (complete study data)	**Bioavailability/Bioequivalence** **1. Formulation data same?** a. Comparison of all Strengths (check proportionality of multiple strengths) b. Parenterals, Ophthalmics, Otics and Topicals per 21 CFR 314.94 (a)(9)(iii)-(v) **2. 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: YES SENT TO EDR 3. In-Vitro Dissolution: NA	☐
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	☐



088169 **AT**	No	FLUOCINOLONE ACETONIDE	CREAM; TOPICAL	0.025%	FLUOCINOLONE ACETONIDE	FOUGERA
012787 **AT**	Yes	FLUOCINOLONE ACETONIDE	CREAM; TOPICAL	0.01%	SYNALAR	MEDICIS
012787 **AT**	Yes	FLUOCINOLONE ACETONIDE	CREAM; TOPICAL	0.025%	SYNALAR	MEDICIS
012787 **AT**	Yes	FLUOCINOLONE ACETONIDE	CREAM; TOPICAL	0.025%	SYNALAR	MEDICIS
087102 **AT**	No	FLUOCINOLONE ACETONIDE	CREAM; TOPICAL	0.01%	FLUOCINOLONE ACETONIDE	TARO
087104 **AT**	No	FLUOCINOLONE ACETONIDE	CREAM; TOPICAL	0.025%	FLUOCINOLONE ACETONIDE	TARO
021737	Yes	FLUOCINOLONE ACETONIDE	IMPLANT; INTRAVITREAL	0.59MG	RETISERT	BAUSCH AND LOMB
019452	Yes	FLUOCINOLONE ACETONIDE	OIL/DROPS; OTIC	0.01%	FLUOCINOLONE ACETONIDE	HILL DERMAC
019452	Yes	FLUOCINOLONE ACETONIDE	OIL; TOPICAL	0.01%	DERMA-SMOOTHE/FS	HILL DERMAC
019452	Yes	FLUOCINOLONE ACETONIDE	OIL; TOPICAL	0.01%	DERMA-SMOOTHE/FS	HILL DERMAC
088168 **AT**	No	FLUOCINOLONE ACETONIDE	OINTMENT; TOPICAL	0.025%	FLUOCINOLONE ACETONIDE	FOUGERA
013960 **AT**	Yes	FLUOCINOLONE ACETONIDE	OINTMENT; TOPICAL	0.025%	SYNALAR	MEDICIS
040041 **AT**	No	FLUOCINOLONE ACETONIDE	OINTMENT; TOPICAL	0.025%	FLUOCINOLONE ACETONIDE	TARO
020001	Yes	FLUOCINOLONE ACETONIDE	SHAMPOO; TOPICAL	0.01%	FS	GALDERMA LABS LP
088167 **AT**	No	FLUOCINOLONE ACETONIDE	SOLUTION; TOPICAL	0.01%	FLUOCINOLONE ACETONIDE	FOUGERA
015296 **AT**	Yes	FLUOCINOLONE ACETONIDE	SOLUTION; TOPICAL	0.01%	SYNALAR	MEDICIS
089124 **AT**	No	FLUOCINOLONE ACETONIDE	SOLUTION; TOPICAL	0.01%	FLUOCINOLONE ACETONIDE	TARO
021112	Yes	FLUOCINOLONE ACETONIDE; HYDROQUINONE; TRETINOIN	CREAM; TOPICAL	0.01%;4%;0.05%	TRI-LUMA	GALDERMA LABS LP
073085 **AB1**	No	FLUOCINONIDE	CREAM; TOPICAL	0.05%	FLUOCINONIDE	ACTAVIS MID ATLANTIC
076586 **AB2**	No	FLUOCINONIDE	CREAM; TOPICAL	0.05%	FLUOCINONIDE EMULSIFIED BASE	ALTANA



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Go Links

Search results from the "OB_Rx" table for query on "019452."

Active Ingredient:	FLUOCINOLONE ACETONIDE
Dosage Form;Route:	OIL; TOPICAL
Proprietary Name:	DERMA-SMOOTHE/FS
Applicant:	HILL DERMAC
Strength:	0.01%
Application Number:	019452
Product Number:	001
Approval Date:	Feb 3, 1988
Reference Listed Drug	Yes
RX/OTC/DISCN:	RX
TE Code:	
Patent and Exclusivity Info for this product:	View

Active Ingredient:	FLUOCINOLONE ACETONIDE
Dosage Form;Route:	OIL; TOPICAL
Proprietary Name:	DERMA-SMOOTHE/FS
Applicant:	HILL DERMAC
Strength:	0.01%
Application Number:	019452
Product Number:	002
Approval Date:	Nov 9, 2005
Reference Listed Drug	Yes
RX/OTC/DISCN:	RX
TE Code:	
Patent and Exclusivity Info for this product:	View

Active Ingredient:	FLUOCINOLONE ACETONIDE
Dosage Form;Route:	OIL/DROPS; OTIC
Proprietary Name:	FLUOCINOLONE ACETONIDE
Applicant:	HILL DERMAC
Strength:	0.01%
Application Number:	019452
Product Number:	003
Approval Date:	Nov 9, 2005
Reference Listed Drug	Yes
RX/OTC/DISCN:	RX
TE Code:	
Patent and Exclusivity Info for this product:	View

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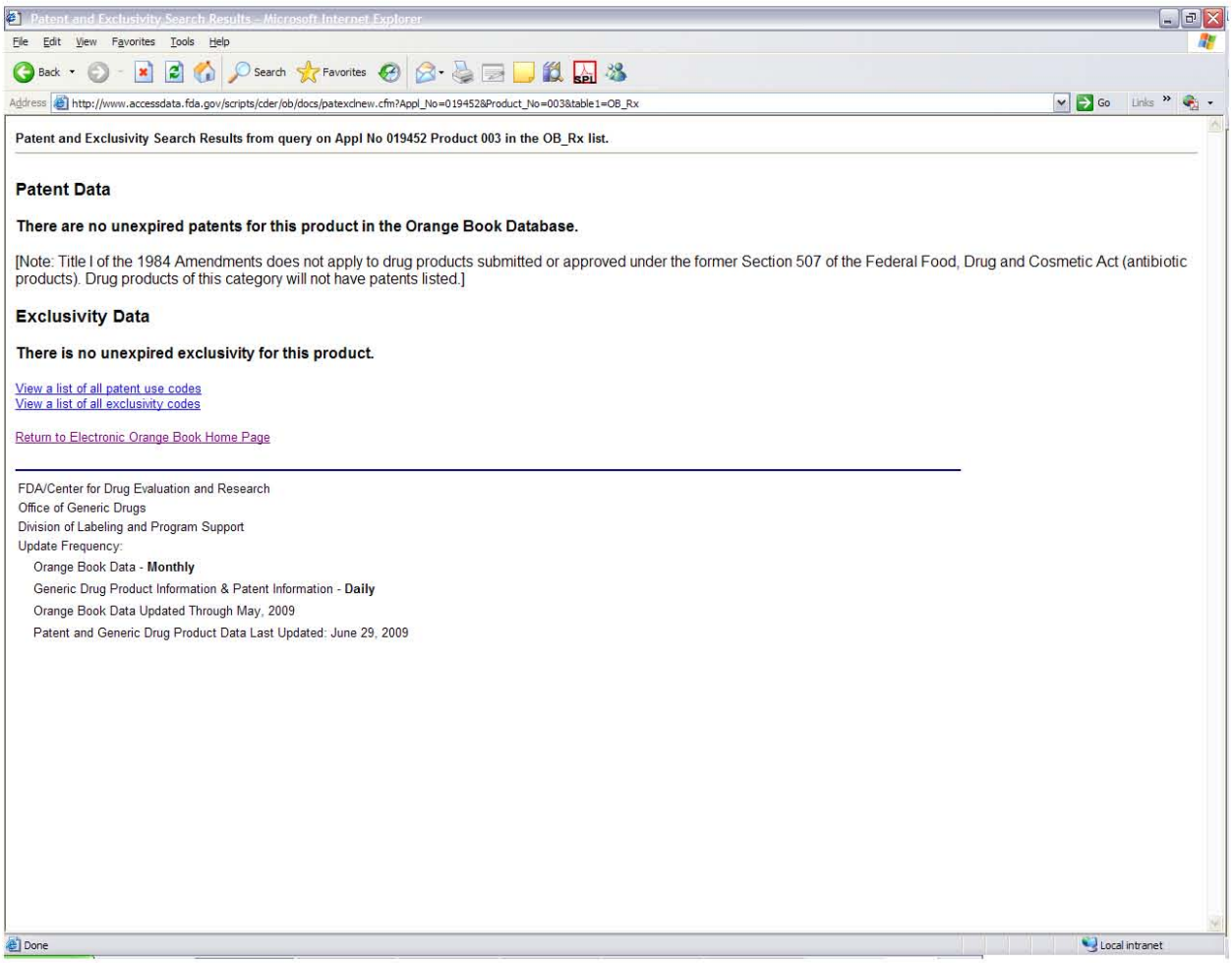

Patent and Exclusivity Search Results -- Microsoft Internet Explorer

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Address http://www.accessdata.fda.gov/scripts/cder/ob/docs/patexclnew.cfm?Appl_No=019452&Product_No=003&table1=OB_Rx

Go Links

Patent and Exclusivity Search Results from query on Appl No 019452 Product 003 in the OB_Rx list.

Patent Data

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

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

Exclusivity Data

There is no unexpired exclusivity for this product.

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

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FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through May, 2009
Patent and Generic Drug Product Data Last Updated: June 29, 2009

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From Pharm/Tox review dated 6/23/2003 in DFS:

Relevant INDs/NDAs/DMFs:

1) IND 33,448 (Derma-Smooth FS for treatment of psoriasis of the scalp; submitted 7/27/89; HFD-540)
2) NDA 12-787 (Synalar Cream, fluocinolone acetonide, 0.025%; Corticosteroid responsive dermatoses; HFD-540; approved 2-15-63)
3) NDA 13-960 (Synalar Ointment, fluocinolone acetonide, 0.025%; Corticosteroid responsive dermatoses; HFD-540; approved 6-19-63)
4) NDA 15-296 (Synalar Solution, fluocinolone acetonide, 0.01%; Corticosteroid responsive dermatoses; HFD-540; approved 5-27-64)
5) NDA 16-161 (Synalar HP cream; fluocinolone acetonide; Corticosteroid responsive dermatoses; HFD-540; approved 7-25-67)
6) NDA 20-001 (FS shampoo, fluocinolone acetonide, 0.01%; Seborrheic dermatitis; HFD-540; 8-27-90)
7) NDA 21-112 (Tri-luma cream, fluocinolone acetonide, 0.01%, hydroquinone, 4%, tretinoin, 0.05%; Cutaneous melasma; HFD-540; 1-18-02)
8) DMF (b) (4)
9) DMF

Drug class: Corticosteroid

Indication: Atopic dermatitis and psoriasis of the scalp

Clinical formulation:

Each gram of Derma-Smoothe FS topical oil contains approximately 0.11 mg of fluocinolone acetonide in a blend of oils which contains isopropyl alcohol, isopropyl myristate, light mineral oil, oleth-2, refined peanut oil NF and fragrances.

Ingredient	Percentage
Refined peanut Oil, NF[a]	(b) (4)
White Mineral Oil, USP	
Oleth-2	
Isopropyl Myristate, NF	
Isopropyl Alcohol, NF	
Cream Fragrance (b) (4)	
Balsam Pine Fragrance (b) (4)	
Fluocinolone Acetonide, USP	0.010

a – Refined peanut oil, NF has been heated at 475 °F for 15 minutes to denature possible peanut allergens

Table 1: Unit Composition (maximum daily dose = 10 drops, 0.0228 mL)

Ingredient	w/v	w/w%	IIG limits	Purpose
Fluocinolone Acetonide, USP	0.01 g	0.011 (b)	NA	Active ingredient
Isopropyl Alcohol, USP	(b) (4)			
Isopropyl Myristate, NF				
Oleth-2				
Light Mineral Oil, NF				
Refined Peanut Oil, NF				
Total	100.00 mL	(b) (4)	NA	NA

Table 10: Bulk Batch Number 04AX02 Reconciliation			
Process Step	**Exhibit Catch Result**	**Target**	**Limit**
Transfer of bulk	(b) (4)		
Packaging Reconciliation			
Theoretical Bulk Yield: (b) (4) **kg**		**Actual Bulk Yield:** (b) (4) **kg**	
Withdrawn for Testing: (b) (4) g (pg 10 of 10 of BPR)			
Packaging Batch Numbers:		**02AX02A**	**02AX02B**
Packaging Description	(b) (4)		
Total weight of product packaged			
Amount not packaged			
Average fill per bottle			
Total number of bottles packaged			
Total packaged			
Amount sampled for chemistry testing (refer to page 6 of 10 Pkg Record)			
Amount sampled for micro testing (refer to page 5 of 10 Pkg Record)			
Amount sampled for stability testing (refer to page 5 of 10 Pkg Record)			
Number of retains			
Total amount withdrawn			
Amount returned to warehouse after initial packaging			
Additional Test and/or Samples Withdrawals			
Current Inventory			

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/s/

IAIN MARGAND
10/14/2009

MARTIN H Shimer
10/15/2009

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 91-306

SciRegs International, Inc.
U.S. Agent for: Identi Pharmaceuticals, LLC
Attention: Jeanne Taborsky
6333 Summercrest Drive
Columbia, MD 21045

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.

Reference is also made to the telephone conversation dated September 29, 2009 and your correspondence dated October 6, 2009.

NAME OF DRUG: Fluocinolone Acetonide Oil, 0.01% (Otic)

DATE OF APPLICATION: April 16, 2009

DATE (RECEIVED) ACCEPTABLE FOR FILING: April 20, 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.

Should you have questions concerning this application, contact:

Nitin Patel
Project Manager
240-276-8548

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-91306	ORIG-1	IDENTI PHARMACEUTICALS	FLUOCINOLONE ACETONIDE

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/s/

MARTIN H Shimer
10/15/2009
Signing for Wm Peter Rickman

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

October 6, 2009

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0003 Telephone Amendment

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.60, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a telephone amendment to our abbreviated new drug application (ANDA) for Fluocinolone Acetonide Oil 0.01% Ear Drops. Reference is made to the original submission eCTD 0000, on April 16, 2009 and the gratuitous amendments eCTD 0001, submitted August 26, 2009 and eCTD 0002, submitted on August 27, 2009. Reference is also made to the telephone request made by Ian Margand, Pharm. D., Regulatory Reviewer, on September 29, 2009.

The agency's requests and our response are as follows;

1) *Please provide a revised debarment certification for Identi Pharmaceuticals with the wording "to the best of our knowledge" removed.*

   As requested, we have removed the wording *"to the best of our knowledge,"* from the Identi debarment certification. The revised certification is located in Module 1 Section 1.3.3 Debarment Certification.

2) *Your patent certification lists NDA 21-930. Please revise the patent certification to reference the currently listed reference listed drug NDA number.*

   Please be advised that at the time of our filing, *NDA 21-930*, was the correct listing for the reference listed drug for the Hill otic product. It appears that since that time, the innovator has collapsed this NDA into their other NDA which includes a topical body treatment and a scalp treatment. As requested, we have provided the revised patent information in for NDA 19-452 in Module 1 Section 1.3.5 Patent Information. Please be advised that our submission covers only the otic product.

3) *Please revise your Identi Certificate of Analysis for Fluocinolone Acetonide, USP to clearly indicate which laboratories are performing the testing and their certificates of analysis.*

The contract testing laboratories are all using Identi specifications for the testing. The Identi certificate of analysis (CoA) form has been revised. For the test batch, the drug substance testing was conducted by (b) (4). The CoA was completed by (b) (4)

Please be advised that Identi has continued to conduct studies for this ANDA and has made some improvements in the contract testing laboratories. When the product was first tested and manufactured, (b) (4) conducted the release testing on the components and (b) (4) conducted testing on the finished product. (b) (4) conducted testing on the residual solvents.

For the revised CoA, the optical rotation and residual solvent testing is now being preformed by (b) (4), the particle size testing is still preformed by (b) (4) and the remaining tests are performed by (b) (4) enters the data on our CoA form, and Identi releases the material. The individual results certificates are provided by the separate testing facilities. The revised blank CoA is provided in Module 3 Section 3.2.S.4.4 Batch Analysis, along with the assay results from (b) (4) on the lot used for the test batch. The results for the all testing laboratories were provided in the original submission eCTD 0000 and in the gratuitous amendment eCTD 0001.

4) *Please provide a revised cGMP cert for* (b) (4)

The cGMP certification for (b) (4) was provided in the original submission (eCTD 0000) in Module 3 Section 3.2.P.1 Manufacturer. (b) (4) had been contracted to perform residual solvent testing. At the present time, Identi has transferred this testing to (b) (4) The certifications for (b) (4) were provided in submission eCTD 0001 on August 26, 2009.

5) *Please revise the bioequivalence waiver to site the Code of Federal Regulations Title 21 §320.00(b)(1)(i-ii).*

The Bioequivalence waiver has been updated to include the 21 *CFR* reference and is provided in Module 1 Section 1.12.15 Bio Waiver.

6) *Please provide a copy of Module 2 in word format.*

The word versions of the requested sections were provided to the agency on a separate disk along with the original submission on April 16, 2009. For ease of reference, the word versions of Module 2 and the Labeling are provided herein.

This completes our submission. This ANDA is filed in eCTD format with a word version of Module 2 and the labeling. Letters of Non-Repudiation have been submitted to the Agency under separate cover. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky
US Regulatory Agent
SciRegs International Inc.

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research
Food and Drug Administration
Silver Spring MD 20993

Tel 301-769-2110
Fax 301-796-9895

M E M O R A N D U M

Date: August 20, 2009

From: Joanna Ku, MD, Medical Reviewer, Division of Dermatology and Dental Products (DDDP)

Through: Jill Lindstrom, MD, Dermatology Team Leader, DDDP
Susan Walker, MD, Division Director, DDDP

To: Deanah L. Mitchell, PhD, Pharmacology Reviewer, Division of Bioequivalence, Office I (DBE_1), Office of Generic Drugs (OGD)
Hoainhon T. Nguyen PhD, Acting Deputy Director, DBE_1/OGD

CC: Theresa Liu, RPM, DBE_1/OGD
Paul J. Phillips, RPM, DDDP
E. Dennis Bashaw, PhD, Clinical Pharmacology Division Director, DCP3
Barbara J. Gould, CPMS, DDDP
Maria Walsh, ADRA, ODE III, CDER
Julie Beitz, MD, Director, ODE III, CDER

Re: DDDP #1175, Memo to DBE_1/OGD Consult Request (July 2, 2009):

DBE_1/OGD: Request opinion as to the whether the formulation difference between the RLD product, DermOtic® (Fluocinolone Acetonide Oil), 0.01% Ear Drops (with fragrances) and Identi Pharmaceutical's test drug product of Fluocinolone Acetonide Oil, 0.01% Ear Drops (without fragrances) is acceptable, and whether it will have any influence on the safety and/or efficacy of the proposed test drug product.

Materials Reviewed:

1) ANDA 091-306, Original Submission 000 dated April 16, 2009
2) Product labeling: DermOtic® (Fluocinolone Acetonide Oil), 0.01% Ear Drops
3) FDA Guidance for Industry: Nonsterile Semisolid Dosage Forms. Scale-Up and Post Approval Changes: Chemistry, Manufacturing, and Controls; In Vitro

> Release Testing and In Vivo Bioequivalence Documentation ("SUPAC-SS Guidance," May 1997)

Review:

Background

Identi Pharmaceutical's ANDA 91-306 for Fluocinolone Acetonide Oil, 0.01% Ear Drops (the Test Product) is the first generic drug application for Fluocinolone Acetonide Oil/Drops (Otic), 0.01%. The drug is a low-to-medium potency topical corticosteroid indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years and older. The Reference Listed Drug (RLD) product is DermOtic® Oil (Fluocinolone Acetonide Oil, 0.01% Ear Drops), which is marketed by Hill Dermaceuticals, approved under NDA 19-452 in 2005. DermOtic® Oil is also marketed as Derma-Smoothe/FS Body Oil® for the treatment of atopic dermatitis, and as Derma-Smoothe/FS Scalp Oil® for the treatment of psoriasis of the scalp. Fluocinolone Acetonide in DermOtic® Oil has a molecular weight of 452.50. It is a white crystalline powder that is odorless, stable in light, and melts at 270°C with decomposition. It is soluble in alcohol, acetone and methanol, slightly soluble in chloroform, and insoluble in water. Each gram of DermOtic® Oil contains approximately 0.11 mg of Fluocinolone Acetonide in a blend of oils, which contains isopropyl alcohol, isopropyl myristate, light mineral oil, oleth-2, refined peanut oil NF and fragrances.

OGD finds that the Sponsor's Test Product appears to be qualitatively (Q1) and quantitatively (Q2) "equivalent" to the RLD product, except for the lack of fragrances, which are present in the RLD product only. Specifically, the Q1 and Q2 differences in the formulation are within + 5% based on the % volume/volume comparison of each of the inactive ingredients, and the differences in the formulation pertain to the two fragrances, Cream Fragrance (b) (4) and Balsam Pine Fragrance (b) (4). The Test Product does not contain these or any other fragrances, and the deletion of fragrance is viewed by the Sponsor as a "product improvement." With the assertion that the two products are otherwise qualitatively and quantitatively equivalent, i.e., containing the same active and inactive ingredients in the same concentration as the RLD product,[1] the Sponsor submitted a waiver request of *in vivo* bioequivalence (BE) requirements for its Fluocinolone Acetonide Oil, 0.01% Ear Drops, based on 21 CFR § 320.22(b)(1)(i-ii):

> 320.22 - Criteria for waiver of evidence of in vivo bioavailability or bioequivalence.
>
> (b) For certain drug products, the in vivo bioavailability or bioequivalence of the drug product may be self-evident. FDA shall waive the requirement for the submission of evidence obtained in vivo measuring the bioavailability or demonstrating the bioequivalence of these drug products. A drug product's in vivo bioavailability or bioequivalence may be considered self-evident based on other data in the application if the product meets one of the following criteria: (1) The drug product: (i) Is a parenteral

[1] The Sponsor also believes that they are (b) (4), as disclosed in a patent for another product.

> solution intended solely for administration by injection, or an ophthalmic or otic solution; and (ii) Contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application.

OGD requests DDDP to review the formulations of the Test Product and the RLD product in order to determine whether the difference in formulation as it pertains to fragrances is acceptable, and whether it will have an impact on the safety and/or efficacy of the proposed Test Product.

Review of Formulation Differences
FDA's NDA review for the RLD product and its formulation composition is summarized as follow (Tables 1 and 2):

Table 1 Excipients data for the RLD, submitted in the original NDA

D: Raw Excipients of NDA 19452[4]

PRODUCT NAME: DERMA-SMOOTHE/FS TOPICAL OIL
PRODUCT FORM: Oil Lotion
PRODUCT DISTRIBUTED BY: Hill Dermaceuticals
INTERNAL ORDER NUMBER
DATE BEGIN: 01-26-84 DATE END: 01-26-84
RAW MATERIALS
NAME | QUANTITY KG GM LT | Allowed Override | Formula per
BATCH MANUFACTURING STEPS | Theoretical Yield per Step

(b) (4)

Table 2 Active ingredient and excipients composition data for the RLD, submitted in the original NDA

A: NDA Formulation[1,2] (NDA # 19452): (NOT FOR RELEASE UNDER FOIA)

Ingredient	Percentage
Fluocinolone Acetonide, USP	0.010
Refined peanut Oil, NF[a]	(b) (4)
White Mineral Oil, USP	
Oleth-2	
Isopropyl Myristate, NF	
Isopropyl Alcohol, NF	
Cream Fragrance (b) (4)	
Balsam Pine Fragrance (b) (4)	

Note: For the inactive ingredients, the "Percentage" in the RLD formulation is based on Volume/Volume (v/v) * 100
For the active ingredient, the "Percentage" in the RLD formulation is based on weight/volume (w/v) * 100
a- Refined peanut oil, NF has been heated at 475 °F for 15 minutes to denature possible peanut allergens.
*The RLD labeling states that Light Mineral Oil is an inactive ingredient in Fluocinolone Acetonide Oil. Therefore, in the table above, White Mineral Oil, USP is used interchangeably as Light Mineral Oil.

In Table 3, the Test Product formulation is summarized (copied electronically from the Sponsor's ANDA submission, as Table 1 Unit Composition, Section 2.3.P.1 Description and Composition of the Drug Product):

Table 3 Active ingredient and excipients data for the Test Product, submitted in the current ANDA

Table 1: Unit Composition (maximum daily dose = 10 drops, 0.0228 mL)				
Ingredient	**w/v**	**w/w%**	**IIG limits**	**Purpose**
Fluocinolone Acetonide, USP	0.01 g	0.011 (b) (4)	NA	Active ingredient
Isopropyl Alcohol, USP	(b) (4)			
Isopropyl Myristate, NF				
Oleth-2				
Light Mineral Oil, NF				
Refined Peanut Oil, NF				
Total	100.00 mL	(b) (4)	NA	NA

Reviewers Comment:
Please note that in Table 3, the first row is for the active ingredient, Fluocinolone, which is listed as 0.01g (weight); the other ingredients from the rows below are excipients, which are listed as ml (volume). Therefore, the column heading for column 2, w/v (which denotes weight by volume) is accurate only for the first row, Fluocinolone, 0.01 g/100 mL. For the rest of the cells in that column, which contain values for the excipients, the heading should be v.

Note to other reviewers: Table 4 RLD Unit Composition, in Module 2 Section 2.3.P.1 Drug Product (page 2/38) contains multiple errors, and was not used for this consult. This reviewer understands the above referenced table to be the correct version.

Using data from the above tables (Tables 1, 2, and 3), the OGD Pharmacology Reviewer (Dr. D. Mitchell) in DBE_1/OGD compiled the following comparisons between the Test Product and the RLD Product:

Table 4 Formulation differences between Test and the RLD products[2]

C: Formulation Differences between the Test and Reference Products

Ingredient	w/v of Test Product* per 100 mL	v/v of RLD Product per 100 mL	Q1/Q2 % Difference between RLD and Test Product**
Fluocinolone Acetonide	0.01 g	0.01 g	0.0%
Ingredient	**v/v of Test Product* per 100 mL**	**v/v of RLD Product per 100 mL**	**Q1/Q2 % Difference between RLD and Test Product****
Isopropyl Alcohol	(b) (4)		
Isopropyl Myristate			
Oleth-2			
Light Mineral Oil			
Refined Peanut Oil			
Cream Fragrance # (b) (4)			
Balsam Pine Fragrance (b) (4)			
Total			

*As calculated by the firm, Identi Pharmaceuticals, LLC.
** Percent difference is calculated as: (Test – Reference)/ Reference * 100

Conclusion/Recommendation:
We understand that OGD concludes that the Q1/Q2 differences in the excipients (other than fragrances) between the RLD and the Test Product do not exceed 5%. Based on OGD's analysis, it appears that the only other difference between the Test Product and the RLD is the *lack of*, or deletion of fragrances in the Test Product. We understand that these differences are considered by the OGD to be unlikely to have any detectable impact on formulation quality and performance, and that OGD is currently recommending waiving the requirement for the submission of evidence obtained *in vivo* measuring the bioavailability or demonstrating the bioequivalence of the drug products.

If this product were a semi-solid dosage form, the SUPAC-SS Guidance would apply, which states that deletion of an ingredient intended to affect fragrance is unlikely to have any detectable impact on formulation quality and performance, and that it would be considered a Level 1 change and no bioequivalence testing would be necessary. The

[2] The OGD reviewer confirmed that refined peanut oil v/v % (column 3) for the RLD should be (b) (4), consistent with the number in Tables 1 and 2. The number (b) (4) is a typo.

Guidance also states that any change in an excipient up to 5% of approved amount of that excipient is also unlikely to have any detectable impact on formulation quality and performance (however, please note the total additive effect of all excipient changes should not be more than 5%). Though the Test Product is not a semi-solid dosage form, the SUPAC-SS Guidance nevertheless provides a useful regulatory framework for evaluation. For this instance with the available information that has been provided, we would not object to waiver for bioequivalence testing if the present excipients are within +/- 5% of the RLD, and are not structure forming agents that might impact bioavailability. With regards to the deletion of the fragrances, given that the two fragrances in question are present in the RLD at an extent of (b) (4)% of the total amount (v/v), and that such "minor" changes are explicitly allowed under SUPAC-SS in such situations, we would not object to an in vivo bioavailability waiver on these grounds for this product.

Thank you for this consult; please let us know if we could be of further assistance.

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

/s/

JOANNA W KU
09/03/2009

JILL A LINDSTROM
09/03/2009

SUSAN J WALKER
09/08/2009

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

August 26, 2009

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0001 Gratuitous Amendment - Additional Analytical Information

Dear Sir/ Madam:

Pursuant to *Code of Federal Regulations* Title 21 § 314.60, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits a gratuitous amendment to our abbreviated new drug application (ANDA) for Fluocinolone Acetonide Oil 0.01% Ear Drops. Reference is made to the original submission eCTD 0000, on April 16, 2009.

Since the filing of the original submission Identi has continued to work to improve the analytical information for this drug product by conducting additional tests on the raw materials and drug product.

The following amendment contains additional analytical information, test methods, and validation reports and provides for two additional outside testing facilities; (b) (4) for residual solvent testing of the raw materials. Information on the facilities is provided in Attachment 1 to the filing form and in Module 3 Section 3.2.P.3.1 Manufacturer. Debarment certifications are provided in Module 1 Section 1.3.3 Debarment. CGMP certifications are provided in Module 3 Section 3.2.P.3.1 Manufacturer. Test results for the residual solvents in the drug substance are provided in Module 3 Section 3.2.S.4.4 Justification for API Specifications. Test results for the residual solvent in the excipients are provided in Module 3 Section 3.2.P.4.4 Justification for Excipient Specifications. Test methods used to test for residual solvents in the excipients are provided in Module 3.2.P.4.2 Analytical Procedures. (b) (4) The specifications for the Mineral Oil, NF and the Oleth 2 have also been updated and are provided in Module 3 Section 3.2.P.4.1 Excipient Specifications.

Stability studies were conducted under a stability protocol that is in conformance with the ICH Stability Guidelines. All stability data to date including the 9-months test results are provided in Module 3 Section 3.2.P.8.3 Stability Data. Additional investigative studies including HPLC/mass spectroscopy have determined that two of the reported impurites/degradants have been demonstrated to be *unrelated* to the drug. These peaks may be evidence of migrants from the plastic components used during the filing operation, or trace amounts of components of the excipients. The stability data report has been amended to correct the listing of one of the impurites listed as (b) (4) Based on the characterization, the stability reports, analytical method and validation reports have been revised. A copy of the revised Validation of Analytical Procedures and the report of the investigation into the structures of the degradants by HPLC /Mass spectroscopy are provided in Module 3 Section 3.2.P.5.3 Validation of Analytical Procedures.

During the course of HPLC testing, it was determined that one auto injector was injecting less than the desired amount of drug product and therefore, yielding lower assay results. A report and revised systems suitability requirements have been added.

This completes our submission. This ANDA is filed in eCTD format. Letters of Non-Repudiation have been submitted to the Agency under separate cover. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky
US Regulatory Agent
SciRegs International Inc.

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION			REQUEST FOR CONSULTATION Consult No: 2009-0336	
TO *(Division/Office)* DDDP - HFD-540 Thru: Maria Walsh, ODEIII			FROM: Hoainhon Caramenico	
DATE: 7/2/2009	IND NO.	~TYPE~ NO. 091306	TYPE OF DOCUMENT ~TYPE_OF_DOCUMENT~	DATE OF DOCUMENT 4/16/2009
NAME OF DRUG FLUOCINOLONE ACETONIDE		PRIORITY CONSIDERATION 30 days	CLASSIFICATION OF DRUG CORTICOSTEROIDS	DESIRED COMPLETION DATE 8/1/2009

NAME OF FIRM IDENTI PHARMS

REASON FOR REQUEST

I. GENERAL

- Γ NEW PROTOCOL
- Γ PROGRESS REPORT
- Γ NEW CORRESPONDENCE
- Γ DRUG ADVERTISING
- Γ ADVERSE REACTION REPORT
- Γ MANUFACTURING CHANGE/ADDITION
- Γ MEETING PLANNED BY _____
- Γ PRE NDA MEETING
- Γ END OF PHASE II MEETING
- Γ RESUBMISSION
- Γ SAFETY/EFFICACY
- Γ PAPER NDA
- Γ CONTROL SUPPLEMENT
- Γ RESPONSE TO DEFICPENCY LETTER
- Γ FINAL PRINTED LABELING
- Γ LABELING REVISION
- Γ ORIGINAL NEW CORRESPONDENCE
- Γ FORMULATIVE REVIEW
- X *OTHER ('specify below)*

II.BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
Γ TYPE A OR B NDA REVIEW Γ END QF PHASE II MEETING Γ CONTROLLED STUDI ES Γ PROTOCOL REVIEW Γ OTHER	Γ CHEMISTRY Γ PHARMACOLOGY Γ BIOPHARMACEUTICS Γ OTHER

III.BIOPHARMACEUTICS

- □ DISSOLUTION
- □ PROTOCOL-- BIOPHARMACEUTICS
- □ IN--VIVO WAIVER REQUEST
- □ DEFICIENCY LETTER RESPONSE
- □ BIOAVAILABILITY STUDIES
- □ PHASE IV STUDIES

IV.DRUG EXPERIENCE

- □ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- □ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- □ CASE REPORTS OF SPECIFIC *REACTIONS(List below)*
- □ COMPARATIVE RISK ASSESSEMENT ON GENERIC DRUG GROUP
- □ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- □ SUMMARY OF ADVERSE EXPERIENCE
- POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

□ CLINICAL □ PRECLINICAL

COMMENTS

DBE1/OGD is requesting the evaluation of the test formulation for any clinical and safety concerns: The test and Reference Listed Drug (RLD) product, DermOtic Oil, 0.01% Ear Drops contain the same active and inactive ingredients in the same concentrations (+/-5%) EXCEPT for the fragrances, Cream Fragrance and Balsam Pine Fragrance, which are present in the RLD product but not in the test product, which contains NO FRAGRANCES. (Please see attached documents for additional information)Please cc Theresa Liu, HFD-617 (Theresa.Liu@fda.hhs.gov) on the review when it is being checked into DFS. Thank you.

SIGNATURE OF REQUESTER	METHOD OF DE LIVERY *(Check one)* □ MAIL □ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

FORM FDA 3291 (7/83)

cc: ANDA
Drug File Folder

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20852

To: Susan Walker, M.D., Director Division of Dermatology and Dental Products, Office of Drug Evaluation III

From: Deanah L. Mitchell, Ph.D., Reviewer, Division of Bioequivalence, Office of Generic Drugs

Through: Hoainhon Nguyen, Acting Deputy Director, Division of Bioequivalence I, Office of Generic Drugs

Re: Request opinion as to the whether or not the formulation difference between the RLD product, DermOtic® (Fluocinolone Acetonide Oil), 0.01% Ear Drops (with fragrances) and Identi Pharmaceutical's test formulation of Fluocinolone Acetonide Oil, 0.01% Ear Drops (without fragrances) is acceptable, and whether it will have any influence on the safety and/or efficacy of the proposed (test) drug product.

Introduction: The Division of Bioequivalence is requesting a clinical consult to determine the acceptability of Identi Pharmaceutical's Fluocinolone Acetonide Oil, 0.01% Ear Drops (ANDA # 91-306). This is a First Generic application for Fluocinolone Acetonide Oil/Drops (Otic), 0.01%. The Reference Listed Drug (RLD) is DermOtic® Oil (Fluocinolone Acetonide Oil), 0.01% Ear Drops by Hill Dermaceuticals (NDA# 019452 approved on November 09, 2005). The drug is a low to medium potency corticosteroid indicated for the treatment of chronic eczematous external otitis in adults and pediatric patients 2 years and older.

Background Information: On April 16, 2009, Identi Pharmaceuticals submitted a waiver request of *in vivo* bioequivalence (BE) requirements for its Fluocinolone Acetonide Oil, 0.01% Ear Drops based on 21 CFR § 320.22(b)(1)(i-ii).

Issue: The firm's test product is qualitatively (Q1) and quantitatively (Q2) the same to the RLD product, ***except for the lack of fragrances*** which are present in the RLD product. The Q1 and Q2 differences in the formulation are within + 5% based on the % volume/volume comparison of each of the inactive ingredients. The differences in the formulation pertain to the two fragrances (Cream Fragrance (b) (4) and Balsam Pine Fragrance (b) (4)) that the RLD product contains, but the test product does not contain.

Identi Pharmaceutical's states the following in Module 2: Quality Summary concerning the formulation difference, *"The only difference in the formulation of our product and the RLD is the deletion of the fragrance which Identi views as a product improvement."*

Question: Please review the formulations of the test and RLD products, in order to determine whether or not the difference in formulation as it pertains to fragrances is acceptable and whether or not it will have an impact on the safety and/or efficacy of the proposed drug product.

Additional Data/Supportive Information: The firm's complete application is located in the Electronic Document Room, letter date: 16-Apr-09, http://edr fda.gov:7777/edr/EDR_Main.jsp.

The tables provided below contain the formulations of the test product, the RLD product and calculation of the formulation differences between the test and RLD product:

A: NDA Formulation[1,2] (NDA # 19452): (NOT FOR RELEASE UNDER FOIA)

Ingredient	Percentage
Fluocinolone Acetonide, USP	0.010
Refined peanut Oil, NF[a]	(b) (4)
White Mineral Oil, USP	
Oleth-2	
Isopropyl Myristate, NF	
Isopropyl Alcohol, NF	
Cream Fragrance (b) (4)	
Balsam Pine Fragrance # (b) (4)	

Note: For the inactive ingredients, the "Percentage" in the RLD formulation is based on Volume/Volume (v/v) * 100
For the active ingredient, the "Percentage" in the RLD formulation is based on weight/volume (w/v) * 100
a- Refined peanut oil, NF has been heated at 475 °F for 15 minutes to denature possible peanut allergens.
*****The RLD labeling states that Light Mineral Oil is an inactive ingredient in Fluocinolone Acetonide Oil. Therefore, in the table above, White Mineral Oil, USP is used interchangeably as Light Mineral Oil.

B: ANDA Formulation: Fluocinolone Acetonide Topical Oil, 0.01% (Ear Drops)[3]

RLD Unit Composition (maximum daily dose = 10 drops or 0.0228 mg Fluocinolone Acetonide)			
Ingredient	**Generic**		**RLD**
	v/v %	**w/w %**	**amount**
Fluocinolone Acetonide, USP	0.01 g	0.011	(b) (4)
Isopropyl Alcohol, USP	(b) (4)		
Isopropyl Myristate, NF			
Oleth-2			
Mineral Oil, USP			
Peanut Oil, NF			
Cream Fragrance (b) (4)			
Balsam Pine fragrance (b) (4)			
Total	**100.00 mL**	(b) (4)	

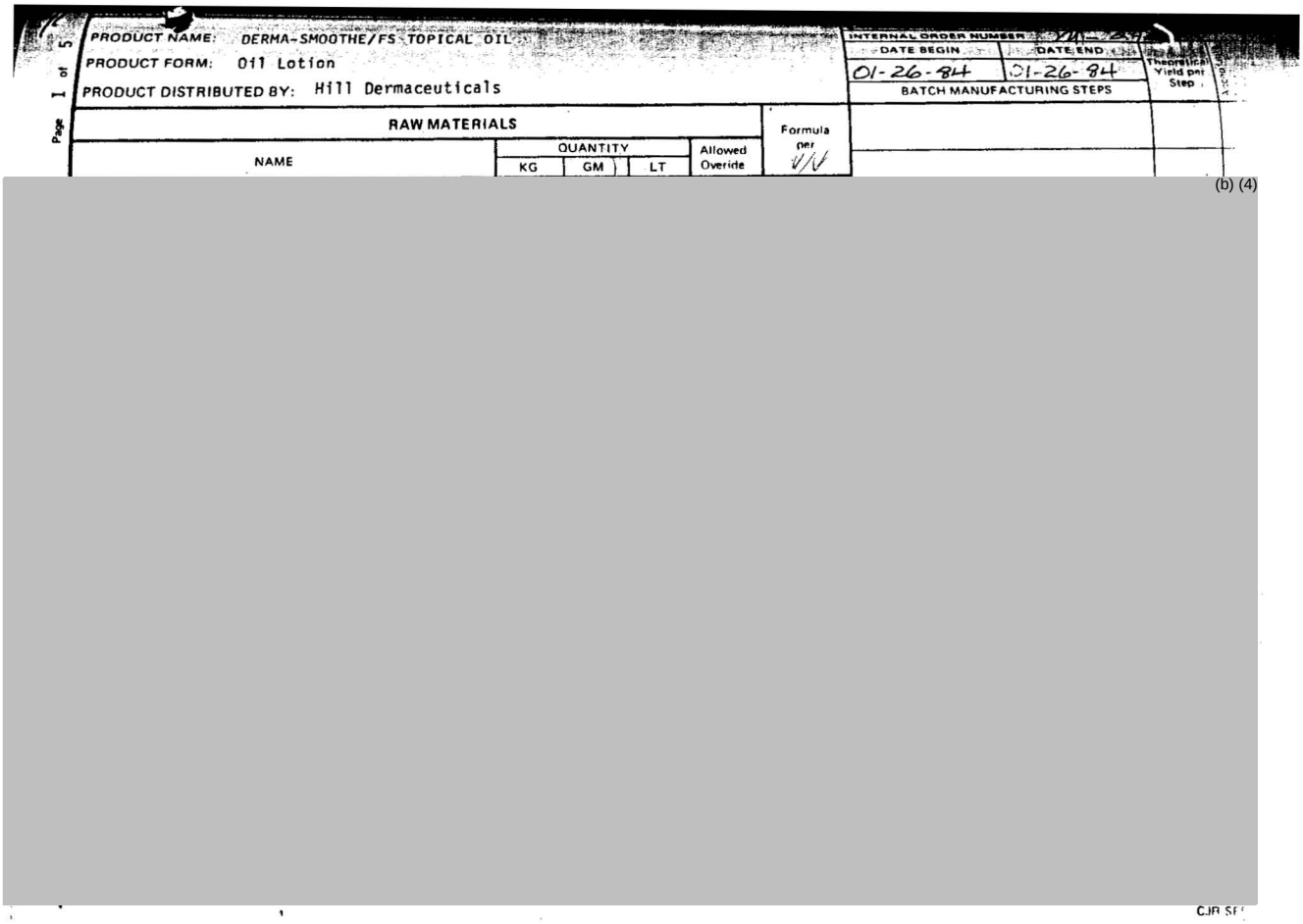
[1] Division of System Files v. 2.0; SE5-024: Pediatric effica, Pharmacologist; N 019452 SE5 024 12-Feb-2007. Review Sign off date: 06/13/2007.
[2] Archival Copy of NDA 19452; Volume 1.1. Date: August 14, 1985. Page 167.
[3] ANDA submission, Section 2.3.P.1: Formulation Composition

C: Formulation Differences between the Test and Reference Products

Ingredient	w/v of Test Product* per 100 mL	v/v of RLD Product per 100 mL	Q1/Q2 % Difference between RLD and Test Product**
Fluocinolone Acetonide	0.01 g	0.01 g	0.0%
Isopropyl Alcohol Isopropyl Myristate Oleth-2 Light Mineral Oil Refined Peanut Oil Cream Fragrance (b) (4) Balsam Pine Fragrance (b) (4)	(b) (4)		
Total	100 mL	100 mL	

*As calculated by the firm, Identi Pharmaceuticals, LLC.
** Percent difference is calculated as: (Test – Reference)/ Reference * 100

D: Raw Excipients of NDA 19452[4]



Page 1 of 5

PRODUCT NAME: DERMA-SMOOTHE/FS TOPICAL OIL
PRODUCT FORM: Oil Lotion
PRODUCT DISTRIBUTED BY: Hill Dermaceuticals

INTERNAL ORDER NUMBER: [illegible]
DATE BEGIN: 01-26-84 | DATE END: 01-26-84

RAW MATERIALS

NAME	QUANTITY KG	GM	LT	Allowed Overide	Formula Per	BATCH MANUFACTURING STEPS	Theoretical Yield per Step

(b) (4)

[redacted]

[4] Archival Copy of NDA 19452; Volume 1.1. Date: August 14, 1985. Page 167.

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/s/

Theresa Liu

7/2/2009 12:25:53 PM

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE : May 11, 2009

TO : Director
Division of Bioequivalence (HFD-650)

FROM : Chief, Regulatory Support Branch
Office of Generic Drugs (HFD-615)

SUBJECT: Examination of the bioequivalence study submitted with an ANDA 91-306 for Fluocinolone Acetonide Otic Oil, 0.01% to determine if the application is substantially complete for filing and/or granting exclusivity pursuant to 21 USC 355(j)(5)(B)(iv).

Identi Pharmaceuticals, LLC has submitted ANDA 91-306 for Fluocinolone Acetonide Otic Oil, 0.01%. The ANDA contains a certification pursuant to 21 USC 355(j)(5)(B)(iv) stating that patent(s) for the reference listed drug will not be infringed by the manufacturing or sale of the proposed product. Also it is a first generic. In order to accept an ANDA that contains a first generic, the Agency must formally review and make a determination that the application is substantially complete. Included in this review is a determination that the bioequivalence study is complete, and could establish that the product is bioequivalent.

Please evaluate whether the request for study submitted by Identi Pharmaceuticals, LLC on April 16, 2009 for its Fluocinolone Acetonide product satisfies the statutory requirements of "completeness" so that the ANDA may be filed.

A "complete" bioavailability or bioequivalence study is defined as one that conforms with an appropriate FDA guidance or is reasonable in design and purports to demonstrate that the proposed drug is bioequivalent to the "listed drug".

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/s/

Eda Howard
5/13/2009 06:55:45 AM
APPLICATIONS EXA

SciRegs International, Inc.
6333 Summercrest Dr.
Columbia, MD 21045 USA

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

April 16, 2009

RE: ANDA 091-306 Fluocinolone Acetonide Oil 0.01% Ear Drops
eCTD 0000 Original Submission

Dear Sir/ Madam:

Pursuant to Section 505 (j) of the *Federal Food, Drug, and Cosmetic Act*, SciRegs International, Inc., US Agent for Identi Pharmaceuticals, LLC, here within submits an abbreviated new drug application (ANDA) for Fluocinolone Acetonide 0.01% Ear Drops. A copy of our Letter of Appointment as US Agent is provided in Module 1 Section 1.4.1. References.

This application references DermOtic® Oil (fluocinolone acetonide oil) 0.01% Ear Drops listed in the *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the Orange Book), and manufactured by Hill Dermaceuticals, Inc.

The dosage form, route of administration, active ingredient, potency, and labeling (with the exception of brand name, logo, manufacturer, and NDC number) for Fluocinolone Acetonide Oil 0.01% Ear Drops are the same as those for DermOtic® Oil (fluocinolone acetonide oil) 0.01% Ear Drops. An electronic copy of the innovator labeling is provided in Module 1 Section 1.14.3.3 Labeling, proposed labeling for Identi's product is provided in Module 1 Section 1.14.1.1 Draft Labeling, and the side-by-sides are provided in Module 1 Section 1.14.1.2 Annotated Draft Labeling Text and Section 1.14.3.1 Annotated Comparison with Listed Drug.

(b) (4) is the manufacturer of the Active Pharmaceutical Ingredient (API), Fluocinolone Acetonide, USP, used in Identi's drug product. (b) (4) facility is responsible for manufacturing, release testing, and stability testing of the API. This API manufacturing facility was last inspected by the US FDA, (b) (4). The API site is ready for inspection. (b) (4) particle size testing on the drug substance is contracted by the drug substance manufacturer to (b) (4). Information on these facilities is provided in Module 3 Section 3.2.S.2 Manufacture. The sites are ready for inspection.

Identi has contracted the residual solvent testing of the raw materials to (b) (4) particle size testing of the drug substance to (b) (4), and the testing of the amino acid content to (b) (4). The release testing of the drug substance, and release testing and stability studies for the drug product are being conducted at (b) (4) where a portion of the stability samples are stored. This testing laboratory is FDA registered and was last inspected, on March 24, 2008. A portion of the stability samples are also being stored at (b) (4) close to (b) (4). Information on all of these facilities is provided in Attachment 1 to the filing form and in Module 3 Section 3.2.P.3.1 Manufacturer.

The drug substance is the subject of an USP monograph; therefore, methods validation was not required for the drug substance compendial tests and was provided only for the drug substance impurities, residual solvents, and the drug product test methods. The Firm commits to provide any additional information and resolve any issues identified in the methods validation process post approval.

The drug product manufactured in support of this ANDA submission was and will be manufactured at the contract manufacturing facility, (b) (4). This facility is also responsible for receiving raw materials and components, manufacturing, and packaging the drug product. The facility is FDA registered. The facility was last inspected by US FDA, in January 2009, and was classified as acceptable. For the test batch, (b) (4) conducted release testing on the raw materials, components, and finished product. The facility is ready for inspection. Additional information regarding this facility is located in Module 3 Section 3.2.P.3.1 Manufacturer.

The entire test batch was packaged in (b) (4) bottles with specially designed continuous thread (b) (4) closures; one half of the containers were fitted with (b) (4) liners and the other half was fitted with (b) (4). Identi is requesting approval of the product packaged with the (b) (4) closure. The container includes an auxiliary dropper assembly to dispense the product. Information on the container/closure systems is provided in Module 3 Section 3.2.P.7 Container Closure System and Module 3.2.R.1.P.2 Information on Components. The components were tested in conformance with USP <661> *Containers*. Additional migration and compatibility studies were conducted on the components.

Stability studies were conducted under a stability protocol that is in conformance with the ICH Stability Guidelines. The drug product is to be stored at USP MKT 25°C and shipped USP refrigerated. Identi requests approval of a two-year expiration dating for these products as supported by one, two, and three month's accelerated stability data (40ºC + 2°C/ 75% + 5% Relative Humidity), testing under intermediate conditions (30°C + 2°C /65% + 5% RH) and controlled room temperature conditions (25°C + 2°C /60% + 5% RH) to date. A copy of the forced degradation studies is also provided in Module 3 Section 3.2.P.5.3 Validation of Analytical Procedures.

Identi is requesting a waiver from in-vivo bioequivalence studies based upon the fact that the formulation for our otic product is the same (with the exception of the fragrance) to the innovator product. The waiver is located in Module 1 Section 1.12.15 Request for Waiver.

This completes our submission. This ANDA is filed in eCTD format. As instructed by Peter Chan, OGD, Module 2 and the labeling are also submitted on a separate disk in WORD format. Letters of Non-Repudiation have been submitted to the Agency under separate cover. Please contact C. Jeanne Taborsky, SciRegs International Inc. at phone (410) 309-3145; fax (410) 309-6145, if you have any questions concerning this submission.

Sincerely yours,

C. Jeanne Taborsky

C. Jeanne Taborsky
US Regulatory Agent
SciRegs International Inc.