CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 72-354

Name: Desowen (desonide lotion) 0.05%

Sponsor: Owen Laboratories

Approval Date: January 24, 1992

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 72-354

CONTENTS

Reviews / Information Included in this Review	
Approval Letter	X
Tentative Approval Letter	
Labeling	X
Labeling Reviews	X
Medical Reviews	
Chemistry Reviews	X
Bioequivalence Reviews	X
Statistical Reviews	
Microbiology Reviews	
Administrative & Correspondence Documents	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 72-354

APPROVAL LETTER

ANDA 72-354

JAN 24 1992

Owen/Galderma
Attention: Ms. Christine E. Shank
6201 South Freeway
PO Box 6600
Fort Worth, TX 76115

Dear Madam:

Reference is made to your abbreviated new drug application dated November 25, 1987, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for DesOwen^{R} (Desonide) Lotion, 0.05%.

We acknowledge receipt of your communications dated November 1, November 15, December 5 (two), December 13, 18, and 19, 1991 amending this application.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Anti-Infective Drug Products has reviewed your bioequivalence testing and has determined that the proposed drug product can be expected to have the same therapeutic effect as that of the listed drug (Desonide Cream of your firm).

Any significant change in the conditions outlined in this abbreviated application requires an approved supplemental application before the change may be made, except for changes made in conformance with other provisions of Section 314.70 of the Regulations.

Postmarketing reporting requirements for this abbreviated application are set forth in *21 CFR* 314.80 and 314.81 of the Regulations.

This administration should be advised of any change in the marketing status of this drug.

For Initial Campaigns: We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your immediate advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising and Communications (HFD-240). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

For Subsequent Campaigns: We call your attention to Section 314.81(b)(3) of the Regulations which requires that materials for any subsequent advertising or promotional campaign, at the time of their initial use, be submitted to our Division of Drug Marketing, Advertising and Communications (HFD-240) with a completed Form FD-2253.

Sincerely yours,

1/24/92

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #72-354
DUP/Division File
HFD-638/PSubramaniam 12-23-91
HFD-82
HFD-320/PVogel
HFD-650/Dighe
HFC-130/JAllen
HFD-634/MSmela/RTrimmer 12-30-91
HFD-632/RPollock/VVashio Washio 12/23/91
HFD-600/Reading File
R/D initialed by MSmela 12/30/91
72354A06.lrt(apprltr)
F/T by jkg/12-23-91
Approval Letter!

Rec'd 12/30/91

1/24/92

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 72-354

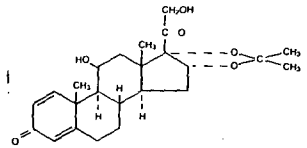
LABELING

DesOwen® (desonide) Cream 0.05% Ointment 0.05% and lotion 0.05%

JAN 24 1992

APPROVED

DESCRIPTION: **DesOwen**® Cream, Ointment and Lotion contain the topical corticosteroid desonide, a nonfluorinated corticosteroid. It has the chemical name: Pregna-1,4-diene-3,20-dione,11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (11β,16α)-; the molecular formula: $C_{24}H_{32}O_6$; molecular weight: 416.51; *CAS-638-94-8*. The structural formula is:



Each gram of **DesOwen** Cream contains 0.5 mg of desonide microdispersed in a compatible vehicle buffered to the pH range of normal skin. It contains propylene glycol, polysorbate 60, emulsifying wax, isopropyl palmitate, stearic acid, synthetic beeswax, citric acid, sodium hydroxide, and purified water. It is preserved with sorbic acid and potassium sorbate.

Each gram of **DesOwen** Ointment contains 0.5 mg of desonide in a base consisting of mineral oil and polyethylene.

Each gram of **DesOwen** Lotion contains 0.5 mg of desonide in a lotion vehicle consisting of sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium, and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.

CLINICAL PHARMACOLOGY: Topical corticosteroids share anti-inflammatory, anti-pruritic, and vasoconstrictive actions.

The mechanism of anti-inflammatory activity of the topical corticosteroids is unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

Pharmacokinetics: The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids. Thus, occlusive dressings may be a valuable therapeutic adjunct for treatment of resistant dermatoses. (See DOSAGE AND ADMINISTRATION).

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

INDICATIONS AND USAGE: **DesOwen** (desonide) Cream 0.05%, Ointment 0.05% and Lotion 0.05% are indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

CONTRAINDICATIONS: Topical corticosteroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparations.

PRECAUTIONS: **General:** Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.

Conditions which augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.

Therefore, patients receiving a large dose of a potent topical steroid applied to a large surface area or under an occlusive dressing should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation 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 steroid.

Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids.

Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity (See PRECAUTIONS – Pediatric Use).

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.

In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

Information for the Patient: 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 use only. Avoid contact with the eyes.
2. Patients should be advised not to use this medication for any disorder other than for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
4. Patients should report any signs of local adverse reactions especially under occlusive dressing.
5. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.

Laboratory Tests: The following tests may be helpful in evaluating the HPA axis suppression:

Urinary free cortisol test
ACTH stimulation 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 topical corticosteroids.

Studies to determine mutagenicity with prednisolone and hydrocortisone have revealed negative results.

Pregnancy Category C: Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. There are no adequate and well controlled studies in pregant women on teratogenic effects from topically applied corticosteroids. Therefore, topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively on pregnant patients, in large amounts or for prolonged periods of time.

Nursing Mothers: It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities *not* likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman.

Pediatric Use: *Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio.*

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestions 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.

Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

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

OVERDOSAGE: Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects (See PRECAUTIONS).

DOSAGE AND ADMINISTRATION: **DesOwen**® (desonide) Cream 0.05%, Ointment 0.05% or Lotion 0.05% should be applied to the affected area as a thin film two or three times daily depending on the severity of the condition. SHAKE LOTION WELL BEFORE USING.

Occlusive dressings may be used for the management of psoriasis or recalcitrant conditions.

If an infection develops, the use of occlusive dressings should be discontinued and appropriate antimicrobial therapy instituted.

HOW SUPPLIED:

DesOwen (desonide) Cream 0.05% is supplied in tubes containing:
15 g **NDC** 0299-5770-15
60 g **NDC** 0299-5770-60

DesOwen (desonide) Ointment 0.05% is supplied in tubes containing:
15 g **NDC** 0299-5775-15
60 g **NDC** 0299-5775-60

DesOwen (desonide) Lotion 0.05% is supplied in bottles containing:
2 fl oz **NDC** 0299-5765-02
4 fl oz **NDC** 0299-5765-04

Storage Conditions: Store below 86°F (30°C). Avoid freezing.

CAUTION: Federal law prohibits dispensing without prescription.

Marketed by:
Owen/GALDERMA
LABORATORIES, INC.
Fort Worth, Texas 76134
Mfd. by: Dermatological
Products of Texas, Inc.
San Antonio, Texas 78296

126500-0390 Revised: March, 1990

ORIG

CAUTION: Federal law prohibits dispensing without prescription.

FOR TOPICAL USE. NOT FOR OPHTHALMIC USE. STORE BELOW 86°F (30°C). AVOID FREEZING. SHAKE WELL BEFORE USING.

Usual dosage: Apply a small amount to affected areas 2 or 3 times daily. See package insert for complete prescribing information.

Lot number and expiration date on bottom of bottle

PROFESSIONAL SAMPLE

NDC 0299-5765-08

DesOwen®
(desonide)
lotion 0.05%

Owen/GALDERMA
8 mL

Contents: Active: desonide 0.05% w/w (0.5 mg g) **Inactive:** sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.

Marketed by
Owen®/GALDERMA®
LABORATORIES INC
Fort Worth, Texas 76134
126495 0390

APPROVED
JAN 24 1992

CAUTION: Federal law prohibits dispensing without prescription.

FOR TOPICAL USE. NOT FOR OPHTHALMIC USE. STORE BELOW 86°F (30°C). AVOID FREEZING. SHAKE WELL BEFORE USING.

Usual dosage: Apply a small amount to affected areas 2 or 3 times daily. See package insert for complete prescribing information.

Lot number and expiration date on bottom of bottle

PROFESSIONAL SAMPLE

NDC 0299-5765-08

DesOwen®
(desonide)
lotion 0.05%

Owen/GALDERMA
8 mL

Contents: Active: desonide 0.05% w/w (0.5 mg g) **Inactive:** sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.

Marketed by
Owen®/GALDERMA®
LABORATORIES INC
Fort Worth, Texas 76134
126495 0390

APPROVED
JAN 24 1992

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Usual dosage: Apply a small amount to affected areas 2 or 3 times daily. See package insert for complete prescribing information.

Lot number and expiration date on bottom of bottle

PROFESSIONAL SAMPLE

NDC 0299-5765-08

DesOwen®
(desonide)
lotion 0.05%

Owen/GALDERMA
8 mL

Contents: Active: desonide 0.05% w/w (0.5 mg g) **Inactive:** sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.

Marketed by
Owen®/GALDERMA®
LABORATORIES INC
Fort Worth, Texas 76134
126495 0390

JAN 24 1992
APPROVED

PROFESSIONAL SAMPLES

8 mL Each

DesOwen®
(desonide)
lotion 0.05%

CAUTION: Federal law prohibits dispensing without prescription.

FOR TOPICAL USE. NOT FOR OPHTHALMIC USE.

Usual Dosage: Apply a small amount to affected areas 2 or 3 times daily. See package insert for complete prescribing information.

Contains: Active: desonide 0.05% w/w (0.5 mg/g). **Inactive:** sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.

Store below 86°F (30°C). Avoid Freezing.
SHAKE WELL BEFORE USING.

Marketed by:
Owen/GALDERMA
LABORATORIES, INC.
Fort Worth, Texas 76134
Mfd. by: Dermatological Products of Texas, Inc. San Antonio, Texas 78296
OWEN and GALDERMA are registered trademarks.

133154-0390

DesOwen®
(desonide)
lotion 0.05%

APPROVED
JAN 24 1992

Owen/GALDERMA

DesOwen®
(desonide)
lotion 0.05%

FOR TOPICAL USE. NOT FOR OPHTHALMIC USE. STORE BELOW 86°F (30°C), AVOID FREEZING. SHAKE WELL BEFORE USING.

Usual dosage: Apply a small amount to affected areas 2 or 3 times daily. See package insert for complete prescribing information.

Contains: Active: desonide 0.05% w/w (0.5 mg/g). **Inactive:** sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.

Lot number and expiration date on bottom of bottle.

Marketed by:

Owen/GALDERMA
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Fort Worth, Texas 76134
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San Antonio, Texas 78296
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126496-0390

NDC 0299-5765-02

DesOwen®
(desonide)
lotion 0.05%

CAUTION: Federal law prohibits dispensing without prescription

JAN 24 [illegible]

APPROVED

Owen/GALDERMA

2 FL. OZ. (59 mL)

FOR TOPICAL USE. NOT FOR OPHTHALMIC USE. STORE BELOW 86°F (30°C), AVOID FREEZING. SHAKE WELL BEFORE USING.

Usual dosage: Apply a small amount to affected areas 2 or 3 times daily. See package insert for complete prescribing information.

Contains: Active: desonide 0.05% w/w (0.5 mg/g). **Inactive:** sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.

Lot number and expiration date on bottom of bottle.

Marketed by:

Owen/GALDERMA
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Fort Worth, Texas 76134
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San Antonio, Texas 78296
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126496-0390

NDC 0299-5765-02

DesOwen®
(desonide)
lotion 0.05%

CAUTION: Federal law prohibits dispensing without prescription

JAN 24 [illegible]

APPROVED

Owen/GALDERMA

2 FL. OZ. (59 mL)

FOR TOPICAL USE. NOT FOR OPHTHALMIC USE. STORE BELOW 86°F (30°C), AVOID FREEZING. SHAKE WELL BEFORE USING.

Usual dosage: Apply a small amount to affected areas 2 or 3 times daily. See package insert for complete prescribing information.

Contains: Active: desonide 0.05% w/w (0.5 mg/g). **Inactive:** sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.

Lot number and expiration date on bottom of bottle.

Marketed by:

Owen/GALDERMA
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San Antonio, Texas 78296
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126496-0390

NDC 0299-5765-02

DesOwen®
(desonide)
lotion 0.05%

CAUTION: Federal law prohibits dispensing without prescription

JAN 24 [illegible]

APPROVED

Owen/GALDERMA

2 FL. OZ. (59 mL)

2 FL. OZ. (59 mL)

DesOwen® (desonide) lotion 0.05%

FOR TOPICAL USE. NOT FOR OPHTHALMIC USE. STORE BELOW 86°F (30°C), AVOID FREEZING. SHAKE WELL BEFORE USING.

Usual dosage: Apply a small amount to affected areas 2 or 3 times daily. See package insert for complete prescribing information.

Contains: Active: desonide 0.05% w/w (0.5 mg/g). **Inactive:** sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.

Marketed by:
Owen/GALDERMA
LABORATORIES, INC.
Fort Worth, Texas 76134
Mfd. by: Dermatological Products of Texas, Inc.
San Antonio, Texas 78296
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110415-0390

NDC 0299-5765-02

DesOwen®
(desonide)
lotion 0.05%

APPROVED
JAN 24 1992

CAUTION: Federal law prohibits dispensing without prescription

Owen/GALDERMA

2 FL. OZ. (59 mL)

LOT:

EXPIRES:

FOR TOPICAL USE. NOT FOR OPHTHALMIC USE. STORE BELOW 86°F (30°C), AVOID FREEZING. SHAKE WELL BEFORE USING.
Usual dosage: Apply a small amount to affected areas 2 or 3 times daily. See package insert for complete prescribing information.
Contains: Active: desonide 0.05% w/w (0.5 mg/g). **Inactive:** sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.
Lot number and expiration date on bottom of bottle.

Marketed by:
Owen/GALDERMA
LABORATORIES, INC.
Fort Worth, Texas 76134
Mfd. by: Dermatological Products of Texas, Inc.
San Antonio, Texas 78296
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126497-0390

NDC 0299-5765-04

DesOwen®
(desonide)
lotion 0.05%

APPROVED
JAN 24 1992

CAUTION: Federal law prohibits dispensing without prescription

Owen/GALDERMA

4 FL. OZ. (118 mL)

SHAKE WELL BEFORE USING.
Usual dosage: Apply a small amount to affected areas 2 or 3 times daily. See package insert for complete prescribing information.
Contains: Active: desonide 0.05% w/w (0.5 mg/g). **Inactive:** sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.
Lot number and expiration date on bottom of bottle.

Marketed by:
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126497-0390

DesOwen®
(desonide)
lotion 0.05%

APPROVED
JAN 24 1992

CAUTION: Federal law prohibits dispensing without prescription

Owen/GALDERMA

4 FL. OZ. (118 mL)

SHAKE WELL BEFORE USING.
Usual dosage: Apply a small amount to affected areas 2 or 3 times daily. See package insert for complete prescribing information.
Contains: Active: desonide 0.05% w/w (0.5 mg/g). **Inactive:** sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.
Lot number and expiration date on bottom of bottle.

Marketed by:
Owen/GALDERMA
LABORATORIES, INC.
Fort Worth, Texas 76134
Mfd. by: Dermatological Products of Texas, Inc.
San Antonio, Texas 78296
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126497-0390

DesOwen®
(desonide)
lotion 0.05%

APPROVED
JAN 24 1992

CAUTION: Federal law prohibits dispensing without prescription

Owen/GALDERMA

4 FL. OZ. (118 mL)

4 FL. OZ. (118 mL)

DesOwen® (desonide) lotion 0.05%

FOR TOPICAL USE. NOT FOR OPHTHALMIC USE. STORE BELOW 86°F (30°C), AVOID FREEZING. SHAKE WELL BEFORE USING.

Usual dosage: Apply a small amount to affected areas 2 or 3 times daily. See package insert for complete prescribing information.

Contains: Active: desonide 0.05% w/w (0.5 mg/g). **Inactive:** sodium lauryl sulfate, light mineral oil, cetyl alcohol, stearyl alcohol, propylene glycol, methylparaben, propylparaben, sorbitan monostearate, glyceryl stearate SE, edetate sodium and purified water. May contain citric acid and/or sodium hydroxide for pH adjustment.

Marketed by:
Owen/GALDERMA
LABORATORIES, INC.
Fort Worth, Texas 76134
Mfd. by: Dermatological Products of Texas, Inc.
San Antonio, Texas 78296

110416-0390

NDC 0299-5765-04

DesOwen® (desonide) lotion 0.05%

APPROVED
JAN 28 1992

CAUTION: Federal law prohibits dispensing without prescription

Owen/GALDERMA

4 FL. OZ. (118 mL)

LOT:

EXPIRES:

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 72-354

LABELING REVIEWS

REVIEW OF PROFESSIONAL LABELING

ANDA

DRAFT

DATE OF REVIEW: December 24, 1987

ANDA #: 72-354 NAME OF FIRM: Owen Labs

NAME OF DRUG: Trade: DesOwen Lotion, 0.05%
Generic: Desonide Lotion, 0.05%

DATE OF SUBMISSION: November 27, 1987

COMMENTS:

General Comment: Potency Statement: To Chemist

We question the expression of potency as a percent weight/weight. USP monographs for lotions of similar products express potency as a percent weight/volume. We feel that the formulation should also be expressed as a percent weight/volume. Please review and discuss with me.

Carton: Not Satisfactory

1. fl oz (rather than "Fl. Oz.")

2. Usual dosage - 2 or 3 times (rather than "2 to 3 times")

3. Professional Samples Carton

"...86°F (30°C). Avoid Freezing."
(not (b)(4)°F")

Container: Not Satisfactory
(2 fl oz, 4 fl oz, 8 mL Sample)

1. See A. 1. (2 fl oz, 4 fl oz)

2. See A. 2.

Insert: Not Satisfactory

1. CLINICAL PHARMACOLOGY (Pharmacokinetics)
Paragraph 3, line 4 - Corticosteroids...

2. HOW SUPPLIED

Revise "Storage" statement to read, "Store below 86°F (30°C). Avoid Freezing."

RECOMMENDATIONS:

1. Inform the firm of the above comments.

2. Request the firm revise their labels and labeling. We cannot request final printed copy until the question regarding expression of potency has been resolved.

3. For The Record:

   The "For topical use" phrase is used on labels of firm's other products. This statement is acceptable per discussion by G. Johnston and K. Johnson.

Gordon Johnston

cc:
HFN-238
GJohnston/KJohnson/je/12-28-87
rpl
7699A/ pg 1-2

1/4/88

REVIEW OF PROFESSIONAL LABELING

Orig. Amendment

DRAFT

DATE OF REVIEW: June 28, 1988

ANDA #: 72-354 NAME OF FIRM: Owen Labs

NAME OF DRUG: Trade: Desowen Lotion 0.05%
Generic: Desonide Lotion 0.5%

DATE OF SUBMISSION: June 6, 1988

COMMENTS:

Carton: We question your content statement. Your composition statement lists citric acid and/or sodium hydroxide as present in the formulation. However, the carton labeling indicates that these components may be present. Please comment.

Container: See comment under carton labeling.

Insert: See comment under carton labeling.

RECOMMENDATIONS:

1. Inform the firm of the above comments.

2. We cannot request final printed copy until the issue regarding the composition has been resolved.

3. NOTE TO CHEMIST: Please review my comment to the firm and inform me if any change is required.

G Johnston 6/30/88

Gordon Johnston

cc:
HFD-238
GJohnston/KJohnson/je/6-29-88
rpl
7887A/ pg 8

REVIEW OF PROFESSIONAL LABELING

Orig. Amendment; DRAFT

DATE OF REVIEW: January 10, 1989

ANDA #: 72-354 NAME OF FIRM: Owen Labs

NAME OF DRUG: Trade: Des Owen Lotion
Generic: Desonide Lotion 0.05%

DATE OF SUBMISSION: November 28, 1988

COMMENTS:

Insert: Satisfactory

RECOMMENDATIONS:

1. Inform the firm of the above comments.

2. Request the firm prepare and submit final printed container labels and carton labeling. We cannot request final printed insert labeling until your Bio data has been found satisfactory and we have had a chance for review and comment.

3. NOTE TO CHEMIST: If the Bio data has been found satisfactory prior to issuing an action letter, I will revise our request for FPL insert labeling.

G Johnston 1/13/89
Gordon Johnston

cc:
HFD-238 1/13/89
GJohnston/KJohnson/je/1-12-89
rpl
8167A/pg 8

OWEN/GALDERMA LABELING WORKSHEET

ANDA #: 72354 ANDA#: _____ ANDA#: _____

PRODUCT NAME: DES OWEN LOTION (DESONIDE LOTION 0.05%)

NDA HOLDER(S): MILES PHARMACEUTICALS (FOR CREAM & OINTMENT OWEN LABORATORIES. 0.05%);

NDA NUMBER(S): 17-010 (MILES) 19-048 (OWEN)

LABELING OF THE LISTED DRUG

DATE NOTED:	FIRM:	NDA#:	APPROVAL DATE:	REV. DATE:
	MILES	17010	2-12-76	1-84
	OWEN	19-048	11-23-88	1-87

CONTAINER LABELS:

APPROVED COPY ON FILE? ✓ Y ___ N _____ COMMENT

USP CONTAINER/CLOSURE REQUIREMENTS: N/A

OTHER KEY ISSUES: DESONIDE CREAM OR OINTMENT IS NOT A USP PRODUCT

INSERT LABELING:

PATENT ISSUES: NONE

EXCLUSIVITY ISSUES: NONE

IO ISSUES: NONE

OTHER KEY ISSUES: THE FIRM HAS USED DES OWEN CREAM AS THE REFERENCE DRUG FOR LOTION. GRANTED BY PETITION ON Sept 10, 1987. Firm already has approval Cream and Ointment This is first lotion for this product.

SUMMARY FOR APPLICATION APPROVAL:

CONTAINER LABELS: SATISFACTORY PER SUBMISSION OF ~~4-10-89~~ (2 ltrs, 4 ltrs) ~~UPDATED PER AMENDED SUBMISSION OF~~ 5-30-91.

CARTONING: SAME AS FOR CONTAINER LABELS ABOVE.

LABELING COMMENT/FURTHER REVISION: SAME AS FOR CONTAINER LABELS ABOVE. THE FIRM HAS SUBMITTED COMMITMENT TO REFLECT MANUFACTURER/DISTRIBUTOR RELATIONSHIP (5-30-91)

DATE: 7-24-91 REVIEWER: Vaijayanti Lakshmanan

SUPERVISOR: Sandy Rhodes 7/26/91

8/28/91

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 72-354

CHEMISTRY REVIEWS

CHEMIST'S REVIEW ANDA 72-354

3. NAME AND ADDRESS OF APPLICANT
Owen Laboratories
Divisions of Dermatological Products of Texas, Inc.
6201 South Freeway
Fort Worth, Texas 76134

4. AF NUMBER
Waxman/Hatch

5. SUPPLEMENT(s)
Original 11/25/87

6. NAME OF DRUG
Desowen

7. NONPROPRIETARY NAME
Desonide

8. SUPPLEMENT(s) PROVIDE(s) FOR:
Original submission of a new application

9. AMENDMENTS AND OTHER DATES:
12/11/87 New Correspondence (Type I DMF 1229 material not previously submitted.

10. PHARMACOLOGICAL CATEGORY
Anti-inflammatory

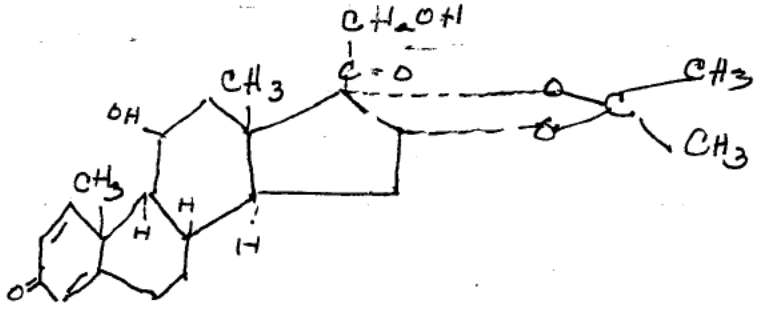
11. HOW DISPENSED
RX

13. DOSAGE FORM(s)
Lotion

14. POTENCY
0.05%

15. CHEMICAL NAME AND STRUCTURE
Pregna-1,4-diene-3,20-dione,11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(11β,16)

Formula: $C_{24}H_{32}O_6$; molecular weight: 416.5



17. COMMENTS
505(J)(2)(A) information is satisfactory as per D. Rosen. Application found acceptable as per the petition process. See letter dated 9/10/87 (Dr. Reinstein). We await evaluation by Div. of Anti-Infectives of the vasoconstrictor study.

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable with deficiencies identified.

19. REVIEWER:
Brenda T. Arnwine

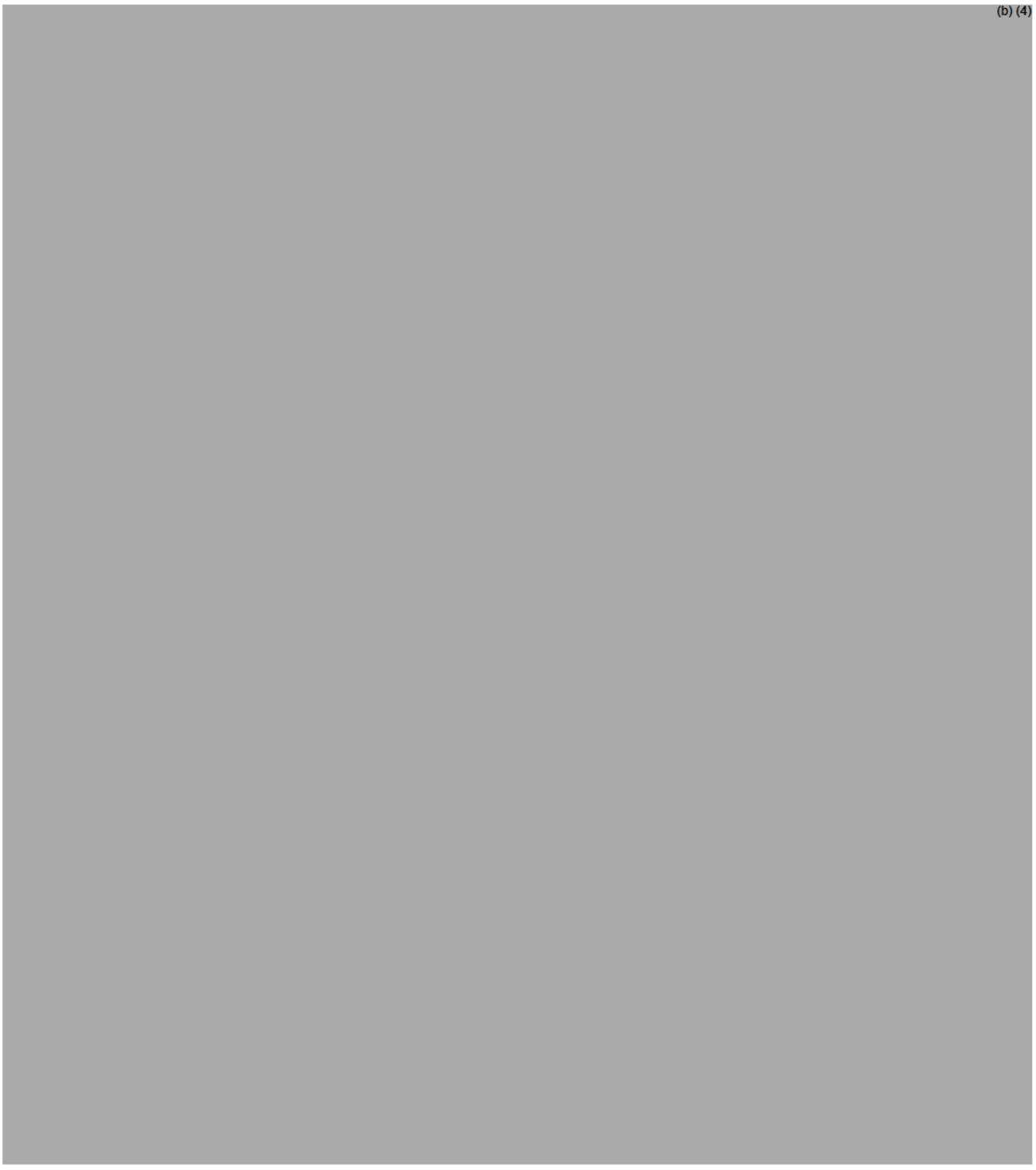
DATE COMPLETED:
5/1/88

5/17/88

R/D INITIALED BY R.M. Patel 5/11/88

(b) (4)

[redacted]


(b) (4)

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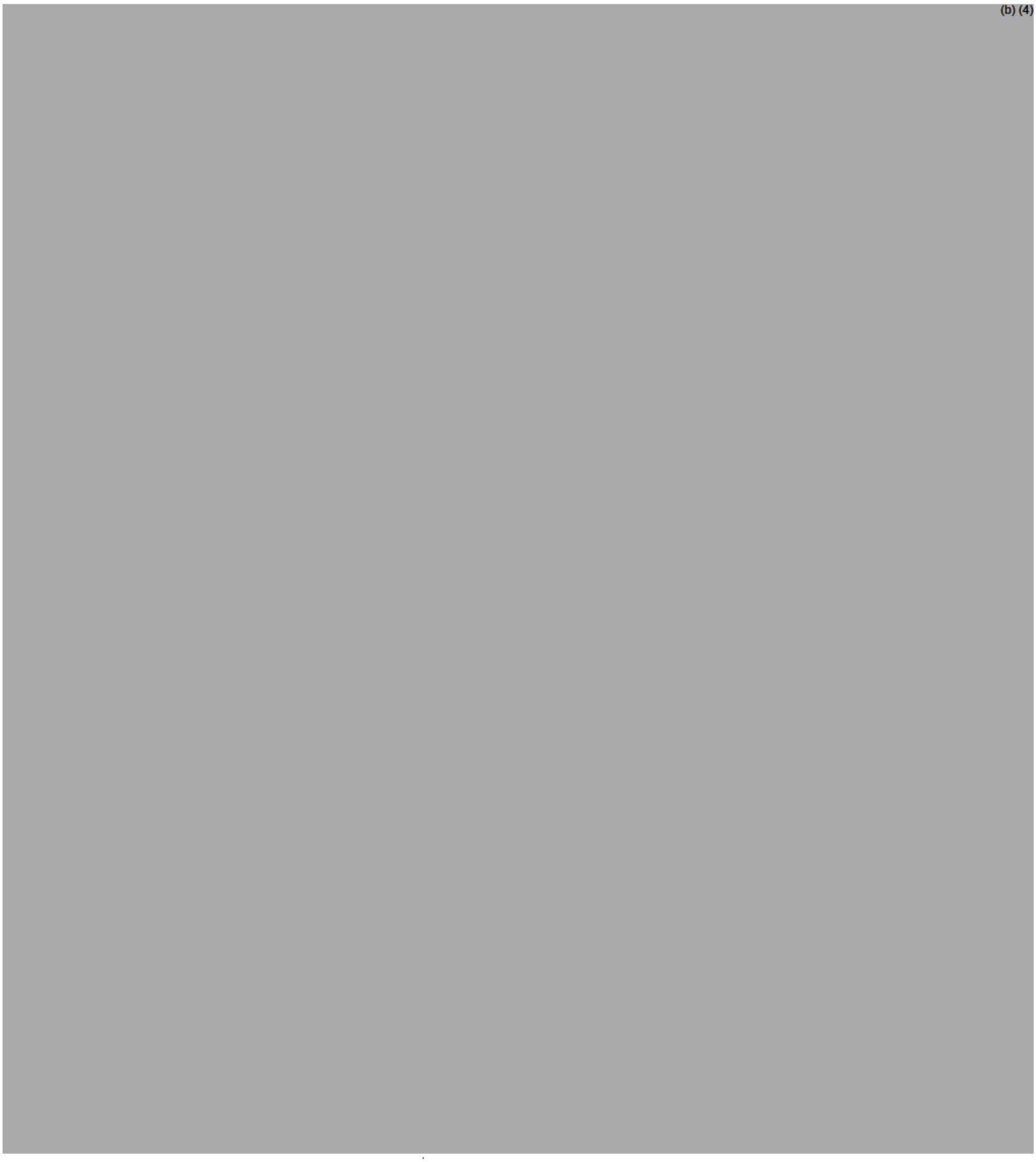


ANDA 72-354 CHEMIST'S REVIEW FOR ANDA OR SUPPLEMENT

NAME AND ADDRESS OF APPLICANT:
Owens Laboratories
Div. of Dermatological Products of Texas, Inc.
Fort Worth, TX 76115

PURPOSE OF AMENDMENT/SUPPLEMENT
6-6-88 Draft labeling and manufacturing and control information
6-24-88 Samples sent to Dallas for methods validation

PHARMACOLOGICAL CATEGORY	NAME OF DRUG	HOW DISPENSED
Anti-inflammatory	DesOwen (desonide)	Rx

DOSAGE FORM	POTENCY
Lotion	0.05%

SAMPLES
We await methods validation as per Dallas District. Quality assurance testing of nds is ok as per companion application 71-425.

RELATED IND/NDA/DMF
71-425

LABELING
Not satisfactory - See labeling review as per G.Johnston 6-28-88.

BIOLOGIC AVAILABILITY
Not satisfactory - Firm is to provide more information. See letter dated July 1, 1988.

ESTABLISHMENT INSPECTION
Satisfactory as per D.Sylvia 1-6-88

COMPONENTS, COMPOSITION, MANUFACTURING, CONTROLS
Not satisfactory
Firm has submitted Certificates of Analysis for the raw materials used in the drug product. Firm was requested to define the term "suitable" in the manufacturing instructions. The revision submitted contains more specific times and temperatures; the equipment is specified only by terms like round bottom as more specific identification. Firm should name specific equipment used.

PACKAGING
Satisfactory - See Chemist Review dated 5-17-88

STABILITY
Not satisfactory
Firm has submitted challenge condition stability data and cycling studies with a request for 18 months. Data are satisfactory. However, protocol should be revised to express test stations in months rather then weeks.

REMARKS AND CONCLUSION
Not approvable

BTArnwine
r/d RPatel - 11-8-88

11/10/88

3

ANDA 72-354 CHEMIST'S REVIEW FOR ANDA OR SUPPLEMENT

NAME AND ADDRESS OF APPLICANT:
Owen Laboratories
Div. of Dermatological Products of Texas, Inc.
Fort Worth, TX 76115

PURPOSE OF AMENDMENT/SUPPLEMENT
11/28/88 Draft labeling and manufacturing and control information
11/16/88 Bio Material
4/18/89 Bio material and FPL

PHARMACOLOGICAL CATEGORY	NAME OF DRUG	HOW DISPENSED
Anti-inflammatory	DesOwen (desonide)	Rx

DOSAGE FORM	POTENCY
Lotion	0.05%

SAMPLES
Methods validation is satisfactory as per Dallas District. Quality assurance testing of nds is ok as per companion application 71-425.

RELATED IND/NDA/DMF
71-425

LABELING
Not satisfactory - Request for FPL cannot be made until bio data have been found satisfactory as per G Johnston. see labeling review 1/10/89.

BIOLOGIC AVAILABILITY
Not satisfactory - Firm has provided more information. We await evaluation by Division of Anti-Infectives.

ESTABLISHMENT INSPECTION
Satisfactory as per D.Sylvia 1-6-88

(2) COMPONENTS, COMPOSITION, MANUFACTURING, CONTROLS
~~Not S~~atisfactory
Firm has submitted Certificates of Analysis for the raw materials used in the drug product. Firm was requested to define the term "suitable" in the manufacturing instructions. The revision submitted contains more specific times and temperatures; the equipment is specified only by terms like round bottom as more specific identification. Firm should name specific equipment used. By amendment firm has identified equipment.

PACKAGING
Satisfactory - See Chemist Review dated 5-17-88

STABILITY
~~Not~~ Satisfactory
Firm has submitted challenge condition stability data and cycling studies with a request for 18 months. Data are satisfactory. Protocol has been revised to express test stations in months rather then weeks.

REMARKS AND CONCLUSION
Not approvable

Brenda T. Arnwine
jth: 0009j 5/12/89

5/12/89

File in ANDA

1. *CHEMIST's REVIEW #4*

2. **ANDA 72-354**

3. APPLICANT, Name/Address/Telephone:
Owen/Galderma Laboratories, Inc.
Attention: Christine E. Shank
Manager, Regulatory Affairs
6201 South Freeway
PO Box 6600
Fort Worth, TX 76115
Tel. 617-293-0450; Fax 817-551-8079.

6. PROPRIETARY NAME: DesOwen[R] Lotion, 0.05%
7. NON-PROPRIETARY NAME: Desonide Lotion, 0.05%

9. AMENDMENTS and Other DATES:
A. **FIRM:**
11-25-87 O Application.
05-19-89 NC re NA letter of 5-15-89.
01-12-90 NC
03-26-90 Amendment re telecon of 3-12-90
05-30-90 Amendment ("NC") re telecon with Dr.S.Dugar.
08-17-90 Amendment
05-30-91 Amendment re FPL
08-09-91 Amendment re telecons of 8-7 & 8th-1991.
08-14-91 Amendment re our conversation of 12, 13 & 14 August.

B. **FDA:**
05-12-89 3rd (last) CR.
05-15-89 NA re Bioeq. & labeling
07-26-89 Clinical Review by Div. of Anti-infective D.P.
03-12-90 Telecon by S.D. to Ms.C.Shank at Owen.
04-06-90 Telecon by S.D. to Ms.C.Shank
05-11-90 Telecon by S.D. to Ms.C.Shank
06-28-90 Telecon by R.T. to Ms.C.Shank
03-07-91 Info. letter re contract manufacturer
07-23-91 Satisfactory labeling.
08-07-91 Telecon re batch records & stability data.
08-08-91 Telecon re low temp.(35°) accelerated studies.
08-12-91 Telecon re manuf. of containers.
08-13-91 Telecon re subject of degradation products (DP).
08-14-91 Telecon re change of limits of DP from (b)(4) %.

10. PHARMACOLOGICAL CATEGORY: Corticosteroid: anti-inflammatory

11. Rx or OTC: R_x

12. RELATED ANDA/DMF's:
Desonide Cream (#19-048) & Desowen Ointment (#71-425)
Tridesilon[R] (innovator product)

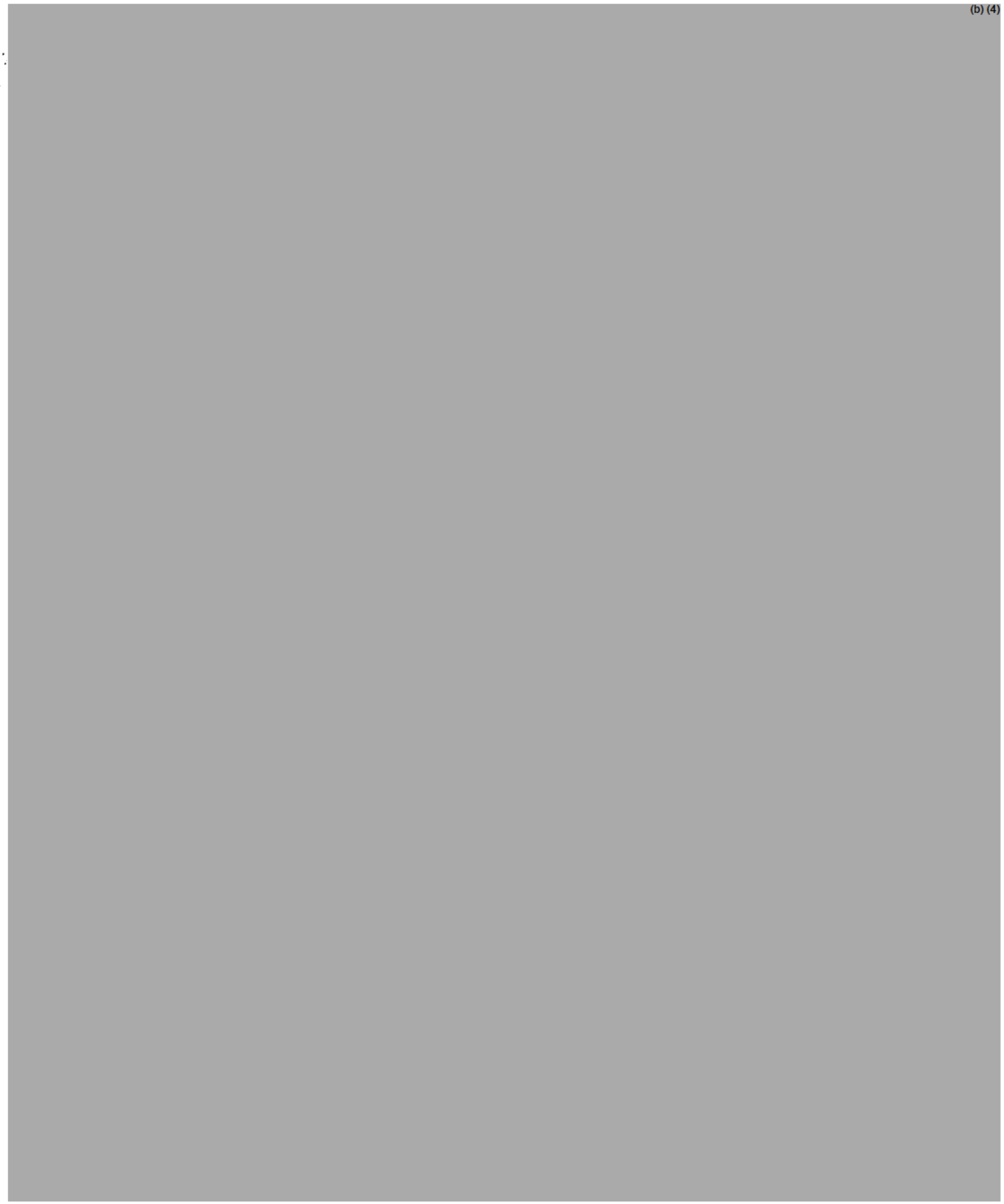
13. DOSAGE FORM: lotion
14. POTENCY: 0.05%

15. Chemical Name. 11,21-Dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-(11ß,16α)-pregna-1,4-diene-3,20-dione. Also: Desfluorotriamcinolone Acetonide. $C_{24}H_{32}O_6$

17. COMMENTS.

(b) (4)

[redacted]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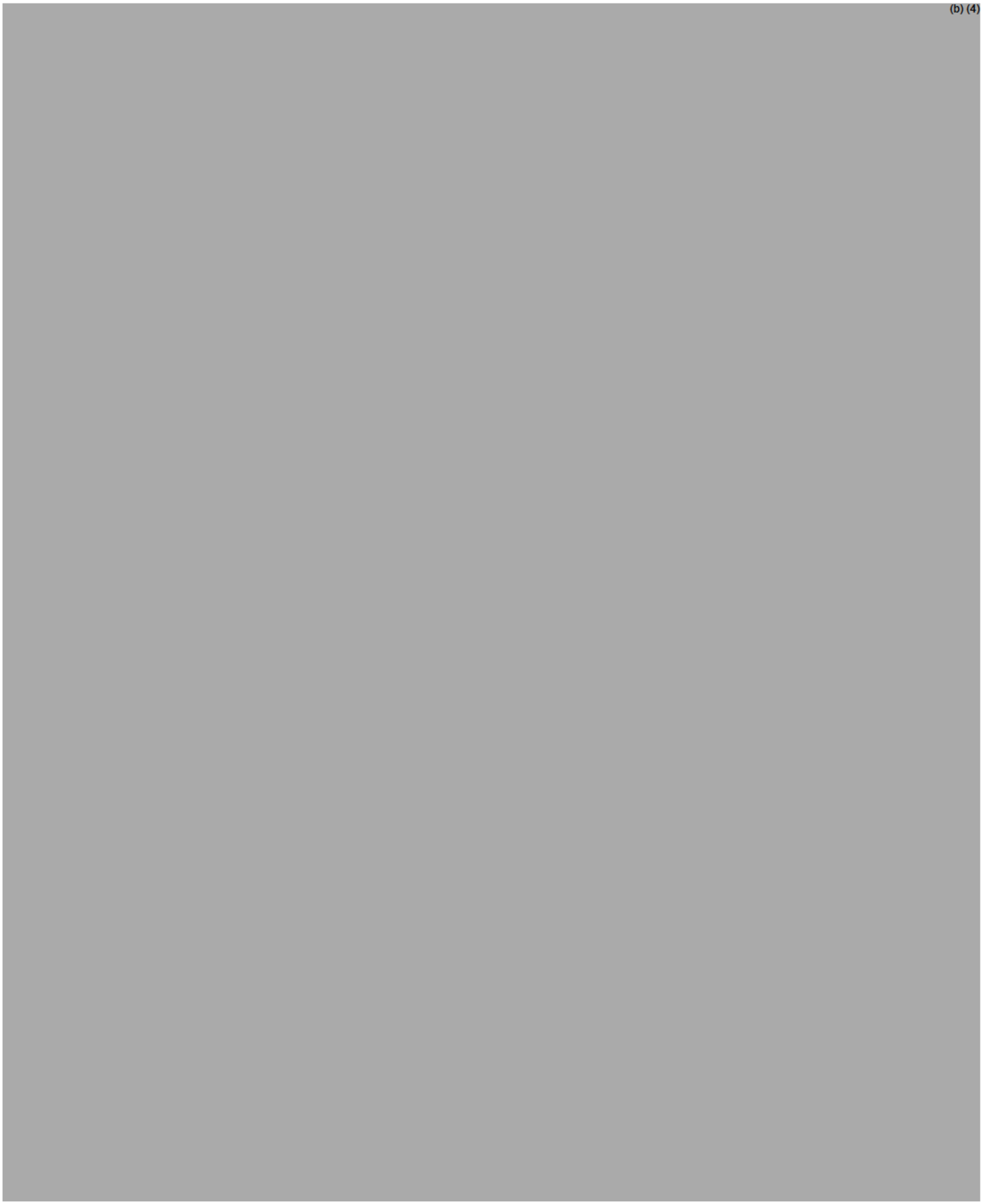
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(b) (4)

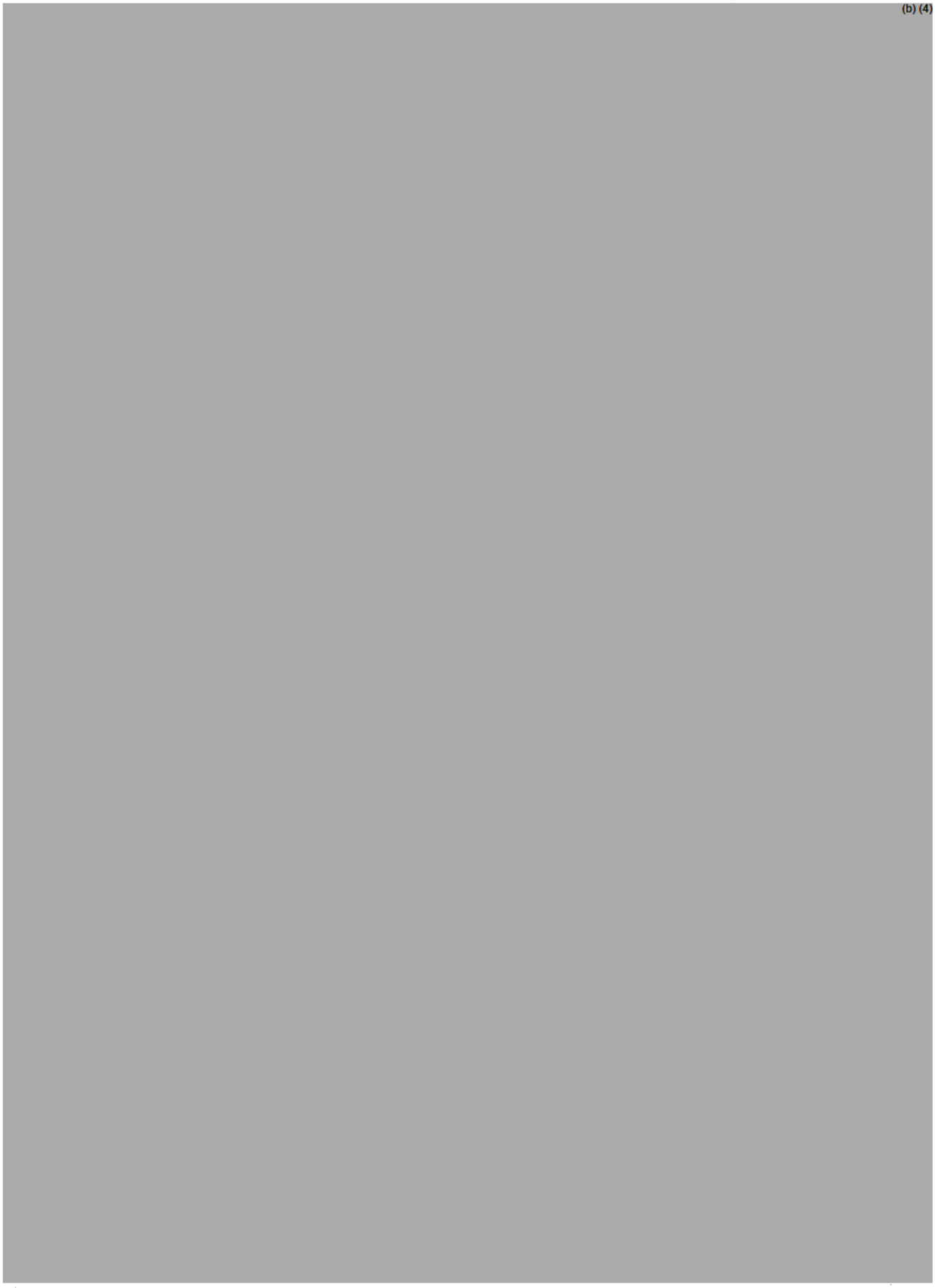
[redacted]

18. CONCLUSIONS and RECOMMENDATIONS:
Approval

19. REVIEWER:
Robert W. Trimmer, Ph.D.
Branch II, Div. of Chemistry II, OGD

Date Started: 8-02-91
Completed: 8-15-91

8-26-91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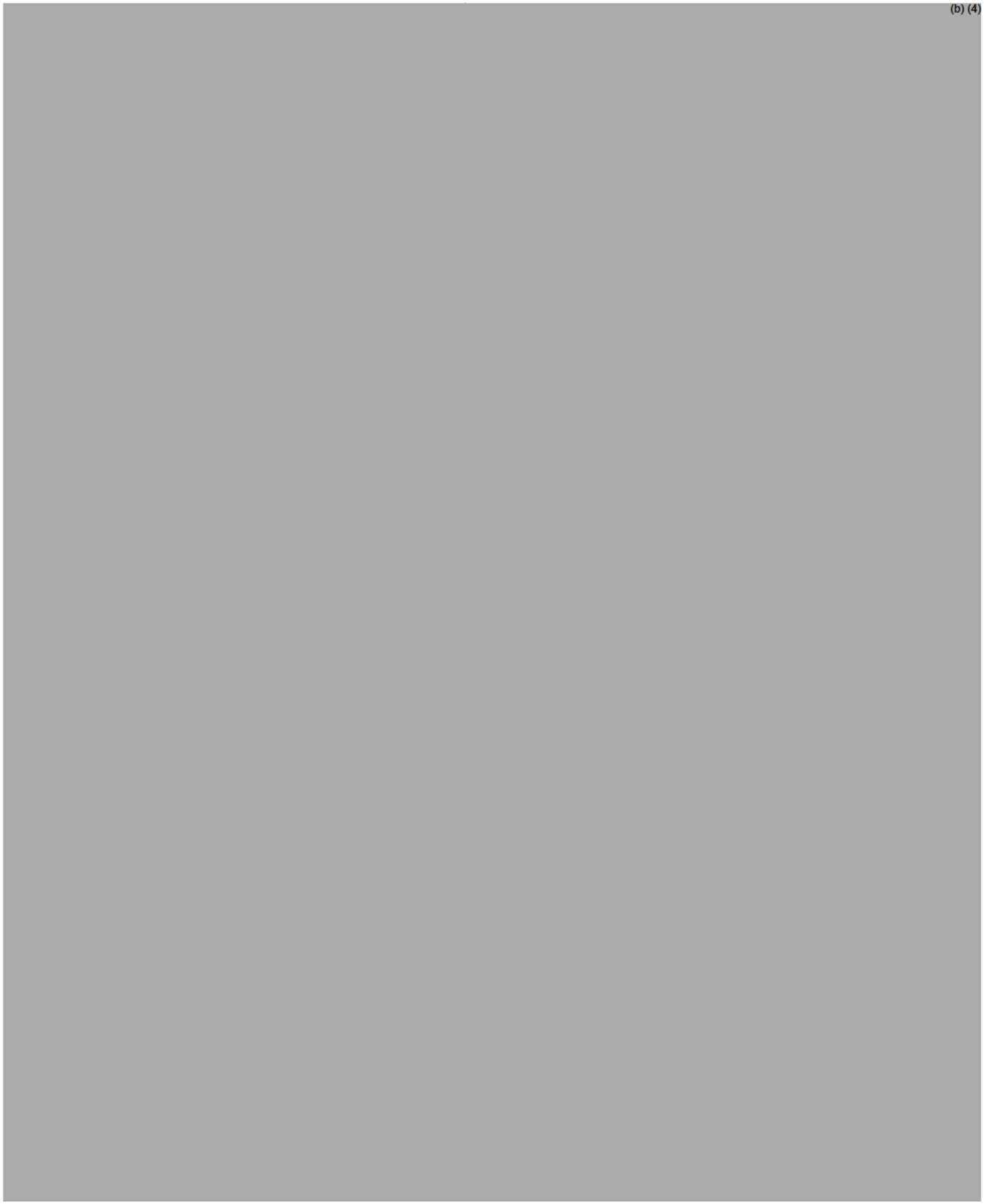
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RWT File #72354R-4.RRT
72354A04.RRT

cls/08/22/91/d:72-354.REV

File in ANDA

1. ***CHEMIST's REVIEW #5***

2. **ANDA 72-354**

3. APPLICANT, Name/Address:
Owen/Galderma Laboratories, Inc.
Attention: Ms. Christine E. Shank
6201 South Freeway
Fort Worth, TX 76115

6. PROPRIETARY NAME: DesOwen^{R} Lotion, 0.05%
7. NON-PROPRIETARY NAME: Desonide Lotion, 0.05%

9. AMENDMENTS and Other DATES:
A. **FIRM:**
11-25-87 O Application.
B. **FDA:**
6/17-21/91 EI of Derm. Products of Texas facility.

10. PHARMACOLOGICAL CATEGORY: Corticosteroid: anti-inflammatory
11. Rx or OTC: R_x

12. RELATED ANDA/DMF's:
Desonide Cream (#19-048) & Desowen Ointment (#71-425)
Tridesilon^{R} (innovator product)

13. DOSAGE FORM: lotion
14. POTENCY: 0.05%

17. COMMENTS.
A. Comments to be Included in the Action Letter:

During the FDA inspection of your production facilities, Dermatological Products of Texas, it was learned, among other things, that at least two of your test batches were filled and QC tested at an unreported plant in Fort Worth, Texas.

1. Please amend your application to includes all details of this previously unreported filling operation at the ALCON facilities including all equipment, container/closure systems utilized, complete test batch records which includes the filling process, etc.

Please be advised we await CGMP compliance status of the ALCON facilities.

2. Please submit the time limits for the various phases of production. This may be done on the master batch record.

3. Please note that your SOP #108.1010 is considered too general. Please amend your application to include specific case procedures or withdraw said SOP and after approval of this ANDA you may supplement the application as per 21 *CFR* 314.70 (b)(2)(x).

B. General Comments:

A Clinical-Consult to David Bostwick regarding this new pH range was found acceptable 2-8-1991.

A (b)(4) kg representative batch production record was submitted (max. future production size).

The reason for the use of 35° rather than 40° for accelerated studies was stated, namely, that at 40° the emulsion breaks down.

<u>The following are our comments regarding the 483 items listed in the August 27th Memo to the Office of Generic Drugs</u>.

<u>FDA 483 Items.</u>

#1 & 2: The EI uncovered information showing that the bio batches AHE-1911 & AIE-2059 were transferred to another plant (ALCON) for filling; this facility is not a part of the contract manufacturer of Dermatological Products of Texas (DPT) nor Owen/Galderma the applicant.

We agree this is a violation and will issue the applicant a NA letter requesting specific amendments to the filling issue and will issue an EER for the ALCON facility. See above #17.A.

#3: The EI questioned the use of 15-30°C (59-86°F) as controlled room temperature conditions and thinks the firm should do room temp. stability studies at the higher point, namely, 30°C. They also question the accelerated conditions of 35°.

a. Since last spring we have been recommending 25-30° (USP 15-30°) for room temperature studies but do not reject studies that commenced before that time using 15-30°.

b. The accelerated studies were carried out at 35° instead of the recommended 40° as the applicant stated that at above 37° the lotion breaks up. In lieu of the 40° accelerated conditions we accepted two years data at room temperature.

c. The need to change recorder charts to the proper frequency and sign & initial charts is a CGMP matter.

#4: The EI report criticizes the firm for doing validation only on (b)(4) kg batches and questioning the validity of these results for scaling up to a (b)(4) kg batch. Time limits are also discussed.

a. The area of batch sizes falls within the OGD *Guide #22-90* allowing a ten fold scale-up from test batch. The applicant has agreed in writing to limit production scale-up to (b)(4) kg.

b. We agreed to tell the applicant to set time limits for the various phases of production. See section #17.A. above.

#5: This involves rework procedures and we generally agree that specific rework procedures need to be in the application or supplemented after approval of said application. See #17.A. above.

#6: Compliance wants the firm to establish a correct sanitation procedure with validation data for equipment which is consistent with the firm's SOP - CGMP issue.

<u>Other points:</u>

#1.

The EI criticized the firm for the lowered pH formulation. In the application we received a satisfactory Medical Consult for the change which change affords increased stability of the drug product and have satisfactory stability data. We ourselves requested this change.

#2.

Compliance criticized the (b) (4) kg batch ticket but we have a commitment from the firm that (b) (4) kg will be their largest production batch size under the present approval package.

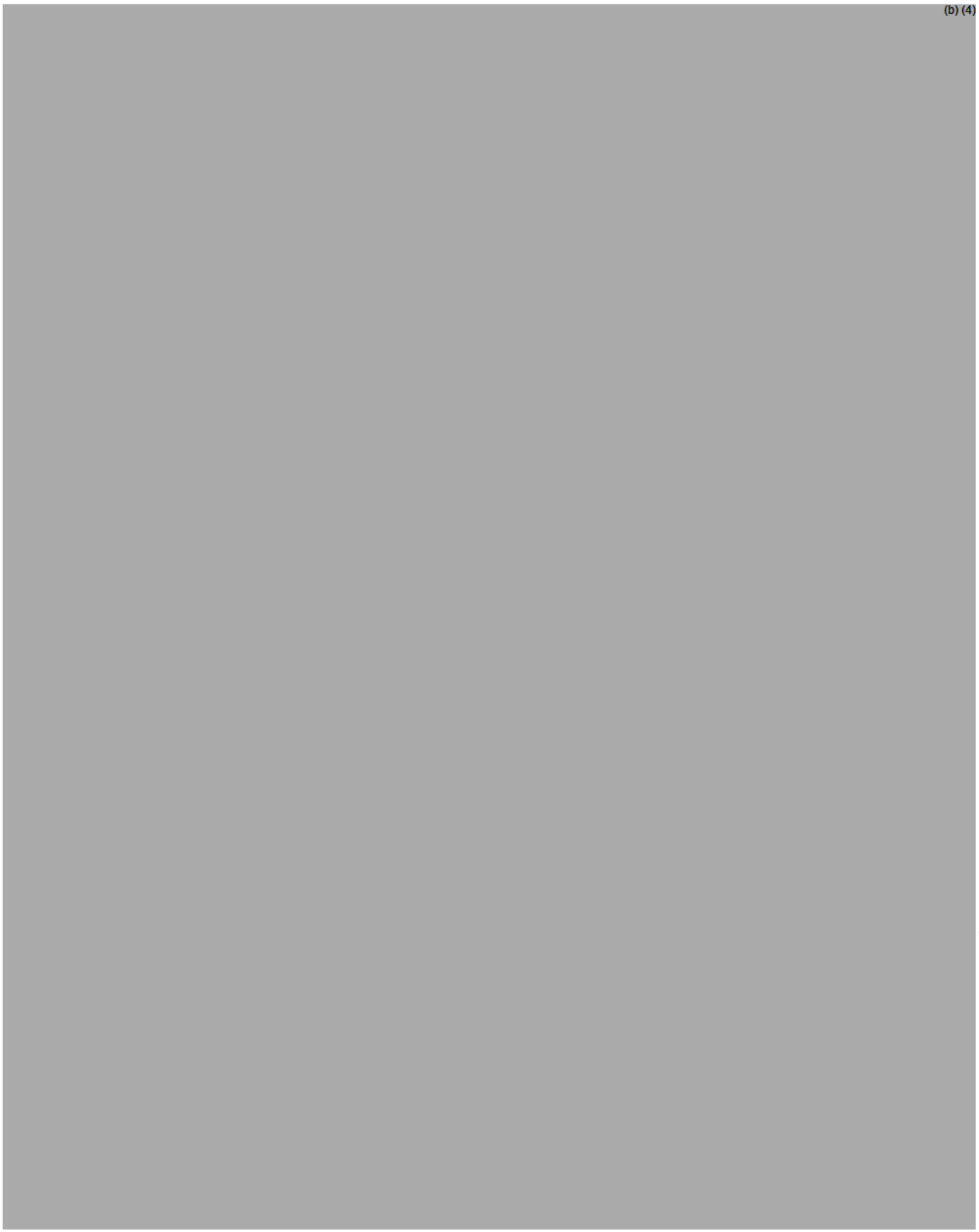
18. CONCLUSIONS and RECOMMENDATIONS:
Not Approvable. MINOR Amendment.

19. REVIEWER:
Robert W. Trimmer, Ph.D. Date Started: 10-15-91
Branch II, Div. of Chemistry I, OGD Completed: 10-16-91

10-18-1991

cc: ANDA 72-354
72-354/Division File
72-354/Dup
HFD-634/RTrimmer

Endorsed Michael Smela Jr.
10/18/91


(b) (4)

MEMORANDUM

Department of Health & Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

Date: October 16, 1991

Subject: Comments for EIR of 6/17-21/91 (ANDA 72-354):
Dermatological Products of Texas
San Antonio, TX

Applicant:
Owen/Galderma Laboratories, Inc.
6201 South Freeway
Fort Worth, TX 76115

Drug Product:
DesOwen^{R} Lotion, 0.05%

See FDA 483 Items in the Report of August 27, 1991

To: HFD-320
Through David Doleski
Attention: Ann L. deMarco

The following are our comments regarding the 483 items listed in the August 27th Memo to the Office of Generic Drugs.

FDA 483 Items.

#1 & 2:

The EI uncovered information showing that the test batches AHE-1911 & AIE-2059 were transferred to another plant (ALCON) for filling; this facility is not a part of the contract manufacturer of Dermatological Products of Texas (DPT) nor Owen/Galderma the applicant.

We agree this is a deficiency in the ANDA and will issue the applicant a NA letter requesting specific amendments to the filling issue and will issue an EER for the ALCON facility.

#3:

The EI questioned the use of 15-30°C (59-86°F) as controlled room temperature conditions and thinks the firm should do room temp. stability studies at the higher point, namely, 30°C. They also question the accelerated conditions of 35°.

a. Since last spring we have been recommending 25-30° (USP 15-30°) for room temperature studies but do not reject studies that commenced before that time using 15-30°.

b. The accelerated studies were carried out at 35° instead of the recommended 40° as the applicant stated that at above 37° the lotion breaks up. In lieu of the 40° accelerated conditions, we accepted two years data at room temperature.

c. The need to change recorder charts to the proper frequency and sign & initial charts is a CGMP matter.

#4:

The EI report criticizes the firm for doing validation only on (b)(4) kg batches and questioning the validity of these results for scaling up to a (b)(4) kg batch. Time limits are also discussed.

a. The area of batch sizes falls within the OGD *Guide #22-90* allowing a ten fold scale-up from test batch. The applicant has agreed in writing to limit production scale-up to (b)(4) kg.

b. We agree to tell the applicant to set time limits for the various phases of production in our NA letter.

#5:

This involves rework procedures and we generally agree that specific rework procedures need to be in the application or supplemented after approval of said application and shall so indicate in our NA letter.

#6:

The investigators want the firm to establish a correct sanitation procedure with validation data for equipment which is consistent with the firm's SOP. This is a CGMP issue.

Other points:

#1.

The investigators criticized the firm for the lowered pH formulation.

We received a satisfactory Medical Consult for the change which change affords increased stability of the drug product and have received satisfactory stability data on the drug product with the lower pH. We ourselves requested this change.

#2.

The investigators criticized the (b)(4) kg batch ticket but we have a written commitment from the firm that (b)(4) kg will be their largest production batch size under the present approval package.

Robert Trimmer
Review Chemist
Branch II, OGD

Michael Smela
Branch Chief
Branch II, OGD

1. ***CHEMIST's REVIEW #6***

2. **ANDA 72-354**

3. APPLICANT, Name/Address/Telephone/Fax:
Owen/Galderma Laboratories, Inc.
Attention: Ms. Christine E. Shank
6201 South Freeway
Fort Worth, TX 76115
Tel. 817 293-0450 or 551-8516; Fax 817 551-8079

6. PROPRIETARY NAME: DesOwen^{R} Lotion, 0.05%
7. NON-PROPRIETARY NAME: Desonide Lotion, 0.05%

9. AMENDMENTS and Other DATES:
A. **FIRM:**
11-25-87 O Application.
*11-01-91 Amendment
*11-15-91 Amendment
*12-05-91 Amendment from **Owen** w 15th mo. stability.
12-06-91 Telecon of clarification: Owen will make clear container/closure descriptions ([redacted] (b) (4) correspond with description in Package Specs, Ms. Shank will consolidate stab. data, & will contact supplier for data for USP tests.
*12-13-91 Amendment with USP data.
*12-18-91 Fax Amendment with time limits.
*12-19-91 Amendment with [redacted] (b) (4) information.
B. **FDA:**
06-17-91 EI of Derm. Products of Texas facility.
11-08-91 Telecon to our San Antonio, TX office: J.Davis.
11-14-91 Telecon to Owen re ALCON facilities.
11-15-91 Telecon from Owen re ALCON facilities.
11-26-91 Telecon requesting stability data for new test batches.
12-05-91 NC Telecon stating 15th mo stab. data sent via Fax; I told of need yet for time limits info & need for COA's for c/c from DPT & USP tests - Biol. Reactivity Test as per *21 CFR* 211.84.
12-05-91 EI found acceptable.

10. PHARMACOLOGICAL CATEGORY: Corticosteroid: anti-inflammatory
11. Rx or OTC: R_x

12. RELATED ANDA/DMF's:
Desonide Cream (#19-048) & Desowen Ointment (#71-425)
Tridesilon^{R} (innovator product)
DMF #1229 Type I for DPT, Inc. of San Antonio, TX.
[redacted] (b) (4)

[redacted] (b) (4)

13. DOSAGE FORM: lotion
14. POTENCY: 0.05%

17. COMMENTS.
A. Comments to be Included in the Action Letter:
For Approval

B. General Comments:
1. A Clinical-Consult to David Bostwick regarding this new pH range was found acceptable 2-8-1991 for the revision in pH specification from [redacted] (b) (4)

2. A [redacted] (b) (4) kg representative batch production record was submitted (max. future production size).

3. The reason for the use of 35° rather than 40° for accelerated studies was stated, namely, that at 40° the emulsion breaks down. I would recommend granting an 18 month expiration dating based on this data alone; a 15th month station was submitted to this point on the new bio batch and 24 months on the old bio batches (old = batches were the drug product was filled by an unauthorized facility, namely Alcon).

4. Satisfactory USP testing of the [redacted] (b) (4) containers which testing included section <87> submitted 12-13-91.

5. This application was previously AP pending EI then consequently found deficient in the 483. Since the 483 the issues have been resolved.

C. Comments concerning the Last NA Letter (483 related):
1. "During the FDA inspection of your production facilities, Dermatological Products of Texas, it was learned, among other things, that at least two of your test batches were filled and QC tested at an unreported plant in Fort Worth, Texas. Please amend your application to includes all details of this previously unreported filling operation at the ALCON facilities including all equipment, container/closure systems utilized, complete test batch records which includes the filling process, etc.

Please be advised we await CGMP compliance status of the ALCON facilities.
Response to #1: Satisfactory.
Two of the batches identified in the ANDA (#AIE-2059 and AHE-1911) were filled and tested at Alcon Labs and were done basically to see if Alcon could handle such a operation.

Since the applicant has stated there will no involvement at all with the Alcon facilities we are to look now at just Derm. Products of Texas, Inc. (DPT) manufactured test batches:

Three new test batches were produced of (b) (4) kg each, using the in-process pH adjustment outlined August 17, 1990, using (DPT) production scale equipment which included (b) (4) & filling equipment and DPT quality control testing. These three batches are considered representative standards for the commercial production of the drug product. See section #25.

(b) (4)

[redacted]

The applicant certified that there will be no utilization of the ALCON facilities for post-approval manufacture or quality control for the commercial product (11-15-91).

2. Please submit the time limits for the various phases of production. This may be done on the master batch record.
Response to Comment #2 re time limits: Satisfactory. Amendment of 12-18-91 incorporated requested time limitations for the different production phases.

3. Please note that your SOP #108.1010 is considered too general. Please amend your application to include specific case procedures or withdraw said SOP. After approval of this ANDA, you may supplement the application for reprocessing a batch of the drug product as per *21 CFR* 314.70 (b)(2)(x)".
Response to #3: Satisfactory.
The applicant made a commitment that no reprocessing of any batch will be performed without prior approval of a supplement to the application.

18. CONCLUSIONS and RECOMMENDATIONS:
Approval. A min. 18 mo expiration dating is recommended based on previous satisfactory 24 mo RT (old bio batches), accelerated studies of 3 months at 35° + cycle studies at 4° to 35°.

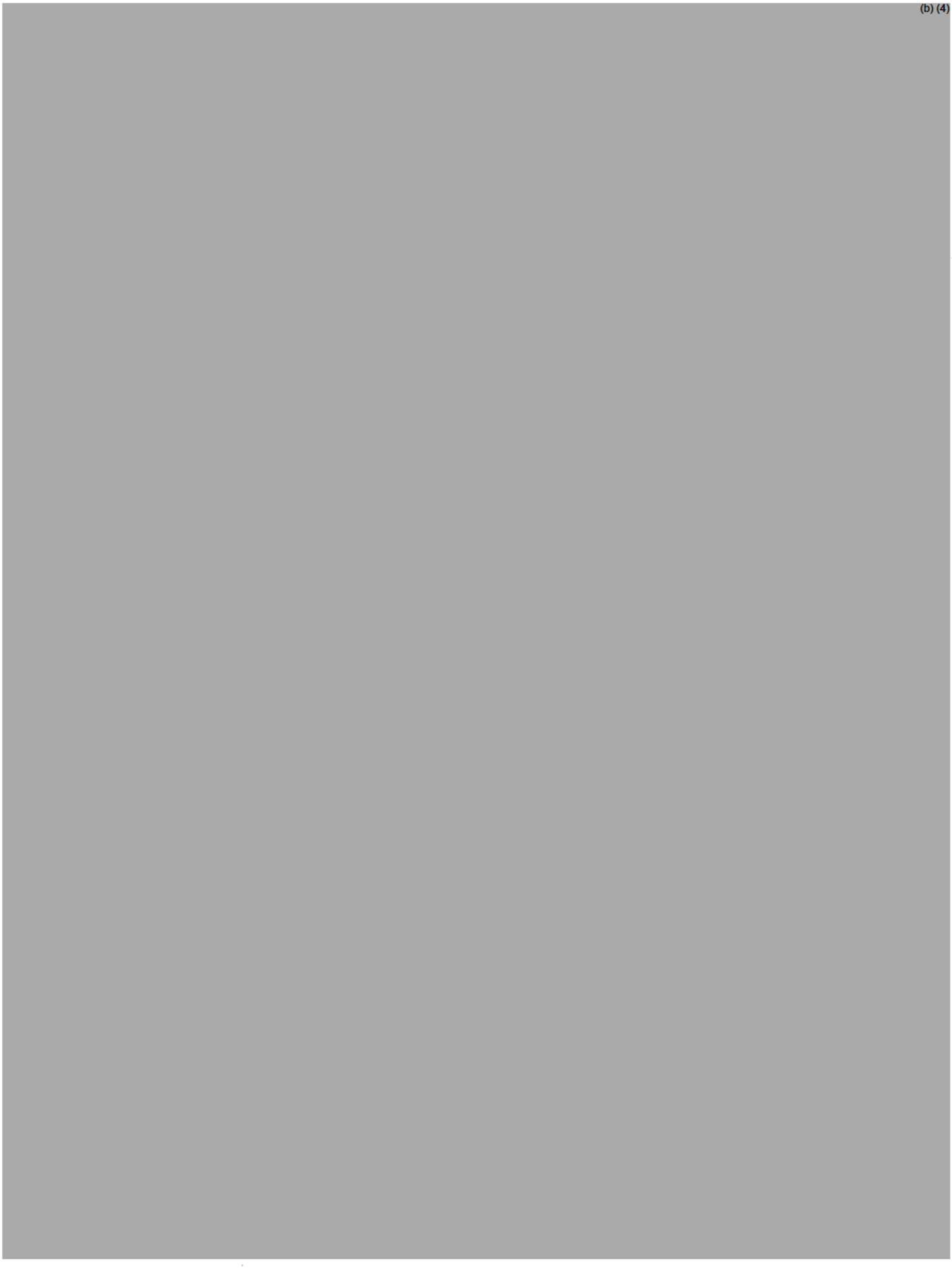
19. REVIEWER:

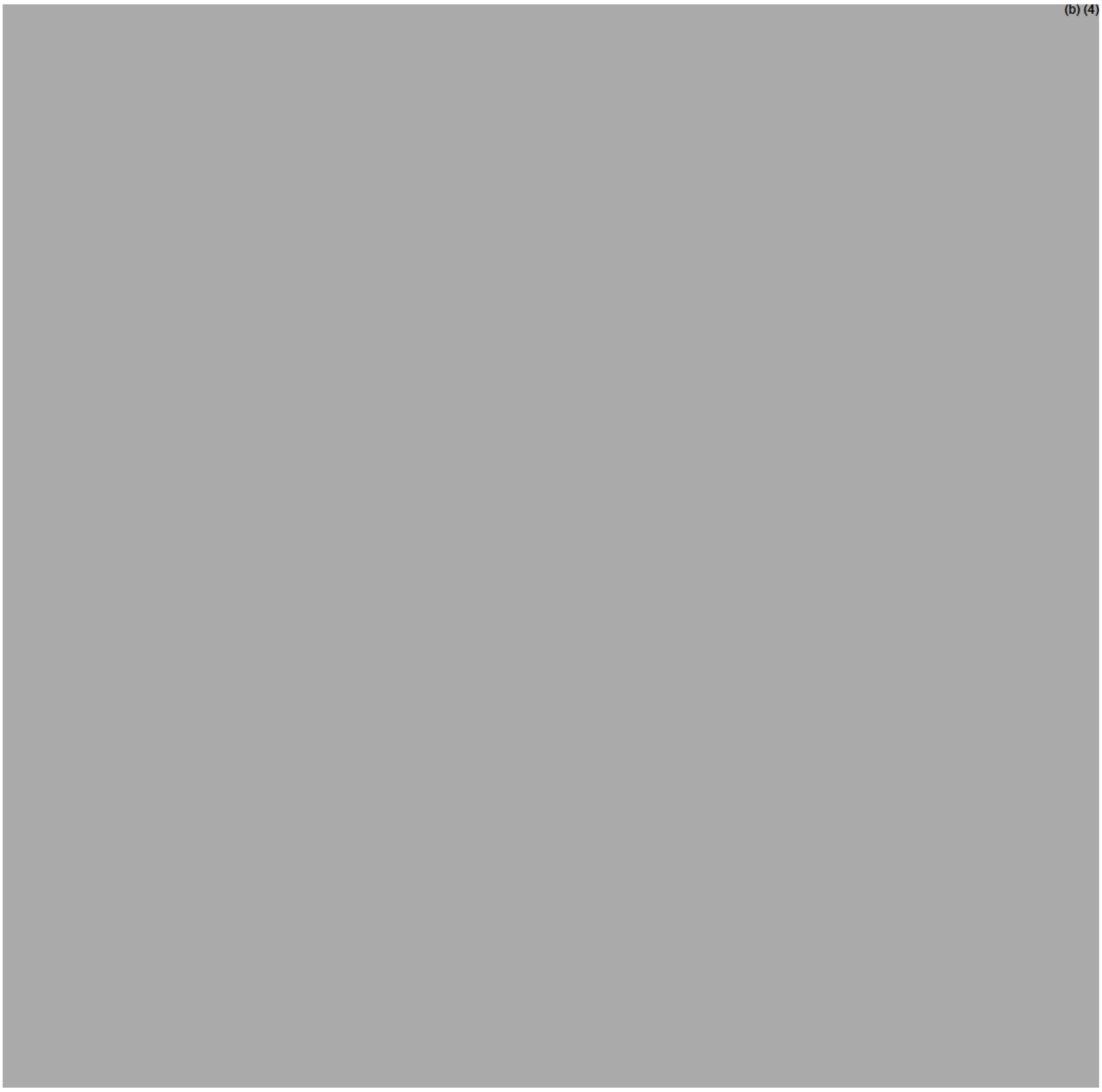
12-30-91
Robert W. Trimmer, Ph.D.
Branch II, Div. of Chem. I, OGD

12/30/91
Michael J. Smela, Jr.
Branch Chief

Date Started: 11-16-91
Completed: 12-18-91

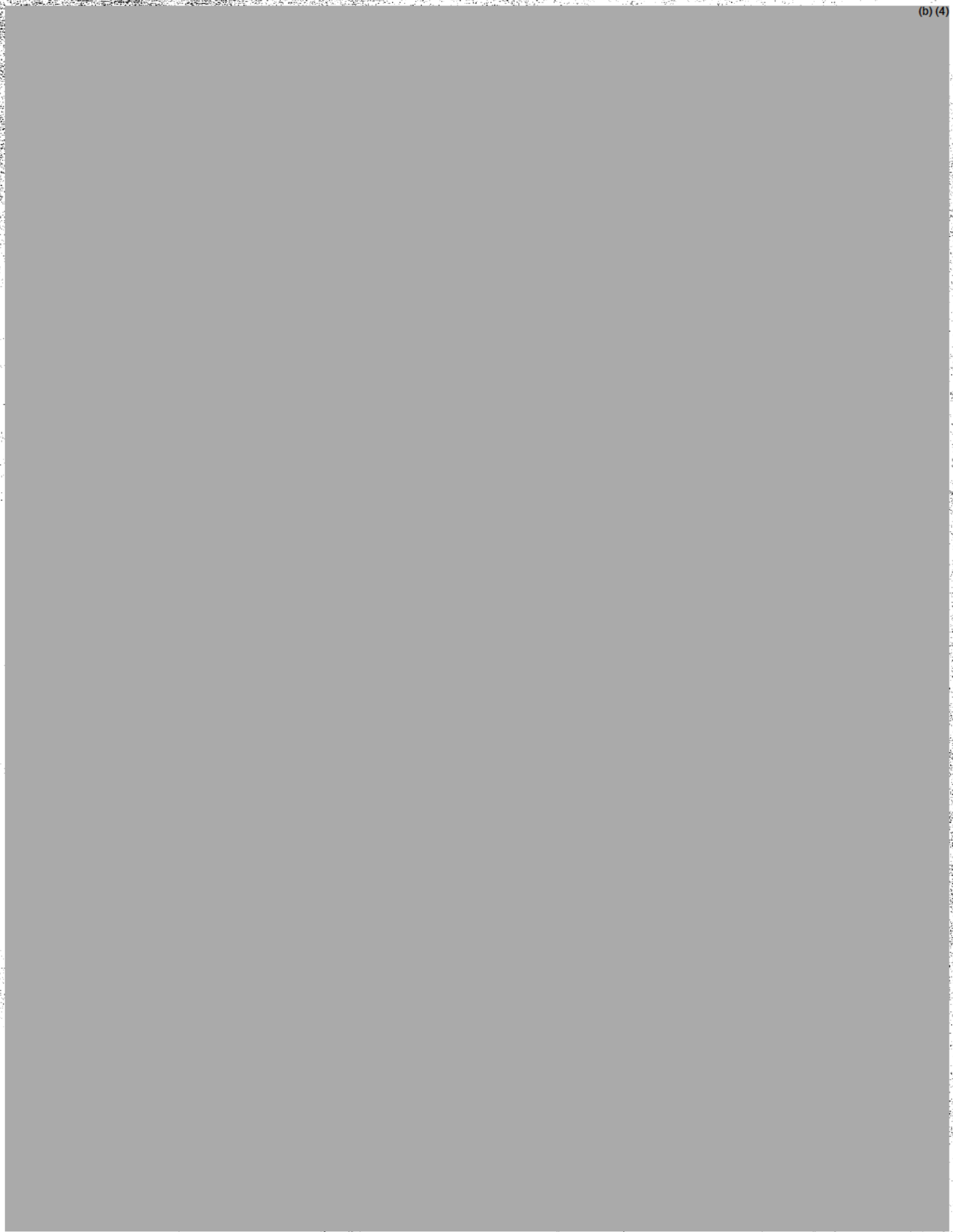
cc: ANDA 72-354
72-354/Division File
72-354/Dup
HFD-634/RTrimmer


(b) (4)


(b) (4)

ANDA 72-354

(b) (4)



ANDA 72-354

(b) (4)

[redacted]

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 72-354

BIOEQUIVALENCE REVIEWS

ANDA 72-354 April 20, 1988

Consultative Review of Clinical Protocol

Sponsor: Owen Laboratories
Forth Worth, Texas 76134

Product: DesOwen (desonide) Lotion, 0.05%

Formulation: Not provided

Indication: Corticosteroid-responsive dermatoses

Date of Submission: November 25, 1987

Background: DesOwen Lotion has been found to be eligible for submission of an Abbreviated NDA (ANDA) through an ANDA suitability petition. In order for the ANDA to be approved, it is necessary that two studies be performed: a vasoconstrictor protocol and a small clinical study in patients with diseased skin to establish that the ANDA formulation is bioequivalent to the reference product (in this case, DesOwen Cream 0.05%, which is the subject of the approved NDA 19-048). The ANDA sponsor has submitted protocols for both studies for comment prior to initiation of the studies.

Proposed Clinical Studies:

1. Vasoconstrictor Assay
   The vasoconstrictor assay is to be performed by Dr. R. B. Stoughton in volunteer subjects. The protocol is a standard one and is satisfactory.

2. Bioequivalency Protocol
   The investigator for this study will be H.I. Katz, M.D. Dr. Katz's qualifications have not been provided.

A. Study design: This is an investigator-blinded, randomized, paired comparison of DesOwen Cream and DesOwen Lotion in 36 patients with bilateral eczema.

B. Patient selection: Males and females with a minimum age of 6 with varying degrees of bilateral eczema which could normally be treated with low-potency topical steroids.

C. Treatment regimen: The medications are to be applied to affected areas three times daily. One medication will be applied to the left side of the body and the other to the right side. Medications will be color-coded (left side blue and right side yellow). The study is to continue for three weeks with four investigator evaluations; one prior to therapy and weekly thereafter.

4. Effectiveness parameters: Patients will be evaluated for erythema, scaling, excoriations, pruritus, oozing/weeping, and overall severity on a scale of 0-9 as follows:

Clear	Mild	Moderate	Severe
0	1, 2, 3	4, 5, 6	7, 8, 9

Evaluation: This protocol presents two major difficulties: the choice of eczema as the disease to be treated, and the choice of a paired comparison methodology.

Topical steroids are normally required to show effectiveness in both atopic dermatitis and psoriasis prior to approval. If only one clinical study is to be performed, the more difficult indication (psoriasis) should be studied, since a product which is effective against psoriasis may be expected to also be effective against atopic dermatitis. On the other hand, effectiveness against atopic dermatitis does not necessarily indicate that a product will be useful in psoriasis.

In addition, parallel groups of patients should be studied (one group on cream, and the other on lotion). Use of the paired comparison technique greatly increases the chance of medication mix-up, especially if the patients themselves are to apply the drugs.

It is also felt that a global evaluation should be performed according to a scale of improvement from baseline (rather than the overall severity score on a scale of 0-9 as proposed by the sponsor). The global evaluation is intended to view the improvement of the patient over the length of therapy. The overall severity score would essentially reevaluate signs and symptoms which have already been evaluated individually.

A small vehicle group should also be included in order to assess the clinical effect of the excipients in the formulation.

Recommendation: The following general protocol is an example:

> The study should be an investigator-blinded comparison of DesOwen Cream (20 patients), DesOwen Lotion (20 patients) and lotion vehicle (10 patients). Parallel groups of patients with psoriasis are to be entered into the study for each treatment group in a randomized fashion. The patients should be comparable in terms of disease state, demographic characteristics, etc. The study should run for three weeks. Drug applications are to be three times daily with investigator evaluations prior to therapy and weekly thereafter.

The effectiveness parameters proposed by the sponsor are satisfactory, except that the "overall severity" rating of signs and symptoms should be replaced by a global evaluation using the following scale:

1 = "Cleared" - 100% clearance of signs, except for residual discolorations.

2 = "Marked Improvement" - between 76% and 99% clearance of signs monitored.

3 = "Moderate Improvement" - 50% to 75% clearance of signs monitored.

4 = "Slight Improvement" - less than 50% clearance of signs monitored.

5 = "No Change" - no detectable improvement from pretreatment (baseline) evaluation.

6 = "Exacerbation" - flare of sites monitored.

Data Reporting:

Data should be reported both in terms of weekly results and in terms of "endpoint"; that is, one set of data should view all patients at the last valid treatment visit. The endpoint evaluation is the best method of assessing the effect of patient dropouts. Signs and symptom scores should be reported individually and as a total score. Global evaluation should be reported as noted above. The qualifications of the investigator and the complete formulation of each test material should be submitted.

Conclusion:

The proposed clinical protocol is not acceptable. Changes have been suggested.

David C. Bostwick, Chemist

C. Carnot Evans, M.D.

cc:
Orig ANDA
HFD-520
HFD-340
HFD-520/CCEvans
HFD-520/DCBostwick/llm/5/7/88
4018m

6/20/88

ANDA 72-354

Date Review Begun: July 26, 1989
Date Review Completed: July 26, 1989

Clinical Review of ANDA
(referred by Division of Generic Drug, HFD-230)

Sponsor: Owen Laboratories
Fort Worth, Texas

Product: DesOwen (desonide) Lotion, 0.05%

Formulation:

Ingredient	mg Per Gram	Percent (w/w)
Desonide	[redacted] (b) (4)	
Propylparaben, USP/NF		
Methylparaben, USP/NF		
Edetate Sodium		
Sodium Lauryl Sulfate, USP/NF		
Cetyl Alcohol, USP/NF		
Glyceryl Stearate SE (Self emulsifying)		
Stearyl Alcohol, USP/NF		
Sorbitan Monostearate, USP/NF		
Propylene Glycol, USP		
Light Mineral Oil, USP/NF		
Citric Acid, USP and/or Sodium Hydroxide		
Purified Water, USP		

Indication: Corticosteroid-responsive dermatoses.

Dates of Submission: June 6, 1988 (vasoconstrictor study). April 18, 1989 (clinical bioequivalence study).

Background: Please see our previous review of this ANDA dated April 20, 1988. This product represents a line extension (new formulation) for an already approved topical steroid which was first marketed after 1962. Under these conditions, two studies are necessary for approval of an ANDA: a vasoconstrictor assay and a limited clinical study in patients with psoriasis. In this case, the reference drug is DesOwen Cream 0.05% (NDA 19-048).

Clinical Studies:

A. Vasoconstrictor assay.

Investigator: Richard Stoughton, M.D.
La Jolla, California

Method: Thirty healthy adults (16 males, 14 females) were entered into the study.

Three test materials were used: DesOwen Lotion, 0.05%, DesOwen Cream, 0.05% and the DesOwen Lotion vehicle. Each subject was treated with each test material on each forearm, giving a total of six treatment sites per subject. Each site was approximately 3 cm in diameter, with 35 mg. of each test material being used. All applications and readings were double-blind.

The test sites were protected by a nonocclusive plastic guard for 16-20 hours. The sites were then washed and readings for vasoconstriction taken one hour later. The degree of vasoconstriction was read according to the following scale:

0 = no pallor
1 = mild pallor
2 = moderate pallor
3 = maximum pallor

Results: Since both arms were used, there are twice as many readings as patients.

Number of Patients per Blanching Score

Product	0	1	2	3	Mean	Total Patients
DesOwen Lotion	4	19	28	9	1.7	30
DesOwen Cream	3	20	27	10	1.7	30
Vehicle	52	7	0	1	0.2	30

These data indicate that DesOwen Lotion and Cream are equivalent in their vasoconstrictor activity.

B. Comparison of DesOwen Lotion, DesOwen Cream and Lotion Vehicle in Psoriasis.

Investigator: Alan Greenspan, M.D.
TKL Research, Inc.
Maywood, N.J. 07607

Method: This was a double-blind parallel-group comparison of DesOwen Lotion, DesOwen Cream and the lotion vehicle in patients with mild to moderate psoriasis. Thirty patients were entered into each active treatment group and twenty were entered into the vehicle group on a random basis. The patients were males and females aged 20-77 years. The patients had not been on any interfering topical medication for 7 days prior to initiation of therapy.

The study was three weeks in length with evaluations made at baseline and weekly thereafter.

The disease was evaluated for erythema, scaling, induration and pruritis on a scale of 0 to 9 as follows: clear (none) = 0; mild = 1, 2, 3; moderate = 4, 5, 6; and severe = 7, 8, 9. In addition, a global evaluation was made to assess the overall improvement/exacerbation of the disease at all affected sites. This global evaluation was made at Weeks 1, 2 and 3. The following grading system was used: 1 = clear; 2 = 76-99% improvement; 3 = 50-75% improvement; 4 = < 50% improvement; 5 = exacerbation of the disease. The following list of definitions was used in grading the signs and symptoms.

Erythema

Mild: Faintest-detectable erythema; very light-pinkish color.

Moderate: Very distinguishable, dull redness.

Severe: Deep, intense, beefy-red color.

Scaling

Mild: Barely-perceptible shedding, noticeable only on light scratching.

Moderate: Obvious but not profuse; some scales adhering to clothing.

Severe: Heavy scale production, obvious shedding upon removal of clothing with imbedding of scales in clothing; profuse shedding.

Induration

Mild: A slight hardening or firmness of the tissue at the site of psoriatic plaque.

Moderate: Marked hardening of the tissue at the site of a psoriatic plaque; a thickened feel.

Severe: Gross hardening of the tissue at the site of a psoriatic plaque; feels like a lump on the skin.

Pruritus

Mild: Occasional, slight itching; not really bothersome.

Moderate: Constant or intermittent itching; itching that is somewhat bothersome; may or may not require treatment for relief of symptom.

Severe: Bothersome itching that has caused patient to obtain treatment for relief. Excoriations of the skin from scratching.

Safety was determined at the end of therapy by the investigator and patient. Safety is defined as stinging/burning and general irritation. The investigator assessed safety visually and through patient interview.

Results: Eighty patients entered the study and were analyzed for safety. Nine patients failed to finish the study. Five discontinued for "personal reasons". Two patients in the placebo group quit because of exacerbation of their disease. One patient was a protocol deviation and the last was hospitalized for an unrelated back injury. We will analyze the data both in terms of those patients who completed the study and in terms of the last valid patient visit (endpoint analysis).

1. Signs and symptoms

a. Erythema

Average Scale Readings and % Reduction

Test Product	Baseline	Week 1	Week 2	Week 3	Endpoint
DesOwen Cream	3.80	3.14(17%)	2.79(27%)	2.70(29%)	2.67(30%)
DesOwen Lotion	3.63	3.26(10%)	2.63(28%)	2.63(28%)	2.70(26%)
Vehicle	4.00	3.72(7%)	4.00(0%)	3.93(2%)	4.20(+5%)

b. Scaling

Average Scale Readings and % Reduction

Test Product	Baseline	Week 1	Week 2	Week 3	Endpoint
DesOwen Cream	4.37	2.83(35%)	2.75(37%)	2.44(44%)	2.40(45%)
DesOwen Lotion	4.63	2.85(38%)	2.19(53%)	2.15(54%)	2.27(51%)
Vehicle	4.75	3.67(23%)	3.37(29%)	3.47(27%)	3.65(23%)

c. Induration

Average Scale Readings and % Reduction

Test Product	Baseline	Week 1	Week 2	Week 3	Endpoint
DesOwen Cream	3.67	2.86(22%)	2.61(29%)	2.67(27%)	2.57(30%)
DesOwen Lotion	4.10	3.19(22%)	2.74(33%)	2.41(41%)	2.53(30%)
Vehicle	4.15	3.89(6%)	3.71(11%)	4.07(2%)	4.10(1%)

d. Pruritus

Average Scale Readings and % Reduction

Test Product	Baseline	Week 1	Week 2	Week 3	Endpoint
DesOwen Cream	3.33	1.72(48%)	0.93(72%)	0.79(77%)	0.73(78%)
DesOwen Lotion	3.23	1.37(58%)	0.89(72%)	0.69(79%)	0.90(72%)
Vehicle	3.55	2.50(30%)	1.93(46%)	2.40(32%)	2.65(25%)

2. Global assessment. We will present data for the end of the study only.

Week 3 Global Evaluation (Number of Patients and % of Total)

Test Product	76 - 99% Improvement	50 -75% Improvement	50% Improvement	Exacerbation
DesOwen Lotion	10(37%)	6(22%)	9(33%)	2(7%)
DesOwen Cream	7(26%)	9(33%)	11(41%)	0
Vehicle	0	3(20%)	9(60%)	3(20%)

3. Safety Evaluation: In addition to the two placebo patients noted above who suffered exacerbation of their disease, one patient on the Cream formulation reported intense erythema following the initial application of the drug. This resolved with no further consequences.

4. Effectiveness Evaluation: This study establishes that DesOwen Lotion and DesOwen Cream are comparable in their clinical effect. Both products are superior to the vehicle for the lotion. Differences between the active products are not statistically significant.

Recommendation: The vasoconstrictor assay and clinical study in psoriasis establish that DesOwen Lotion is clinically bioequivalent to the previously approved DesOwen Cream. We have no objection to the approval of this ANDA.

David C. Bostwick
Chemist

C. Carnot Evans, M.D.
Group Leader/DERM

Original ANDA
HFD-340
HFD-520
HFD-520
HFD-520/DCBostwick:elp/08/07/89
HFD-520/CCEvans
5047m

ANDA 72-354 DATE OF REVIEW: February 8, 1991

Clinical Review of Amendment
(Referred by Division of Generic Drugs, HFD-630)

Sponsor: Owen Laboratories
Fort Worth, TX

Product: DesOwen (desonide) Lotion, 0.05%

Indication: Corticosteroid - responsive dermatoses

Date of Submission: August 17, 1990

Background: This ANDA was approved in 1990. The sponsor has determined that the finished dosage form is more stable at a pH between [redacted] (b)(4) than the [redacted] (b)(4) range which was originally approved. The Division of Generic Drugs is reviewing an amendment to the ANDA which would change the acceptable pH range to [redacted] (b)(4) They have the following questions:

1. Would a lotion manufactured at the lower pH range be acceptable on the skin?

2. Would the efficacy of the lotion be adversely impacted at such pH levels?

Material Reviewed: Standard references state that the pH of normal skin is in the range of 4.0-7.0. Many topical lotion formulations have pH ranges lower than that proposed for DesOwen Lotion. Examples are [redacted] (b)(4) which has a pH range of [redacted] (D)(4); and [redacted] (b)(4), which has a pH range of [redacted] (D)(4) Neither of these applications exhibited unusual adverse reactions in clinical testing which might be attributable to low pH. Therefore, it is not expected that a lotion which has a pH range of [redacted] (b)(4) would be unacceptable to the skin.

Further, there is no reason to expect the effectiveness of the product would be changed or compromised by this relatively minor pH revision.

Conclusions and Recommendations: There is no objection to a revision in the pH specification for DesOwen Lotion from [redacted] (b)(4)

David C. Bostwick

2/20/90

MD
Wiley Chambers, MD

Orig ANDA 72-354
cc: HFD-340
HFD-520
HFD-520/DCBostwick
HFD-520/WChambers
HFD-520/RCook
HFD-520/Alam
HFD-520/WDeCamp

DBB 9-2-91

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 72-354

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

ANDA NUMBER: 72-354

DATE APPROVAL LETTER ISSUED: 1-24-92

TO: Press Relations Staff (HFI-40)

FROM:
- [x] Bureau of Drugs
- [ ] Bureau of Veterinary Medicine

ATTENTION

Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.

TYPE OF APPLICATION
- [ ] ORIGINAL NDA
- [ ] SUPPLEMENT TO NDA
- [x] ABBREVIATED ORIGINAL NDA
- [ ] SUPPLEMENT TO ANDA

CATEGORY
- [x] HUMAN
- [ ] VETERINARY

TRADE NAME *(or other designated name)* AND ESTABLISHED OR NONPROPRIETARY NAME *(if any)* OF DRUG: Des Owen® (Desonide)

DOSAGE FORM: Lotion 0.05%

HOW DISPENSED
- [ ] RX
- [ ] OTC

ACTIVE INGREDIENT(S) *(as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)*

Desonide

NAME OF APPLICANT *(Include City and State)*

Owen/Galderma Laboratories, Inc.
6201 South Freeway
P.O. Box 6600
Fort Worth, Texas 76115

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY: Corticosteroid, topical

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

FORM PREPARED BY

NAME: Robert W. Trimmer, Ph.D. — DATE: 12-18-1991

FORM APPROVED BY

NAME: Michael J. Smula, Jr. — DATE: 12/18/91

FORM FD 1642 (2/75) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.

ANDA ACTION LETTER ROUTING RECORD

ANDA # 72-354
AADA # ——
Drug Desonide
Dosage Form Lotion
Strength 0.05%
Applicant Owen Laboratories
Manufacturing Site(s) DPT, 307 E Josephine St San Antonio, TX
Proposed Action (AP) AE

Original Rec'd Date 11-27-87
Amendment Date(s) 12/ 87 5/ /88, 1/6/88
Chemistry Reviewer Arnowe/Dugan/Tenner 6/24/
Supervisor Patel/Smith 3/20/
Bio Reviewer Bartchuk/HFD-520 5/30/
Supervisor- Cramer/Ekwenstein/Evans 5/30/
Patent Certification [illegible] 11/1/
5/30/
8/8/
8/9/9
8/14/
11/1/9
12/5/
12/3/9
12/13/
12/16/91

REVIEWER: RECEIPT ACTION

1. R. Pollock, M.S
Chief, Program Support Staff
Date 12/27/91 Initials [illegible]
Date 12/27/91 Initials
Comments:
EER Acceptable 12/5/91

2. S. Dighe, Ph.D.
Director, Bioequivalence
Date 12/30/91 Initials SVD
Date 12/30/91 Initials SVD
Comments: The firm's ANDA suitability petition was approved in 1987. The ANDA (72-354) for the lotion was originally approved to manufacture the test product at pH [redacted]. The firm has determined that at pH [redacted] the lotion is more stable and wants to manufacture the product at pH [redacted]. The Div. of Anti Infective Drug Products has determined that this change in pH is not a problem and therefore permitted. Waiver of bioequivalence study is appropriate as noted.

3. K. Johnson, M.S.
Associate Director
Office of Generic Drugs
Date 12-30-91 Initials KJ
Date 12-30-91 Initials KJ
Comments: Labeling is satisfactory.

4. Director of Chem. I ~~or II~~
Office of Generic Drugs
Date 12/30/91 Initials RK
Date 12/30/91 Initials RK
Comments: The CGMP issues are resolved. From the controls viewpoint this ANDA is satisfactory for approval of the lotion dosage form.

5. R. Jerussi, Ph.D.
Office Level OGD Review
(if necessary) Yes X No__
Date Initials
Date 1/24/92 Initials RJ
Comments: O.K. for approval.
See 1/22/92 memo. Controls O.K. for a lotion.

FIRST LOTION

6. Office Level Bio Review
Date 1/24/92 Initials ATH
Date 1/24/92 Initials ATH
Comments: Bio waived. Firm conducted 2 studies (vasoconstrictor assay + eczema patient) to show safe + effective. OK for approval.

7. R. Williams, M.D.
Director
Office of Generic Drugs
Date Initials
Date 1/28/92 Initials RW
Comments:

LETTER SIGNED: [signature]
(Date)

(revision date 12-16-91)
(C:Forms)

Memorandum of Telephone Conversation
between Jan.22,1992

Christine Shank, Owen/Galderma
and
RA Jerussi, OGD

Subject: ANDA 72-354, Desonide Lotion 0.05%

I spoke to Ms. Shank about two items:

1. This application has as a spec for the desonide drug substance, residue on ignition of (b)(4) whereas the previously approved ANDA 71-425 for desonide ointment 0.05% seemed to have a spec of (b)(4) (in the original submission). I was concerned which was correct. She indicated that the (b)(4) was but we both searched and spoke again. On page 0019 of the original submission for 71-425 it was listed as (b)(4) and therefore was listed twice with two different values. However, I disocvered Report 07 dated 6/89 which had it listed as (b)(4) which she said is the spec.

2. The specifications for the desoniude drug substance do not contain a test for organic volatile impurities. However, the vendors test the product for (b)(4) and for batch 109023 found (b)(4) I pointed this out to Ms. Shank. This data is on page 0015 of the origianl application so I was not revealing confidential information. I strongly urged her to get her firm to set limits for these (b)(4) solvents and said that the amount of (b)(4) is rather high nd perhaps they should reduce it. This would be true for 71-425 also and for all their NDSs. Limits for solvents are now in the USP and FDA has set some limits for (b)(4) solvents. Its about time the firm got with it. I said this could be done without a supplement since it is adding a spec.

Robert A. Jerussi,Ph.D.
Robert A. Jerussi 1/22/92

cc:
ANDA 72-354 Orig.
" " " Dup/Div. File
ANDA 71-425 Orig.
" " " Dup/Div. File
Dr. Trimmer, HFD-600
M. Smela, " "
Dr. Patel, " "
Dr. Jerussi, " "

ANDA Approval Summary

72-354
ANDA Number

OWEN/Galderma
Applicant Name

Desonide
Established Name of Drug

Lotion
Dosage Form

0.05%
Strength

(Physicians Package) (b) (4) mL, 2+4 fl.oz.
Container size(s)

	Date Found Satisfactory	Comment
Labeling	7-23-91	Pari Subramanian
Chemistry, Manufacturing, and Controls	(b) (4)	Robert W. Trimmer, Ph.D.
GMP's		
Manufacturer – Finished Dosage Form		Owen/Galderma Labs.
Outside Facilities		
Manufacturer(s) – Active Ingredient(s)	(b) (4)	(b) (4)

Robert W. Trimmer, Ph.D. — Chemist Reviewer — 12-18-1991 — Date

Michael J. Smela, Jr. — Branch Chief — 12/18/91 — Date

Petition Required	No	✓ Yes		9-10-87	Date of Petition approved STP-C105/CP
Listed Drug Information 505(j)(2)(A)				12-4-87	
Patent Certification 505(j)(2)(B)				12-4-87	No Patents N/A
Date Patent/Exclusivity Expires (if applicable)				12-4-87	
Bioequivalence Section					
Dissolution Required?	✓ No	Yes	DB: ✓ DGD		
In vivo study(s) required?	No	✓ Yes			Vasoconstrictor Assay Waiver Study approved acceptable by HED-520
Study(s) Found Acceptable				2/20/91	
Waiver Request Granted					
Total Bioequivalence Requirement Met				4-2-91	Reviews concurred by Dr Sundaram

Administrative Reviewer — 12/17/91 — Date

Approved _____

Disapproved _____

Director, Division of Generic Drugs — Date

Comments:

ANDA

AIRBORNE EXPRESS

December 19, 1991

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

Owen/GALDERMA
6201 South Freeway
P.O. Box 6600
Fort Worth, Texas 76115
(817) 293-0450
CHRISTINE E. SHANK
Manager
Regulatory Affairs

N-000 AM

ATTENTION: Document Control Room
SUBJECT: ANDA 72-354
DesOwen (Desonide) Lotion, 0.05%

Dear Dr. Trimmer:

Reference is made to our telephone conversations of December 18, 1991 and the two Telefax transmissions made to you in support of the pending application for DesOwen Lotion, 0.05%.

Please find herewith, in duplicate, copies of the Telefax transmissions for formal incorporation into the ANDA 72-354 document.

I would like to express my sincere appreciation of your time and consideration extended in the review of this application. It has been a pleasure working with you.

Sincere regards.

Christine E. Shank
Manager, Regulatory Affairs

CES/dw

ORIGINAL

RECEIVED
DEC 20 1991
GENERIC DRUGS

DaP with Dr. Trimmer returned 12-16-91 Doc 229 OPI

AIRBORNE EXPRESS

Owen/GALDERMA
6201 South Freeway
P.O. Box 6600
Fort Worth, Texas 76115
(817) 293-0450
CHRISTINE E. SHANK
Manager
Regulatory Affairs

December 13, 1991

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

NDA ORIG AMENDMENT
N-000 / AM

ATTENTION: Document Control Room
SUBJECT: ANDA 72-354
REFERENCE: Telephone conversation of December 6, 1991

Dear Dr. Trimmer:

Pursuant to our conversation of last Friday, efforts have been made to obtain as much of the documentation on the containers and closures as is available at this time.

First of all, as promised, please find with this submission stability reports for the 2 fl. oz. and 4 fl. oz. sizes which have been updated with the 15 month test data and have been corrected to accurately reflect the packaging component materials and the fabricators (suppliers). The reports provided are from the "test batches" described in my previous submissions.

Batch No.	Stability Lot	Size
DECE	53540786	2 fl. oz.
DECE	53540787	4 fl. oz.
DFCE	53540789	2 fl. oz.
DFCE	53540790	4 fl. oz.
DFC	53540792	4 fl. oz.
DFC	53540793	2 fl. oz.

You will note that for the lots which employ the containers made with [redacted] (b) (4) is identified as the fabricator. A letter of authorization to reference their Drug Master File # [redacted] (b) (4) is provided. I apologize for the error in identifying the supplier for these containers as it was simply a mistake in our haste to provide the stability data and it was generally assumed that [redacted] (b) (4) was the supplier.

RECEIVED
DEC 16 1991
GENERIC DRUGS

After contacting [redacted] (b) (4) we were able to obtain "Certificates of Compliance" for the containers used in the stability studies. [redacted] (b) (4) was also kind enough to share with us their USP test results for the [redacted] (b) (4) which demonstrate comparative equivalency of the materials.

You will also find enclosed the [redacted] (b) (4) Containers' "Certificates of Compliance" and the Dermatological Products of Texas, Inc. inspection reports for the [redacted] (b) (4) bottles used in the stability studies.

This and the IR scans provided in our December 5, 1991 submission is all the documentation we have for the packaging components. We are of the opinion that substantial verification of the components is provided and that the components as specified are satisfactory for use with a topical lotion dosage form.

We appreciate your continued interest and consideration of the information provided herewith. It is hoped that a final satisfactory decision can be reached in the review of this application.

Sincere regards,

Christine Shank

Christine E. Shank
Manager, Regulatory Affairs

Telephone: (817) 551-8516
FAX: (817) 551-8079

EER Update for APPROVAL

DEPARTMENT OF HEALTH & HUMAN SERVICES 2076

Amendment to 10/16/91 EER

Public Health Service

Memorandum

Date	NOV. 14, 1991		
From	Division of Chem-I OGD	HFD-	632
	Requestor's Name R. TRIMMER	Phone	245-5315
Subject	ESTABLISHMENT EVALUATION REQUEST		
To	Division of Manufacturing & Product Quality (HFD-320)		

Sterile Product ______ Non Sterile Product ✓

Application and Supplement No. 72-354

Brand Name *(if any)* ~~Des~~ Owen® Lotion

Establishment Name, Dosage Form and Strength ~~Desonide Lotion~~ 0.05%

Profile Class Code: LIN

Priority Classification: ASAP for APPROVAL *(See SMG BD-4820.3)*

Applicant's Name: Owen / Galderma

Address: 6201 South Freeway, Ft. Worth, TX 76115

Facilities to be Evaluated: (*Name, full Address, DMF No., and responsibility*)

	For HFD 320 Use Status & Date of Inspection:
1. Dermatological Products of Texas Inc 307 E. Josephine St., San Antonio Texas 78216 Manuf. & testing facility for drug product	AC 6/17/91
3. 4. [redacted] (b) (4)	[redacted] (b) (4)
5.	

* REVISION

Other Information or Special Requests: ~~to~~ Oct 16, 1991 EER (Alcon no longer used as testing or manuf. facility).

****

For HFD-320 Use Only: Date Received: 11/21/91

CGMP Compliance Status of Facilities Evaluated: acceptable

CSO: Melissa Garcia Date Completed: 12/5/91

Distribution: Original and First Copy: HFD-320
Remaining Copies: Requesting Office Use

ANDA Approval Summary

72-354
ANDA Number

OWEN/Galderma
Applicant Name

Desonide
Established Name of Drug

Lotion
Dosage Form

0.05%
Strength

(Physicians Package) (b) (4) mL, 2+4 fl.oz.
Container size(s)

	Date Found Satisfactory	Comment
Labeling	7-23-91	Puri Subramanian
Chemistry, Manufacturing, and Controls	(b) (4)	Robert W. Trimmer, Ph.D.
GMP's		
Manufacturer – Finished Dosage Form		Owen/Galderma Labs.
Outside Facilities		
Manufacturer(s) – Active Ingredient(s)	(b) (4)	(b) (4)

Robert W. Trimmer, Ph.D. — Chemist Reviewer — 12-18-1991 — Date

Michael J. Smela, Jr. — Branch Chief — 12/18/91 — Date

Petition Required		No	✓ Yes	9-10-87	Date of petition approved STP-0105/CP
Listed Drug Information 505(j)(2)(A)				12-4-87	
Patent Certification 505(j)(2)(B)				12-4-87	No Contents N/A
Date Patent/Exclusivity Expires (if applicable)				12-4-87	
Bioequivalence Section					
Dissolution Required?	✓ No	Yes	: ✓ DB	DGD	
In vivo study(s) required?		No	✓ Yes		Vasoconstrictor Assay Bioan
Study(s) Found Acceptable				2/20/91	Study approved acceptable by HFD-520
Waiver Request Granted					
Total Bioequivalence Requirement Met				4-2-91	Review concurred by Dr Burlington

Administrative Reviewer — 12/17/91 — Date

Approved _____

Disapproved _____

Director, Division of Generic Drugs — Date

Comments:

ANDA

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 12-6-1991

NDA NUMBER: 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☒ APPLICANT/SPONSOR ☐ FDA

MADE: ☐ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Desonide

FIRM NAME: Owen/Galderma

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Ms. Christine Shank

TELEPHONE NO.

1. Ms. Shank is searching for data on container/closure systems — both [redacted] (b) (4) I mentioned need for USP test on both [redacted] (b) (4) if both wanted for NF, and USP data need as previously mentioned of Biol. Reactivity Tests (<87>).

2. Ms. Shank will consolidate Stability data sheet info so that there will be no confusion on exactly what container/closure system is being approved.

3. She may contact [redacted] (b) (4) for data re Biol. React. Tests or find it locally or forward to [redacted] (b) (4)

4. [redacted] (b) (4) perhaps to be used in the future.

SIGNATURE: Robert W. Trimmer, Ph.D. 12-6-91

DIVISION: Chemistry I, OGD

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE: 1984-421-976/7124

AIRBORNE EXPRESS

December 5, 1991

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

Owen/GALDERMA
6201 South Freeway
P.O. Box 6600
Fort Worth, Texas 76115
(817) 293-0450
CHRISTINE E. SHANK
Manager
Regulatory Affairs

ATTENTION: Document Control Room
SUBJECT: DESOWEN® (desonide) Lotion, 0.05%

Dear Sir or Madam:

Please find enclosed (in duplicate) copies of the FAX transmissions provided to Dr. Robert Trimmer on November 27, 1991 and December 5, 1991. These documents are to be made a part of the official file for ANDA 72-354.

Sincerely,

Christine E.Shank
Manager, Regulatory Affairs

CES/pc
Enclosures

3.1

Owen/GALDERMA
6201 South Freeway
P.O. Box 6600
Fort Worth, Texas 76115
(817) 293-0450
CHRISTINE E. SHANK
Manager
Regulatory Affairs

AM

NDA DRUG PACKAGE

DATE: December 5, 1991

TO: Dr. Robert Trimmer

FROM: Christine Shank

SUBJECT: ANDA 72-354

REFERENCE: Telephone conversations of November 27 and December 4, 1991

Dear Dr. Trimmer:

Pursuant to our recent conversations please find with this transmittal additional data, documentation, and information to support our request for approval of this pending application for DESOWEN® (desonide) Lotion, 0.05%.

1. Drug Master File reference letter for: [redacted] (b) (4)

2. IR scans of bottle samples employing the [redacted] (b) (4) Each represents a transmission spectrum on a portion of the bottle wall prepared by [redacted] (b) (4) technique described in technical procedure 63.0042000 provided in the original application submission.

3. Packaging description records from the MBRs for each of the 2 fl. oz. and 4 fl. oz. stability lots (reference is made to our FAX of November 27, 1991) are provided as documentation that the closure/liner system used is identical in composition to that described previously in the application. A drawing specification is also provided which details the component. Please note the references to "part number" and "drawing number" are interchangeable terms for component number 104058.

4. After talking with you yesterday, I was in contact with our technical support personnel and was pleasantly surprised to learn that scheduled 15 month stability test data from room temperature studies were available for the 2 fl. oz. and 4 fl. oz. stability lots. I apologize as I was unaware of this scheduled test station and in my absence from the office the last two weeks was obviously unaware that this data was being generated. The reports transmitted with this FAX are the raw data summaries for the following stability lots showing the 15 month test results and should be considered supplementary to the reports provided in our November 27, 1991 FAX.

Stability Lot Code	Size
53540786	2 fl. oz.
53540787	4 fl. oz.
53540789	2 fl. oz.
53540790	4 fl. oz.
53540792	4 fl. oz.
53540793	2 fl. oz.

I can only ask, given the satisfactory stability profile this recent data demonstrates, that you please consider again our request for a tentative 18 month dating.

5. I appreciate your renewed interest in the compliance issue of time limits for the various phases of the [redacted] (b) (4) process. I have again consulted with our technical support personnel and the production support staff at Dermatological Products of Texas, Inc. and have been advised as follows:

Based on historical experience with the production of [redacted] (b) (4)

[redacted] (b) (4)

Given that this information and explanation is not significantly different from my November 1, 1991 response to comment 2, I must rely on the expertise of the Dermatological Products of Texas, Inc. production personnel and their ability to effectively and satisfactorily address the matter during the re-inspection.

I think you will find that I have provided all the materials and information as agreed in our last conversation. I trust your review of the [redacted] (b) (4) DMF will also find things in order. If there is anything you or I can do to help expedite the re-inspection of DPT, Inc. I would welcome some suggestion or input in this regard. This is an anxious time for us and obviously an approval for this application is eagerly anticipated. If there is anything further I can do please do not hesitate to give me a call.

Your continued assistance and interest in this submission is greatly appreciated.

Sincere regards,

Christine Shank

Christine E. Shank
Manager, Regulatory Affairs

Telephone: (817) 551-8516
FAX: (817) 551-8079

File copies sent Airborne Express to OGD Document Control Room

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 12-5-1991

NDA NUMBER: 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☑ APPLICANT/SPONSOR ☐ FDA

MADE: ☑ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Desonide Lotion

FIRM NAME: Owen/Galderma

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Christine Shank; Ms. V. Vashio (FDA)

TELEPHONE NO.:

Ms. Shank called re 15th month stability data being faxed to us.

1. I told her we still need some more info re time limits of a broad nature.

2. I told her we also need COA from container/closure supplier + DPTs own COTS of the new container/closure system. That the USP tests for containers (section >661<) and Biol. Reactivity Test (section >87<) should be followed. See also 21CFR 211.84 & 211.86

SIGNATURE: Robert W. Trimmer, Ph.D. 12-5-91

DIVISION: Chemistry I, OGD

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE: 1984-422-974/7126

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: Nov. 26, 1991

NDA NUMBER: 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☒ FDA

MADE: ☒ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Desmide

FIRM NAME: Owen/Galderma

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD

Ms. C. Shank

TELEPHONE NO.
8-817-293-0450
568-6500
Terry Isaacs

Owen was called to request stability data on their new test batches DECE, DFC + DFE for 2 and 4 fl. oz. (6 mo. previously sent)

Need also to verify that (b) (4) is the NDS source.

SIGNATURE

Robert W. Trimmer, Ph.D. 11-26-91

DIVISION: Chemistry I, OGD

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE: 1984-422-974/7124

Vol. 3.1

AIRBORNE EXPRESS

Owen/GALDERMA
6201 South Freeway
P.O. Box 6600
Fort Worth, Texas 76115
(817) 293-0450
CHRISTINE E. SHANK
Manager
Regulatory Affairs

November 15, 1991

NEW CORRESP

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Document Control Room
SUBJECT: ANDA 72-354
DESOWEN® Lotion, 0.05%

Dear Dr. Trimmer:

Thank you so much for telephoning me yesterday with the update on the review for this application.

As promised, the following statement is offered to fully clarify the question of Alcon Laboratories, Inc. involvement with regard to post-approval manufacture of the drug product:

> The applicant certifies that there will be no utilization of the Alcon facilities for post-approval manufacture or quality control of the commercial product.

If you should have any additional questions please do not hesitate to give me a call.

Sincere regards,

Christine Shank

Christine E. Shank
Manager, Regulatory Affairs
Telephone: (817) 551-8516

CES/pc

RECEIVED
NOV 18 1991
GENERIC DRUGS
ESP

ORIGINAL

EER Update for APPROVAL

DEPARTMENT OF HEALTH & HUMAN SERVICES
Amendment to 05/16/91 EER 2076

Public Health Service

Memorandum

Date Nov. 14, 1991

From Division of Chem-I, OGD — HFD- 632

Requestor's Name R.W. TRIMMER — Phone 295-8315

Subject ESTABLISHMENT EVALUATION REQUEST

To Division of Manufacturing & Product Quality (HFD-320)

Sterile Product _____ Non Sterile Product ✓

Application and Supplement No. 72-354

Brand Name *(if any)* DesOwen® Lotion

Establishment Name, Dosage Form and Strength Desonide Lotion, 0.05%

Profile Class Code: OIN

Priority Classification: ASAP for APPROVAL *(See SMG BD-4820.3)*

Applicant's Name: Owen / Galderma

Address: 6201 South Freeway, Ft. Worth, TX 76115

Facilities to be Evaluated: (*Name, full Address, DMF No., and responsibility*)

For HFD 320 Use
Status & Date of Inspection:

1. Dermatological Products of Texas Inc — AC 6/17/91
2. 307 E. Josephine St., San Antonio Texas 78246 Manuf. & testing facility for drug product
3. _____
4. (b) (4) — (b) (4)
5. _____

2 ✱ REVISION

Other Information or Special Requests: See Oct 16, 1991 EER (ALSO no longer used as testing or manuf. facility).

****

For HFD-320 Use Only:

Date Received: 11/21/91

CGMP Compliance Status of Facilities Evaluated: Acceptable

CSO: Melissa Garcia — Date Completed: 12/5/91

Distribution: Original and First Copy: HFD-320
Remaining Copies: Requesting Office Use

FORM FDA 3274 (3/90)

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 11-14-1991

NDA NUMBER: 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☒ FDA

MADE: ☒ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Desonide

FIRM NAME: Owen/Galderma

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Ms. C. Shank

TELEPHONE NO.: 817-293-0450

Owen was called to verify that the ALCON facility was not used for a testing facility. the letter of 11-1-91 made it clear that ALCON was not to be used in any manufacturing capacity but not as a testing facility

Ms. Shank will post a letter tomorrow stating that ALCON will not be used as a testing or QC facility.

On the tel also from FDA R. Parnassham

SIGNATURE: Robert W. Trimmer, Ph.D. 11-14-91

Ref 11-14-91

DIVISION: Chemistry I, OGD

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE: 1984—421-976/7124

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: November 8, 1991

NDA NUMBER: 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☑ FDA

MADE: ☑ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Desowen

FIRM NAME: Owen/Galderma

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD:
Jack Davis
FDA
San Antonio, Texas

TELEPHONE NO.
PTS (8) 730-4528

We went over the 483 issues per my Review #5 of 10-18-1991. Mr. Davis feels after seeing my memo of Oct 16th that with ALCO out of the way the San Antonio facilities should be OK for AP.

SIGNATURE
Robert W. Trimmer, Ph.D.

DIVISION
Chemistry I, OGD

HFD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE: 1984-422-976/7124

AIRBORNE EXPRESS

Owen/GALDERMA
6201 South Freeway
P.O. Box 6600
Fort Worth, Texas 76115
(817) 293-0450
CHRISTINE E. SHANK
Manager
Regulatory Affairs

November 1, 1991

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

FDA GDIC AMENDMENT
AM

ATTENTION: Document Control Room
SUBJECT: ANDA 72-354
DESOWEN® Lotion, 0.05%

Dear Dr. Trimmer:

Reference is made to the October 23, 1991 deficiency letter for ANDA 72-354 which was received by the applicant on October 28, 1991.

With respect to this submission, the responses are complete for each of the itemized deficiencies. This amendment to the application is to be given consideration as a minor amendment as directed in the October 23, 1991 agency letter.

We appreciate your consideration of the information provided herewith and will continue to keep you apprised of the compliance activities and developments.

Sincere regards,

Christine E. Shank
Manager, Regulatory Affairs

CES/pc
Enclosures

RECEIVED
NOV 4 1991

ANDA 72-354

Owen/Galderma
Attention: Ms. Christine E. Shank
6201 South Freeway
P.O. Box 6600
Fort Worth, TX 76115

OCT 23 1991

Dear Madam:

Please refer to your abbreviated new drug application dated November 25, 1987 submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for DesOwen^{R} (Desonide) Lotion, 0.05%.

Reference is also made to your communications dated March 26, May 30, August 17, 1990, May 30, August 9, and August 14, 1991 amending this application, and new correspondence of May 19, 1989 and January 12, 1990. We also acknowledge your telephone conversation of August 9, 1991.

The application is deficient and therefore not approvable under Section 505 of the Act for the following reasons:

1. During the FDA inspection of your production facilities, Dermatological Products of Texas, it was learned, among other things, that at least two of your test batches were filled and QC tested at an unreported plant in Fort Worth, Texas. Please amend your application to include all details of previously unreported filling and testing operations at the ALCON facilities including all equipment, container/closure systems utilized, complete test batch records which include the filling process, etc. Please advise us if you intend to utilize this facility post-approval.

   Please be advised we await CGMP compliance status of the ALCON facilities.

2. Please submit time limits for the various phases of the drug product production. This must be done on the master batch record and mimic the process used to prepare the bioequivalency batch.

3. Please note that your SOP #108.1010 is considered too general. Please amend your application to include specific case procedures including supporting data or withdraw this SOP. After approval of this ANDA, you may supplement the application for reprocessing a batch of the drug product as per 21 *CFR* 314.70 (b)(2)(x).

The file is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a minor amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

RMPatel 10/21/91

(as revised)
12R
10/23/91

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #72-354
DUP/Division File
HFC-130/JAllen
HFD-600 Reading File
HFD-638/VSubramaniam VSubramaniam 10-18-91
HFD-634/MSmela/RTrimmer/10/17/91 Robert W. Trimmer 10-18-1991
HFD-634/VVashio/10/18/91 VVashio 10/18/91
R/D initialed by MSmela
cls/10/17/91/d:72-354.LTR M Smela 10/18/91
F/T by cls/10/18/91
Not Approvable

EER Update for AP

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Memorandum

Date October 16, 1991

From Division of Chem II, HFD-632

Requestor's Name K W TRIMMER Phone 295-8370

Subject ESTABLISHMENT EVALUATION REQUEST

To Division of Manufacturing & Product Quality (HFD-320)

Sterile Product _____ Non Sterile Product X

Application and Supplement No. 72-354

Brand Name *(if any)* DesOwen & Ointment

Establishment Name, Dosage Form and Strength Desonide Lotion, 0.05%

_____ Profile Class Code: OIN

Priority Classification: _____ *(See SMG BD-4820.3)*

Applicant's Name: Owen Pharmaceuticals

Address: 6701 S. Freeway, Ft Worth, TX

Facilities to be Evaluated: (*Name, full Address, DMF No., and responsibility*) **For HFD 320 Use** Status & Date of Inspection:

1. ALCON, Fort Worth, TX (filling, NDC # drug product)
2. Dermatological Products, Inc., 307 E. Johnson St. San Antonio, Texas 78206 (manufacturer of drug product) to 5305 Distribution Dr.
3. _____
4. (b) (4)
5. _____

Other Information or Special Requests: _____

****

For HFD-320 Use Only: Date Received: _____

CGMP Compliance Status of Facilities Evaluated: _____

CSO: _____ Date Completed: _____

Distribution: Original and First Copy: HFD-320
Remaining Copies: Requesting Office Use

FORM FDA 3274 (3/90)

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: October 15, 1991

NDA NUMBER: 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☒ FDA

MADE: ☒ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Des Owen Latin 0.05%

FIRM NAME: Owen / Galderma

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD:
Jack Davis, Supervisor
James H. Robinson
Gerald J. Berg
Field Investigators
San Antonio, TX

TELEPHONE NO.: 8-730-4528

and

Mike Smela
Br Chief, Branch II

Michael Smela Jr. 10/17/91

James Robinson & Gerald Berg, Field Investigators in San Antonio, TX were called this afternoon re the recent 483. Mr. Robinson called in his supervisor Jack Davis: Mike Smela & I conversed re the 5 items outlined in the memo of Aug 27, 1991 written to HFD-320

Item #1&2: We agreed there was a deficiency in that ALCO was used for the product filling & had not been incl. in this NDA. A NA letter will ask Item for specifics & an EER will be issued for the ALCON facilities.

Item #3: Regarding temperatures used for stability studies,
a. Accelerated was at 35° since the firm earlier reported to us that at above 37° (b) (4) of the lotion occurs.
b. Room temp. studies we recommend currently 25-30°. USP states 15-30°C. The firm would be told the feature RT is recommended at 25-30°.

Item #4: Regards 2 issues, namely, time limits on the manuf. phases and Batch Sizes.
a. We will ask the firm to supply time limits
b. The Field was told the Batch Sizes were adequate as per our guide #7790, the firm has pledged to a max. of (b) (4) kg.

Item #5: Re rework SOP
We will ask the firm to either rewrite specific case SOPs for the product for Drop the SOP # 108,1010 and come back after AP with supplements.

(#6 Not discussed being CGMP issue)

SIGNATURE

Robert W. Trimmer, Ph.D. 10-15-91

DIVISION: Chemistry I, OGD

HFD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE: 1984-422-976/7126

United States Government

MEMORANDUM

DATE: August 27, 1991

REPLY TO: Ann L.deMarco, CSO/ICEB/DMPQ/HFD-320

SUBJECT: REVIEW AND COMMENTS FOR EIR OF 6/17-21/91, ANDA 72-354

Dermatological Products of Texas
San Antonio, Texas
CFN 1628114

TO: OFFICE OF GENERIC DRUGS
THRU ACTING CHIEF ICEB/DMPQ/HFD-320

This report was classified as Bureau Pending and was referred to HFD-320 for review and comment. The following comments relate to the items listed on the FDA 483 and to the additional items discussed with management that were not reported on the FDA 483. These comments are to be forwarded with the EIR to the Office of Generic Drugs for their evaluation.

FDA 483 ITEMS:

483 #1&2 The CSO reports that two clinical lots formulated at the above referenced firm in San Antonio were subsequently filled and Q.C. tested at a different plant in Ft. Worth, Texas.

Comments: According to the ANDA page 03-0088, commercial product is to be manufactured only at San Antonio. Therefore, comparability of the equipment and procedures between the bio batches and commercial production could not be completed at this plant site since filling of biobatches occurred elsewhere.

The following are additional comments based on the exhibits submitted with the report. First, the batch records do not show that the product was transferred from the formulation tank into drums and transported to the Ft. Worth plant. They also do not indicate that filling & Q.C. were performed off the plant site. This information was uncovered by the CSO through verbal comments made by the firm's personnel which, for at least one lot, was confirmed in a memo as having occurred. This type of information should obviously have been

part of the official batch record.

Second, the commercial batch records submitted with this EIR within Exhibit 26a, end after formulation. It is unclear whether or not their firm has established a filling procedure. The ANDA and associated batch records should describe the commercial process, including filling operations.

483 #3 Three items (a,b,c) are listed here, all of which relate to storage of stability samples. They indicate that the firm needs to update its SOP with correct temperatures for accelerated studies; it needs to change recorder charts at proper frequency and sign and initial charts per SOP.

Comments: The CSO does not report any impact on data related to the 483 comments, therefore, they appear to be minor record keeping deficiencies.

However, during a review of the firm's SOP for storage of stability samples (Exh 4), it was noted that the SOP states that controlled room temperature samples can be stored between (b)(4) 86°F. We question the use of a (b)(4) degree range for storing controlled temperature stability samples. Any product labeled with storage statements of (b)(4) 86°F should be stored at the highest temperature that will be stated on product labeling, i.e. 86°F (which is 30°C).

483 #4 This issue relates to a lack of time limits for various phases of production which the firm should establish as part of its process validation studies.

Comments: The following are additional comments relating to the validation report submitted with the EIR in reference to this 483 point. The firm conducted validation studies on two (b)(4) Kg batches from which they have determined the mix times, etc. They conclude that the "process" is validated. The commercial batch size, however, ranges up to (b)(4) Kg. We question if the validation of a (b)(4) Kg batch can assure proper parameters of mix times, etc, for a full scale lot.

483 #5 This 483 item references a minor record keeping discrepancy for documenting rework of a non-conforming batch.

Comments: While the explanation of a record keeping deficiency appears to be plausible, the key issue, we feel, concerns the presence of a general rework provision in the ANDA, i.e. SOP #108.1010. Rework procedures should be specific and be supported by data. If this is not the case, then rework procedures should not be

approved as part of the ANDA. A supplement should be required if the need for rework would arise.

483 #6 This item reports a discrepancy between the procedure actually used for sanitizing equipment and that in the firm's SOP.

Action: The firm should establish a correct sanitization procedure and should have validation data to support their choice. Microbial controls for this topical product are important since it is a water/oil emulsion which can support microbial growth in the water phase.

OTHER DISCUSSIONS WITH MANAGEMENT NOT REPORTED ON THE 483

1. The CSO states that the pH spec for the finished product was changed from (b)(4). The firm indicated that the reviewer was aware of this change but could not produce any documentation to confirm this.

Comments: The CSO states in the report that there are no bioequivalence studies to support the changed spec. This does not appear correct since data in batch records submitted with the EIR show that the two bio lots reviewed by the CSO (AHE-1911 & AIE-2059) had pH values of (b)(4) respectively. These levels appear to correlate to the new specification.

2. The CSO noted that the commercial batch records report batch sizes up to (b)(4) Kg but the ANDA states maximum batch size will be (b)(4) Kg.

Comments: Commercial batch records should be in agreement with ANDA commitments before approval is granted.

Ann L. deMarco
Ann L. deMarco, CSO

ANDA ACTION LETTER ROUTING RECORD

ANDA # 72-354
AADA #
Drug DesOwen (Desonide)
Dosage Form LOTION
Strength 0.05%
Applicant Owen Galderma
Manufacturing Site (s) Dermatologic Products of TEXAS, SAN ANTONIO TX
Proposed Action (AP) AE

Original Rec'd date 4/27/87
Amendment Date(s) 6/24/88, 11/28/88, 4/18/89
Chemistry Reviewer R. Trimmer 3/26/90
Supervisor R. Patel 5/30/90
Bio Reviewer D. Bostwick DAIDP 8/7/90
Supervisor C. Evans DAIDP 5/30/91
Patent Certification H I 8/9/91
8/14/91

REVIEWER:	RECEIPT	ACTION
1. R. Pollock, M.S. Chief, Program Support Staff Comments: EER update req 8/7/91	Date 8/26/91 Initials RP	Date 8/27/91 Initials RP
2. S. Dighe, Ph.D. Director, Bioequivalence Comments: The firm's ANDA (#72-354) was originally approved to manufacture its lotion at pH (b)(4) It has determined that at pH (b)(4) the lotion product is more stable and wants to manufacture it at pH . The Div. of Anti-Infective drug products has determined that there would be no problems. As such waiver of BIE study (clinical) study appropriate & granted	Date 8/27/91 Initials SDW	Date 8/27/91 Initials SDW
3. K. Johnson, M.S. Associate Director Office of Generic Drugs Comments: Labeling Satisfactory. This is the first Desonide Lotion to be approved.	Date 8/28/91 Initials TOJ	Date 8/28/91 Initials TOJ
. R. Jerussi, Ph.D. Acting Director (Chem) DGD Comments:	Date Initials	Date Initials
5. D. Hare Office of Generic Drugs Comments:	Date Initials	Date Initials
6. Office Level Bio Review Comments:	Date Initials	Date Initials
7. R. Williams, M.D. Director Office of Generic Drugs Comments:	Date Initials	Date Initials

LETTER SIGNED: _____
(Date)

(C:Forms)

ANDA Approval Summary

72-354 — ANDA Number
Owen/Galderma — Applicant Name

Desonide — Established Name of Drug
Lotion — Dosage Form
0.05% — Strength
(Physicians Package) (b) (4) 4, 2 + 4 fl. oz, — Container size(s)

	Date Found Satisfactory	Comment
Labeling	7-23-91	Peri S.
Chemistry, Manufacturing, and Controls	8-15-91	RW. Trimmer
GMP's	Awaiting Update	
Manufacturer - Finished Dosage Form	8-7-91	Owen/Galderma Laboratories
Outside Facilities		(b) (4)
Manufacturer(s) - Active Ingredient(s)		

RW Trimmer — Chemist Reviewer — 8-15-91 — Date
RK Cadd, Ph.D. Pending EIR — Branch Chief — 8/16/91 — Date

Petition Required — No ___ Yes ✓ — Petition Affords 9/10/87 87P-0105/CP

Li d Drug Information 505(j)(2)(A) — 12/2/87 — all forms 11/25/87 submission

Patent Certification 505(j)(2)(B) — 12/2/87 — IP I no patents

Date Patent/Exclusivity Expires (if applicable) — N/A

Bioequivalence Section

Dissolution Required? — No ✓ Yes ___ : DB ___ DGD ___

In vivo study(s) required? — No ___ Yes ✓

Study(s) Found Acceptable — Vasoconstrictor assay and Clinical evaluation acceptable by the Division of anti Infective Drug Products all review of 7/26/89. Signed off 8/29/89

~~Waiver Request Granted~~

Total Bioequivalence Requirement Met — 7/26/89

Robert Pollock — Administrative Reviewer — 8/27/91 — Date

Approved ___

Disapproved ___

Director, Division of Generic Drugs — Date

Comments:

OHRA

1763

From: FDA605 Delivered: Wed 21-Aug-91 16:29 EDT Sys 157
Subject: DESONIDE LOTION
Mail Id: IPM-157-910821-148361302

TO: Compliance Evaluation Staff (HFD-320)

INFO: MPQAS (HFC-120)
RFDD (HFR-MA1), Richard Davis

FROM: Mary Woleske, Acting District Director
Dallas District (HFR-SW100)

DATE: August 19, 1991

SUBJECT: ANDA 72-354, Desonide Lotion 0.05%

Establishment: Dermatological Products of Texas, Inc.
San Antonio, Texas

Inspection of Dermatological Products of Texas, June 17-21, 1991, covered ANDA 72-354, Desonide Lotion 0.05%, and the EIR was referred to HFD-300 for evaluation. HFD-320 was advised of inspectional findings on 7/15/91. Approval of ANDA will be dependent upon review of HFD-300. Dallas District is not aware of any adverse information concerning the manufacture of this product, and there is no ongoing inspection covering the product. We considered firm acceptable in Profile Classes LIQ and OIN during EI of 6/17-21/91.

(Robert J. Deininger for)

Mary Woleske

MW:JAK:esl

OUTGOING 08/21/#1 08/21/91 DAE

RECEIVED 8/21/91 AT 4:35 P.M. JMD

ORIGINAL

AIRBORNE EXPRESS

Owen/GALDERMA
6201 South Freeway
P.O. Box 6600
Fort Worth, Texas 76115
(817) 293-0450
CHRISTINE E. SHANK
Manager
Regulatory Affairs

August 14, 1991

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

72-354 AC

ATTENTION: Document Control Room
SUBJECT: DESOWEN® Lotion, 0.05%

Dear Sir or Madam:

Reference is made to telephone conversations with Dr. Robert Trimmer, FDA Reviewer, on August 12th, 13th, and 14th regarding the subject pending ANDA for DesOwen Lotion, 0.05%.

The enclosed communications are hereby formally submitted, in duplicate, as confirmation of the documentation provided by FAX to Dr. Trimmer for his review and consideration.

Sincerely,

Christine E. Shank
Manager, Regulatory Affairs

CES/pc
Enclosure

NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

NDA NUMBER: 72-354

DATE APPROVAL LETTER ISSUED:

TO: Press Relations Staff (HFI-40)

FROM:
- [x] Bureau of Drugs
- [ ] Bureau of Veterinary Medicine

ATTENTION

Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.

TYPE OF APPLICATION
- [ ] ORIGINAL NDA
- [ ] SUPPLEMENT TO NDA
- [x] ABBREVIATED ORIGINAL NDA
- [ ] SUPPLEMENT TO ANDA

CATEGORY
- [x] HUMAN
- [ ] VETERINARY

TRADE NAME *(or other designated name)* AND ESTABLISHED OR NONPROPRIETARY NAME *(if any)* OF DRUG:
DesOwen® (Desonide)

DOSAGE FORM:
Lotion 0.05%

HOW DISPENSED
- [x] RX
- [ ] OTC

ACTIVE INGREDIENT(S) *(as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)*

Desonide

NAME OF APPLICANT *(Include City and State)*
Owen/Galderma Laboratories, Inc.
6201 South Freeway
PO Box 6600
Fort Worth, TX 76115

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY
Corticosteroid, topical

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

FORM PREPARED BY

NAME: David Dimmer, PhD.

DATE: 8-15-1991

FORM APPROVED BY

NAME: Reid, Ph.D. Concurs EI report

DATE: 8-16-91

FORM FD 1642 (2/75) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 8-13-91 and 8-14-91

NDA NUMBER: 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☒ APPLICANT/SPONSOR ☐ FDA

MADE: ☐ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Desonide Lotion 0.05%

FIRM NAME: Owen

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Ms. C. Shank

TELEPHONE NO.: 817-551-8516

Regarding Owen's letter of Aug 17, 1990 - Section E (p. 7 of 33) Limits of Degradation of Desonide

Specifications: "Total degradation products not more than (b)(4)% Label".

Ms. Shank was told this was too high to be acceptable. Last June 28, 1990 she was told typical spec. might be a max. of (b)(4)% total degradation products.

I told her that the results (p. 2 May 30, 1990) for 1.6 yr RT. Stability were only (b)(4)% so ∴ (b)(4)% max. is not unreasonable.

Raw Mat. specs., I was told, allow for no single (b)(4) impurity more than (b)(4)%; related foreign (b)(4) not more than (b)(4)% total."

Listening was Mr Carlos Straw = . CS

8-14-91

Ms. Shank called this AM; I returned the call later in the AM. 11:30.

I suggested getting the NDS cleaned up to meet (b)(4)% (not (b)(4)%) assay. I can then recommend acceptance of up to (b)(4)% total impurities with (6 month exp. dating in Stability Protocol Amendment.

Ms. Shank would agree to this & will fax & send hardcopy of amended protocol.

SIGNATURE: Ted C. Mirmo, Ph.D. Washington

DIVISION: Chem, II, OGD

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE: 1984—422-976/7126

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 8-12-1991

NDA NUMBER: 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☑ APPLICANT/SPONSOR ☐ FDA

MADE: ☑ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: DesOwenkotion

FIRM NAME: Owen/Galderma

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Ms. Shank

Ms. V. Voshio, CSO on the line here.

TELEPHONE NO.: 817-551-8516

Ms. Shank at Owen/Galderma was called today to obtain verification that:

1. In the two stab. lots. for 2+4 fl. oz. containers they are indeed the same (b) (4) as described in the Contain section of the Appl.? Describ manuf. and numbers.

2. Re stab. lot # 53540791 for (b) (4) containers. Are they produced by Alcon" or for Alcon by (b) (4) PE foam #

SIGNATURE: (b) (4)

DIVISION: Gen. Chem. II, OGD

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE: 1984-422-976/7126

3.1 ORIG

AIRBORNE EXPRESS

Owen/GALDERMA
6201 South Freeway
P.O. Box 6600
Fort Worth, Texas 76115
(817) 293-0450
CHRISTINE E. SHANK
Manager
Regulatory Affairs

August 9, 1991

AC

NDA ORIG AMENDMENT

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ATTENTION: Document Control Room
SUBJECT: ANDA 72-354
DESOWEN® Lotion, 0.05%

Dear Sir or Madam:

Reference is made to telephone conversations with Dr. Robert Trimmer, FDA Reviewer, on August 7th and 9th regarding the subject pending ANDA for DESOWEN® Lotion, 0.05%.

Pursuant to these conversations, the applicant submits herewith the requested information for Dr. Trimmer's review and consideration.

Sincerely,

Christine Shank

Christine E. Shank
Manager, Regulatory Affairs

CES/pc
Enclosure

DESK COPY: Dr. Robert Trimmer
HFD-634, Room 229

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: August 9, 1991

NDA NUMBER: 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☒ APPLICANT/SPONSOR ☐ FDA

MADE: ☒ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: DesOwen Lotion 0.05%

FIRM NAME: Owen/Galderma

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Ms. Christine Shank

TELEPHONE NO.: 817-551-8516

I called Ms. Shank of Owen/Galderma twice this AM. Faxed her on the FAX re renewal of (b) (4) + Stability data.

1. I told her the 35° accel. studies was not sufficient for (b) (4) exp. dating + would need min. of 6 month/35° & would need to show us with data that 40° is destructive of the Lotion (b) (4) She is willing to accept (b) (4) month exp. dating — they have (b) (4) months R.T. stability which they will send next week (just on the (b) (4) mL physicians' bottles).

2. The batch ticket for the (b) (4) kg is really to be sent with declaration this production batch will be made by the same process + same or comparable equipment.

3. They have revised the Stability data sheets to list the containers "as their sides or inverted" for said studies + will incl. data such as NDS used, better description of containers/closures + dates when stabilities were analyzed will be done.

On the line also was Mrs. Shirley Brown

SIGNATURE: Ted Berry

DIVISION: Chem. II, OGD

FORM FD 2587 (11/77)

DIVISION FILE

U.S. GOVERNMENT PRINTING OFFICE: 1984-422-976/7126

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: August 7, 1991 (and 8)

NDA NUMBER: 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☒ APPLICANT/SPONSOR ☐ FDA

MADE: ☒ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: DesOwen Lotion

FIRM NAME: Owen/Galderma

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Ms. Christine Shank

TELEPHONE NO.: 817-293-0450
817-551-8516

Called Ms. Christine Shank of Owen Labs Manager Reg. Affairs:

1. Need stability data from test batches for the (b) (4) mL containers.
Ms. S. stated it was submitted 6-6-88. Stab. data however, only from pilot batch. She called back saying will send new data on new (b) (4) kg production batch.
will state same process equipment, if OK Dr. Patel
2. We need batch ticket for projected (b) (4) kg production batch and also executed batch records for test batches #AHE-1911 and #AIE-2059.
OK. She will send.

3. Withdraw (b) (4) as an alternate supplier of the NDS as there is no stability nor batches to report.
Yes, Owen will withdraw (b) (4).

4. Describe how containers were positioned during stability studies.
She didn't agree with containers to be on sides or inverted but would commit to changing stability protocol
they don't know how containers were earlier positioned nor had they been told by any previous Reviewers.

SIGNATURE: R. D. Wilkin Jr.

DIVISION: Div. Chem. II, OND

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE: 1984-422-976/7126

EER UPDATE for APPROVAL

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

1763

Memorandum

Date August 7th 1991

From Division of Chemistry II (OGD) — HFD- 634

Requestor's Name Robt TRIMMER — Phone 295 8370

Subject ESTABLISHMENT EVALUATION REQUEST

To Division of Manufacturing & Product Quality (HFD-320)

Sterile Product _____ Non Sterile Product ✓

Application and Supplement No. 72-354

Brand Name *(if any)* DesOwen® Lotion

Establishment Name, Dosage Form and Strength Desonide, Lotion, 0.05%

Profile Class Code: O/N

Priority Classification: EER Update for AP *(See SMG BD-4820.3)*

Applicant's Name: Owen Labs, Div. of Dermatological Products of Texas, Inc.

Address: 6201 South Freeway, Fort Worth, TX 76134

Facilities to be Evaluated: *(Name, full Address, DMF No., and responsibility)* **For HFD 320 Use**

(b) (4) Dermatological Products of Texas, Inc. (b) (4) Date of Inspection:

DPTS 1. San Antonio, TX 78296 (non-Drug Produ

(b) (4) (b) (4)

4. _____

5. _____

Other Information or Special Requests: _____

****

For HFD-320 Use Only: Date Received: AUG 8

CGMP Compliance Status of Facilities Evaluated: Unacceptable (see attached memo + EIR

CSO: MHampton Date Completed: 9/16/91

Distribution: Original and First Copy: HFD-320
Remaining Copies: Requesting Office Use

FORM FDA 3274 (3/90)

FR
Container labels, carton and package insert labels satisfactory. Purifoy 1-23-91
Jerry Phillips 7/26/91

CERTIFIED MAIL P 672 235 188
Return Receipt Requested

May 30, 1991

Owen/GALDERMA
6201 South Freeway
P.O. Box 6600
Fort Worth, Texas 76115
(817) 293-0450
CHRISTINE E. SHANK
Manager
Regulatory Affairs

Office of Generic Drugs
CDER, FDA
MPN II, HFD-600
5600 Fishers Lane
Rockville, Maryland 20857

RE: ANDA 72-354/AMENDMENT
DesOwen (Desonide) Lotion, 0.05%

Dear Sir or Madam:

Reference is made to our pending Abbreviated New Drug Application for DesOwen (Desonide) Lotion, 0.05%. Reference is also made to your correspondence dated March 7, 1991 (copy enclosed), requesting additional information regarding Dermatological Products of Texas, Inc. (DPT, Inc.) as a contract manufacturer for Owen/Galderma Laboratories, Inc. (Owen/Galderma).

Please find enclosed the information and commitments requested in your March 7, 1991 correspondence. In addition, we are providing Final Printed Labeling which has been revised to accurately reflect the manufacturer and distributor relationship now in effect between DPT, Inc. and Owen/Galderma.

Further, with regard to the approval process for this application, we have been in contact with both the Dallas District Office and the San Antonio Resident Inspection Post concerning the scheduling of the pre-approval inspection. We are now anticipating the inspection of the DPT, Inc. operations relative to production of this product to be conducted during the week of June 17.

It is our sincere hope that you will find the enclosed information and commitments satisfactory and complete. And, it is anticipated that this submission along with a satisfactory pre-approval inspection report will serve to complete the review and approval process for this application. If, however, there are any questions, I would appreciate a call (817) 551-8516.

Sincerely,

Christine Shank
Christine E. Shank
Manager, Regulatory Affairs

CES/pc
Enclosures

7/26
Bob,
I have completed the labeling part + also the labeling approval sheet. Puri

RECEIVED
JUN 4 1991
GENERIC DRUGS

MAR 7 1991

ANDA 72-354
80-426
80-442
80-443
NDA 19-106
AADA 62-522

87-644
84-698
87-204
71-425

Owen/Galderma
Attention: Christine Shank
6201 South Freeway
P.O.Box 6600
Fort Worth, TX 76115

Dear Madam:

Reference is made to your correspondence dated November 27, 1990, informing the Agency that the manufacturing plant in San Antonio, Texas, used in the production of certain of your approved products has been purchased by Dorman-Feik Acquisitons Corporation and that the site will continue to manufacture those products under the approved specifications in the above referenced applications. The new owners will operate this facility under the name of Dermatological Products of Texas.

Reference is also made to the January 15, 1991 telephone conversation between yourself and Mr. John Dawson, Review Support Staff, Office of Generic Drugs concerning this matter.

Please be advised that the Agency views Dermatolgical Products of Texas as a contract manufacturer. Since there has been no transfer of the applications to that group, you must supplement all of your applications for this change. You should provide the following information as a part of those supplemental applications:

1. A commitment from the contract manufacturer that all commitments made in the applications will be followed in the manufacture, control and testing of the drug product. A commitment should also be provided indicating the contract manufacturer will notify the application holder prior to initiating any change that would require prior approval under 21 CFR 314.70 and that such changes will not be implemented prior to obtaining Agency approval for the proposed change.

2. Identify the responsible individuals at the contract facility.

3. Provide information regarding any change in equipment.

4. The applicant may provide right of reference to the contract manufacturer, should the information in the applications be the same information that would be required to be submitted by the contract manufacturer to verify that the promises, equipment, and conditions of manufacturer are the same as those in the applications.

5. The contract manufacturer must address environmental assessment considerations.

6. Please provide a complete description of functions of the contract manufacturer in regard to the functions previously conducted by the applicant and the functions now to be performed by the contract manufacturer (e.g., will the contractor be responsible for manufacturing, packaging, labeling and testing as was the applicant?).

Please be aware that the applicant is responsible for submitting all required information in proper format to the applications. In addition, upon review of the information listed above the Agency may determine that additional information will be required prior to approval of any supplemental application requesting such a change.

You should prepare and submit supplemental applications for each of the applications for which this change is pertinent. Please let us have your response promptly.

Sincerely yours,

Robert A. Jensen 3/6/91

Acting Director
Divisions of Chemistry I and II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 72-354, 80-426, 80-442, 80-443, 87-644, 84-698, 87-204, 71-425
NDA 19-106
AADA 62-522
DUP/Division File
HFD-82
HFD-634/RPatel/RTrimmer/2-15-91 (2 copies)
HFD-634/RPatel/RPermisohn/2/15/91
HFD-634/RPatel/KFurnkranz/2/15/91
HFD-634/RPatel/SSherken/2/15/91
HFD-634/RPatel/JPeichocki/2/15/91
HFD-633/Kishore/PSchwartz/2/15/91
HFD-635/JHarrison/VWalton/2/25/91
HFD-635/JHarrison/RAdams/2/15/91
HFD-632/RPollock/2-15-91
HFD-600/Reading File
R/D initialed by GJohnston
bcw/2-15-91/72354mul.tra
F/T by bcw/3-1-91
Transfer of ownership

GJohnston 3/4/91

2.1 ORIG

AIRBORNE EXPRESS MAIL
#824-076-514

August 17, 1990

Owen/GALDERMA
6201 South Freeway
P.O. Box 6600
Fort Worth, Texas 76115
(817) 293-0450
CHRISTINE E. SHANK
Manager
Regulatory Affairs

Division of Generic Drugs
ATTENTION: Document Control Room
HFD-630, Room 17B-20
Food and Drug Administration
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, Maryland 20857

AC

NDA ORIG AMENDMENT

RE: ANDA 72-354/Amendment
DESOWEN (Desonide) Lotion 0.05%
Response to Chemistry Review Comments

Gentlemen:

Reference is made to a telephone conversation with Dr. Robert Trimmer and Dr. Joseph Piechocki on June 28, 1990 regarding the pending application for DesOwen (Desonide) Lotion, 0.05%.

The applicant submits herewith a response to each of the four comments described by and discussed with Drs. Trimmer and Piechocki. We anticipate that the reviewer will recognize the significant improvements made with regard to the chemistry for detection of potential degradation products and the significance of the proposed product pH profile. If, however, the reviewer wishes to discuss any technical questions or concerns with our chemist, I will be happy to make arrangements for a conference call. Please do not hesitate to contact me if I can be of assistance (817)/551-8516).

Sincerely,

Christine Shank

Christine E. Shank

CES/st

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: June 28th 1990

NDA NUMBER: 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☐ FDA

MADE: ☒ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: DesOwen (Desonide) Lotion 0.05%

FIRM NAME: Owen Laboratories Fort Worth, Texas

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Ms. Christine E. Shank

Dr. R. Trimmer/Dr. J. Pisciotta

TELEPHONE NO.: (817) 293-0450

"In conversation with Ms. Shank of Owen Laboratories was in response to her communications of May 30th 1990 re DesOwen (Desonide) Lotion, 0.05%.

Comment #1 regarding testing for degradation products, she was told that Owen is required to use a validated stability-indicating procedure to monitor for the degradation products which procedure is capable of measuring, quantifing & reporting said degradation products as part of the stability program

Comment #2 regarding the setting of limits for the degradation products Ms. Shank was told that based on their data a typical specification might be (b) (4) % total (max.). degradation products.

Comment #3 regarding pH range, Ms. Shank was asked to justify with data their pH range of (b) (4) since all Owen's data shows only an acidic range of (b) (4) to (b) (4) (lot #53540720; 4 oz. bottle).

Ms. Shank said they will respond after consulting with their people.

cc: Dr. R. Patel

SIGNATURE: Donald W. Trimmer, Ph.D.

DIVISION: DGD

FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE: 1984-422-976/7126

Owen

ALLERCREME

OWEN LABORATORIES
ALLERCREME HYPO-ALLERGENIC COSMETICS

DIVISIONS OF
DERMATOLOGICAL PRODUCTS OF TEXAS, INC.

CHRISTINE E. SHANK
Manager
Regulatory Affairs

AIRBORNE EXPRESS
A/B 519859222

May 30, 1990

ORIG NEW CORRES

Division of Generic Drugs
Attention: Document Control Room
HFD-630, Room 17B-20
Food and Drug Administration
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, Maryland 20857

RE: ANDA 72-354
DESOWEN (Desonide) Lotion 0.05%

Gentlemen:

Reference is made to two telephone conversations on April 6, 1990 and May 10, 1990 with Dr. Sumer Dugar regarding the pending application for DesOwen (Desonide) Lotion, 0.05%.

In the conversations, Dr. Dugar commented that since it appeared that the desonide in DesOwen Lotion may be degrading the applicant should identify the degradation product, set limits and provide for routine analysis. Based on the data and information currently available to the applicant, please find enclosed a response to the comments. If, after Dr. Dugar has had an opportunity to review the enclosed information, there are any technical questions or concerns which he would like to discuss with our chemists directly, we would be happy to make arrangements for a conference call.

If, of course I can be of further assistance, please do not hesitate to give me a call (817/551-8516).

RECEIVED

MAY 3 1 1990

GENERIC DRUGS

Sincerely yours,

Christine Shank
Christine E. Shank

CES/db
Enclosure

Desk Copy: Dr. Sumer Dugar

DPT

OWEN/ALLERCREME
6201 SOUTH FREEWAY FORT WORTH, TEXAS 76134 (817) 293-0450

AN ALCON/NESTLÉ, L'ORÉAL AFFILIATE

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 5/11/90

NDA NUMBER: ANDA 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☐ FDA

MADE: ☒ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Des Owen (Desoinide) Lotion 0.05%

FIRM NAME: Owen Laboratories

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Ms. Christine E. Shank

Dr. Sugar / Dr. Patel

TELEPHONE NO.: (817) 293-0450

This is a follow up to our call of 4/6/90 to get some time frames from the firm for the submission of the information requested.

Ms. Shank has indicated that they are in the process of procuring pure ((b) (4)) material of the degradation product and as soon as it arrives analytical work will be undertaken to collect & submit data / information. She indicates to get in touch with us in about a week or so if any problem develops.

S.

cc: Dr. Patel

SIGNATURE: Sugar

DIVISION: DGD

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE-1984-422-976/7726

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 4/6/90

NDA NUMBER: ANDA 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☒ FDA

MADE: ☒ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: DesOwen (Desonide) Lotion 0.05%

FIRM NAME: Owen Laboratories

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Ms. Christine E. Shank

Dr. Dugar/ Dr. Patel

TELEPHONE NO.: (817) 293-0450

As a follow-up to our telephone call dated 3/12/90, firm submitted the ~~required~~ information asked for. However answer to Q3 was evative. The specific request was to respond if degradation is apparent in the stability testing (gradual decline in potency is noted). The response was "the data indicates that the active ingradient remains within specifications". This was discussed with Dr. Patel and I was advised to call the firm to clarify this issue.

This call was made to re-emphasize the issue and requested firm to respond. If degradation product(s) are visualized (or apparent), firm need to develop analytical methods for the detection/quantitation of the degradation product(s), include the analysis for degradation product(s) in their stability testing protocol and set limits. Also advised to refer to Center's Stability guidelines (page 13) for the requirements if degradation is apparent.

cc: Dr. Patel

SIGNATURE

DIVISION: DGD

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE-1984-432-976/7126

Owen

ALLERCREME

OWEN LABORATORIES
ALLERCREME HYPO-ALLERGENIC COSMETICS

DIVISIONS OF
DERMATOLOGICAL PRODUCTS OF TEXAS, INC.

CHRISTINE E. SHANK
Manager
Regulatory Affairs

AIRBORNE EXPRESS
A/B 470615434

ORIG NEW CORRES

March 26, 1990

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Generic Drugs (HFD-230)
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, Maryland 20857

RE: ANDA 72-354
DESOWEN (Desonide) Lotion 0.05%

Gentlemen:

Reference is made to a telephone conversation on March 12, 1990 with Dr. Sumer Dugar regarding the subject drug product.

Dr. Dugar relayed five additional review comments to which we are responding with this submission. Please find enclosed, by itemized comment, the requested information and data.

We sincerely appreciate the opportunity to discuss these concerns directly with Dr. Dugar and eagerly anticipate the conclusion of the review for this application.

Sincerely,

Christine Shank

Christine E. Shank

CES/db
Enclosure

Desk Copy: Dr. Sumer Dugar

RECEIVED
MAR 27 1990
GENERIC DRUGS

DPT

OWEN/ALLERCREME
6201 SOUTH FREEWAY FORT WORTH, TEXAS 76134 (817) 293-0450

AN ALCON/NESTLÉ, L'ORÉAL AFFILIATE

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 3/12/90

NDA NUMBER: ANDA 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☒ FDA

MADE: ☒ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Des Owen (desoniide) Lotion 0.05%

FIRM NAME: Owen Laboratories

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Ms. Christine E. Shank Mgr. Regulatory Affairs

Dr. Dugar/ Dr. Patel

TELEPHONE NO.: (817) 293-0450 called twice

cc: Dr. Patel

Review of ANDA ready for approval, at the request of Dr. Patel was scanned to ensure every aspect is possibly clearable for approval. Items need discussion with Dr. Patel were flagged, written and responded (by Dr. Patel). The following items were identified for clarification by the firm:

1. Commitment from Firm not to exceed Production batch size of (b) (4) kg.
2. Confirmation on the source of NDS used in manufacture of the clinical batch (RM Lot# A0436 used in (b) (4) kg batch)
3. Clarification on the # of batches manufactured. Batch ticket is only for one ~~lot~~ Batch. However there are 4 batches for stability data
4. Noted a decline in potency by about (b) (4) % at 25°-28°c in 26 weeks and similar decline in 12 weeks at 35°c. Need to clarify if degradation is apparent, if not explanation of this variability.

Firm is asked to send response & Packet by overnight Mail

3/12

SIGNATURE

DIVISION: DGD

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE-1984-432-976/7126

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 2/26/90

NDA NUMBER: 72-354

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☐ FDA

MADE: ☐ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Desowen (Desonide) Lotion 0.05%

FIRM NAME: Galderma

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Christine E. Shank

TELEPHONE NO.: 817-551-8576

I replied by phone to her 2/16/90 letter asking about status. I advised it had been hung up while we decided how to handle biowaivers that came out of DB. I advised the bio materials had now gone to the reviewing chemist for processing.

She thanked me for the reply.

SIGNATURE: M Feinberg

DIVISION:

FORM FD 2587 (11/77)

ORIGINAL IND/NDA

U. S. GOVERNMENT PRINTING OFFICE-1984-432-976/7126

AIRBORNE EXPRESS
A/B 204541562

January 12, 1990

ALCON LABORATORIES, INC.
6201 SOUTH FREEWAY
FORT WORTH, TEXAS 76134-2099
(817) 293-0450 TELEX 758320

Bruce Burlington, M.D.
Acting Director
Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research (HFD-230)
5600 Fishers Lane
Rockville, Maryland 20857

ORIG NEW CORRES

RE: ANDA 72-354
DESOWEN (Desonide) Lotion 0.05%

Dear Dr. Burlington:

Reference is made to our pending Abbreviated New Drug Application (ANDA 72-354) for DESOWEN (Desonide) Lotion 0.05% submitted on November 25, 1987. Please find with this letter, for ease of reference, a chronology of activities relating to this application.

Our application for DesOwen Lotion 0.05% is pending final FDA action which has now exceeded the 180 day statutory requirement. The application was complete with our amendment of April 18, 1989 including bioequivalence results and final printed labeling. Generic Drugs advised us in October 1989 of their receipt of the bioequivalence review by the Anti-Infective Drugs Division recommending approval.

This was the last substantive information we have been given despite numerous calls expressing our concern with regard to final review and approval action. It was finally suggested to us by Mr. Rosen last Friday that a written inquiry be made. While we are keenly aware of the diversions and distractions affecting activities within the Generic Drug Division we are quite anxious to know what to expect concerning this imminently approvable application. I would be pleased to take whatever action may be appropriate to move the application to final approval. If a telephone call or meeting can help resolve the impasse, I am available at (817)551-8920.

Sincerely,

William H. Hubregs, Ph.D.

RECEIVED
JAN 16 1990
GENERIC DRUGS

CES/db

cc: Document Control Room 17B-20 (HFD-230)
File

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO (Division/Office) D. Bostwick HFD-520 Div of Anti-Infective Drug Products			FROM: Div of Generic Drugs	
DATE 8/189	IND NO.	NDA NO. 72-354	TYPE OF DOCUMENT Vasoconstrictor Assay	DATE OF DOCUMENT 6/6/88
NAME OF DRUG Desowen (Desonide) 0.05% Lotion		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE

NAME OF FIRM
Owen Labs

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY _____
- ☐ PRE-NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER (Specify below)

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW	☐ CHEMISTRY
☐ END OF PHASE II MEETING	☐ PHARMACOLOGY
☐ CONTROLLED STUDIES	☐ BIOPHARMACEUTICS
☐ PROTOCOL REVIEW	☐ OTHER
☐ OTHER	

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILITY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL– BIOPHARMACEUTICS
- ☐ IN–VIVO WAIVER REQUEST

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/SPECIAL INSTRUCTIONS (Attach additional sheets if necessary)

Please review the vasoconstrictor assay and provide your comments and recommendations regarding a determination of bioequivalence based on the data submitted

Thanks

Sorry about the delay. This ~~assay~~ included in a chemistry response and was never brought to our attention until now

Note this product also is subject to a "clinical" bio study.

SIGNATURE OF REQUESTER 443 0193 Bob Pollock 17B25 HFD-232	METHOD OF DELIVERY (Check one) ☐ MAIL ☒ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

FORM FDA 3291 (7/83)

Owen

ALLERCREME

Orig

OWEN LABORATORIES
ALLERCREME HYPO-ALLERGENIC COSMETICS

DIVISIONS OF
DERMATOLOGICAL PRODUCTS OF TEXAS, INC.

CHRISTINE E. SHANK
Manager
Regulatory Affairs

CERTIFIED MAIL P-127-239-622
Return Receipt Requested

ORIG NEW CORRES

May 19, 1989

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Generic Drugs (HFD-230)
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, Maryland 20857

RE: ANDA 72-354
DESOWEN (Desonide) Lotion 0.05%

Gentlemen:

We acknowledge receipt on May 18, 1989 of your letter dated May 15, 1989 regarding the subject Abbreviated New Drug Application. Reference is also made to our amendment dated April 18, 1989.

Pursuant to the provisions of 21 CFR 314.120(e) the applicant extends to the Agency sufficient but reasonable time to complete the evaluation of the Clinical Bioequivalence Study submitted in an amendment to the application on April 18, 1989.

As regards labeling for the drug product, Final Printed container, carton and insert labeling (twelve examples each) were also provided in the April 18, 1989 amendment submission. It is our understanding that these items have been received by the Agency and are in queue for review.

In anticipation that the April 18, 1989 submission will be found satisfactory and complete the requirements for approval of this application, we hope to hear from you soon.

Sincerely yours,

Christine E. Shank

Christine E. Shank

CES/db
Enclosures

RECEIVED
MAY 2 0 1989
GENERIC DRUGS

DPT

OWEN/ALLERCREME
6201 SOUTH FREEWAY FORT WORTH, TEXAS 76134 (817) 293-0450

AN ALCON/NESTLÉ, L'ORÉAL AFFILIATE

MAY 15 1989

ANDA 72-354

Owen Laboratories
Division of Dermatological Products of Texas, Inc.
Attention: Ms. Christine Shank
6201 South Freeway
Forth Worth, TX 76134

Dear Madam:

Please refer to your abbreviated new drug application dated November 25, 1987, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for DesOwen (desonide) Lotion, 0.05%.

We acknowledge receipt of your communications dated November 16 and 28, 1988 and April 18, 1989 amending the application.

The application is deficient and therefore not approvable under Section 505 of the Act for the following reasons:

1. We await the evaluation of the Clinical Bioequivalence Study recently submitted. We will communicate with you upon completion of the evaluation.

2. Please prepare and submit final printed container labels and carton labeling. The package insert labeling as submitted is satisfactory, but we cannot request final printed insert labeling until the Bio data have been found satisfactory and we have had a chance for review and comment.

The file is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application, or if you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

Ken G. Johnson (for) 5/15/89

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drug Evaluation and Research

cc:
HFD-230, HFD-234
BTArnwine 5/10/89
R/D INIT. BY RPatel/MSeife
jth: 0009j 5/12/89
G. Johnston.

G. Johnston 5/12/89 per 2nd 5/15/89

Owen

ALLERCREME

OWEN LABORATORIES
ALLERCREME HYPO-ALLERGENIC COSMETICS

DIVISIONS OF
DERMATOLOGICAL PRODUCTS OF TEXAS, INC.

CHRISTINE E. SHANK
Manager
Regulatory Affairs

NDA ORIG AMENDMENT

FEDERAL EXPRESS
A/B 2561337332

AVAILABILITY MATERIAL

FPL

April 18,. 1989

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Generic Drugs (HFD-230)
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, Maryland 20857

RE: ANDA 72-354/Amendment
DESOWEN (Desonide) Lotion 0.05%
CLINICAL BIOEQUIVALENCE STUDY
FINAL PRINTED LABELING

Gentlemen:

Reference is made to our pending abbreviated new drug application, ANDA 72-354, for DesOwen (Desonide) Lotion 0.05%. Reference is also made to your letter dated November 14, 1988 and our response dated November 28, 1988 specifically as regards the matter of the Clinical Bioequivalence Study for the the drug product.

Please find enclosed the Clinical Monitor's Summary Report for the study conducted in patients with psoriasis comparing the proposed drug product, DesOwen (Desonide) Lotion 0.05%, with the listed drug product, DesOwen (Desonide) Cream 0.05%, to demonstrate bioequivalence. This study was conducted under Protocol C-88-52 submitted to this application on November 16, 1988.

Also, please find enclosed Final Printed labeling for the drug product. The Archival copy contains 12 examples of each item. Extra examples are provided in both the Technical Review and the Bioequivalence Review copies of this submission.

OWEN/ALLERCREME
6201 SOUTH FREEWAY FORT WORTH, TEXAS 76134 (817) 293-0450

AN ALCON/NESTLÉ, L'ORÉAL AFFILIATE

This submission constitutes completion of the outstanding issues relating to this application. We sincerely hope the Agency will undertake to expedite the review of this additional information to complete the approval of the application.

Sincerely yours,

Christine E. Shank

Christine E. Shank

CDS/db
Enclosures

Owen

ALLERCREME Orig

OWEN LABORATORIES
ALLERCREME HYPO-ALLERGENIC COSMETICS

DIVISIONS OF
DERMATOLOGICAL PRODUCTS OF TEXAS, INC.

CHRISTINE E. SHANK
Manager
Regulatory Affairs

CERTIFIED MAIL P 834-850-879
Return Receipt Requested

NDA ORIG AMENDMENT

DRAFT LABELING

November 28, 1988

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Generic Drugs (HFN-230)
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, Maryland 20857

RE: ANDA 72-354/Amendment
DesOwen (Desonide) Lotion 0.05%

Gentlemen:

We acknowledge receipt on November 22, 1988 of your letter dated November 14, 1988 regarding our pending ANDA for DesOwen Lotion 0.05%.

Please find enclosed herewith a response to each of the itemized review comments. The actions which are pending for completing this application review are submissions for final printed labeling and the bioequivalence study results. These items will be provided when the bioequivalence study is completed.

Sincerely,

Christine E. Shank

Christine E. Shank

RECEIVED
DEC 6 1988
GENERIC DRUGS

CES/db
Enclosure

OWEN/ALLERCREME
6201 SOUTH FREEWAY FORT WORTH, TEXAS 76134 (817) 293-0450

AN ALCON/NESTLÉ, L'ORÉAL AFFILIATE

Owen

ALLERCREME

OWEN LABORATORIES
ALLERCREME HYPO-ALLERGENIC COSMETICS

DIVISIONS OF
DERMATOLOGICAL PRODUCTS OF TEXAS, INC.

CHRISTINE E. SHANK
Manager
Regulatory Affairs

CERTIFIED MAIL P 834-850-872
Return Receipt Requested

NDA ORIG AMENDMENT

November 16, 1988

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Generic Drugs (HFN-230)
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, Maryland 20857

RE: ANDA 72-354/Amendment
DesOwen (Desonide) Lotion 0.05%
Bioequivalence Study Protocol

Gentlemen:

Reference is made to your letter dated July 1, 1988 regarding the bioequivalence study protocols submitted in our Abbreviated New Drug Application for DesOwen (Desonide) Lotion 0.05%. Reference is also made to a previous review letter dated May 18, 1988 requesting submission of our evaluation of the vasoconstrictor study for the subject drug product.

Please find enclosed herewith a new clinical study protocol, designated Protocol C-88-52, which proposes to compare the new drug product, DesOwen Lotion 0.05%, with the listed drug product, DesOwen Cream 0.05% in patients with psoriasis to demonstrate bioequivalency. In accordance with the Division of Anti-Infective Drug Products recommendations, the study will include a lotion vehicle comparison, global evaluation, randomized parallel groups of patients, and will be investigator blinded.

The study will be conducted under contract by TKL Research, Inc., Maywood, New Jersey. A copy of the responsibilities agreement with this contract facility is provided. Also provided is a curriculum vitae for Allan H. Greenspan, M.D. the investigator designated to conduct the study. The submission also includes formulation composition statements for each of the test materials as requested.

DPT

OWEN/ALLERCREME
6201 SOUTH FREEWAY FORT WORTH, TEXAS 76134 (817) 293-0450

AN ALCON/NESTLÉ, L'ORÉAL AFFILIATE

With regard to the vasoconstrictor assay, the applicant provided a complete evaluation of the study results in the June 6, 1988 amendment to the application. This submission was made in response to the Agency's comments and requests for additional information in the above referenced May 18, 1988 letter.

We would sincerely appreciate hearing from the Agency as soon as possible if there are any significant omissions or deficiencies in this new protocol as we intend to commence with the study this month.

Your time and consideration in review of this amendment is appreciated.

Sincerely,

Christine E. Shank

Christine E. Shank

CES/db
Enclosure

ANDA 72-354

NOV 14 1988

Owen Laboratories
Division of Dermatological Products of Texas, Inc.
Attention: Christine Shank
6201 South Freeway
Fort Worth, TX 76134

Dear Madam:

Please refer to your abbreviated new drug application dated November 25, 1987 submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for DesOwen (desonide) Lotion, 0.05%.

We acknowledge receipt of your communications dated June 6 and 24, 1988 amending the application.

The application is deficient and therefore not approvable under Section 505 of the Act for the following reasons:

1. We await the submission of the additional information requested as per our communication dated July 1, 1988 regarding the bioequivalence of the drug product.

2. Please revise the stability protocol to express the test stations in months rather than weeks.

3. We acknowledge the revisions made in the manufacturing instructions with more specific information. However, it would be preferred if the specific names of the equipment are given.

4. It fails to include in the labeling the following:

   Carton: We question your content statement. Your composition statement lists citric acid and/or sodium hydroxide as present in the formulation. However, the carton labeling indicates that these components <u>may</u> be present. Please comment.

   Container: See comment under carton labeling.

   Insert: See comment under carton labeling.

   We cannot request final printed copy until the issue regarding the composition has been resolved.

5. We await evaluation of the methods by the Dallas District Laboratory.

The file is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application, or if you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

for 11-14-88

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drug Evaluation and Research

cc:
HFD-234
GJohnston/Patel/BTArnwine
r/d Patel/MSeife
mlb 11/10/88 (1892b)
not approvable

11/10/88

11-10-88

Retyped 11/10/88

Owen ALLERCREME

OWEN LABORATORIES
ALLERCREME HYPO-ALLERGENIC COSMETICS

DIVISIONS OF
DERMATOLOGICAL PRODUCTS OF TEXAS, INC.

CHRISTINE E. SHANK
Manager
Regulatory Affairs

CERTIFIED MAIL P 469-888-949
Return Receipt Requested

June 24, 1988

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Generic Drugs (HFN-230)
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, Maryland 20857

RE: ANDA 72-354/Amendment
DesOwen® (Desonide) Lotion 0.05%
Samples Submission for Methods Validation

Gentlemen:

We acknowledge receipt, on June 14, 1988, of your letter dated June 8, 1988 requesting submission of finished dosage form samples for methods validation.

Please find enclosed a complete copy of our correspondence to Mr. James Burkel, HFR-SW160, and the information materials provided with the samples submission.

Sincerely,

C. Shank/db

Christine Shank

CES/db
Enclosure

DPT

OWEN/ALLERCREME
6201 SOUTH FREEWAY FORT WORTH, TEXAS 76134 (817) 293-0450

AN ALCON/NESTLÉ, L'ORÉAL AFFILIATE

ANDA 72-354

Owen Laboratories
Division of Dermatological Products of Texas, Inc.
Attention: Ms. Christine Shank
P.O. Box 6600
Fort Worth, TX 76115

JUL 1 1988

Dear Madam:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for DesOwen (Desonide) Lotion 0.05%.

Reference is also made to the protocols you submitted to establish the bioequivalence of the above product. The protocols have been reviewed by the Division of Anti-Infective Drug Products, HFN-815, and they have the following comments:

"Proposed Studies:

1. Vasoconstrictor Assay
   The vasoconstrictor assay is to be performed by Dr. R. B. Stoughton in volunteer subjects. The protocol is a standard one and is satisfactory.

2. Eczema Protocol
   The investigator for this study will be H.I. Katz, M.D.; Dr. Katz's qualifications have not been provided.

   A. Study design: This is an investigator-blinded, randomized, paired comparison of DesOwen Cream and DesOwen Lotion in 36 patients with bilateral cream.

   B. Patient selection: Males and females with a minimum age of 6 with varying degrees of bilateral eczema which could normally be treated with low-potency topical steroids.

   C. Treatment regimen: The medications are to be applied to affected areas three times daily, One medication will be applied to the left side of the body and the other to the right side. Medications will be color-coded (left side blue and right side yellow). The study is to continue for three weeks with four investigator evaluations; on prior to therapy and weekly thereafter.

3. Effectiveness parameters: Patients will be evaluated for erythema, scaling excoriations, pruritus, oozing/weeping, and overall severity on a scale of 0-9 as follows:

Clear	Mild	Moderate	Severe
0	1, 2, 3	4, 5, 6	7, 8, 9

Evaluation: This protocol presents two major difficulties: the choice of eczema as the disease to be treated, and the choice of a paired comparison methodology.

Topical steriods are normally required to show effectiveness in both atopic dermatitis and psoriasis prior to approval. If only one clinical study is to be performed, the more difficult indication (psoriasis) should be studied, since a product which is effective against psoriasis may be expected to also be effective against atopic dermatitis. On the other hand, effectiveness against atopic dermatitis does not necessarily indicate that a product will be useful in psoriasis.

In addition, parallel groups of patients should be studied (one group on cream, and the other on lotion). Use of the paired comparison technique greatly increases the chance of medication mix-up, especially if the patients themselves are to apply the drugs.

It is also felt that a global evaluation should be performed according to a scale of improvement from baseline (rather than the overall severity score on a scale of 0-9 as proposed by the sponsor). The global evaluation is intended to view the improvement of the patient over the length of therapy. The overall severity score would essentially reevaluate signs and symptoms which have already been evaluated individually.

A small vehicle group should also be included in order to assess the clinical effect of the excipients in the formulation.

Recommendation: The following general protocol is an example:

> The study should be an investigator-blinded comparison of DesOwen Cream (20 patients), DesOwen Lotion (20 patients) and lotion vehicle (10 patients). Parallel groups of patients with psoriasis are to be entered into the study for each treatment group in a randomized fashion. The patients should be comparable in terms of disease state, demographic characteristics, etc. The study should run for three weeks. Drug applications are to be three times daily with investigator evaluations prior to therapy and weekly thereafter.
>
> The effectiveness parameters proposed by the sponsor are satisfactory, except that the "overall severity" rating of signs and symptoms should be replaced by a global evaluation using the following scale:
>
> 1 = "Cleared" - 100% clearance of signs, except for residual discolorations.
>
> 2 = "Marked Improvement" - between 76% and 99% clearance of signs monitored.
>
> 3 = "Moderate Improvement" - 50% to 75% clearance of signs monitores.
>
> 4 = "Slight Improvement" - less than 50% clearance of signs monitored.
>
> 5 = "Exacerbation" - flare of sites monitored.

Data Reporting:

Data should be reported both in terms of weekly results and in terms of "endpoint"; that is, one set of data should view all patients at the last valid treatment visit. The endpoint evaluation is the best method of assessing the effect of patient dropouts. Signs and symptom scores should be reported individually and as a total score. Global evaluation should be reported as noted above. The qualifications of the investigator and the complete formulation of each test material should be submitted."

Please revise the protocol incorporating the above comments and resubmit it for our review. In addition, you are requested to contact Mr. David Rosen at 301-443-0193 to discuss the Eczema protocol.

Sincerely yours,

7/1/88

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drug Evaluation and Research

HFD-232
DRosen
kl/6-28-88/1557b
letter

Owen

ALLERCREME Orig

OWEN LABORATORIES
ALLERCREME HYPO-ALLERGENIC COSMETICS

DIVISIONS OF
DERMATOLOGICAL PRODUCTS OF TEXAS, INC.

CHRISTINE E. SHANK
Manager
Regulatory Affairs

CERTIFIED MAIL P469-888-946
Return Receipt Requested

NDA ORIG AMENDMENT

June 6, 1988

DRAFT LABELING

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Generic Drugs (HFN-230)
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, Maryland 20857

RE: ANDA 72-354/Amendment
DesOwen® (Desonide) Lotion 0.05%

Gentlemen:

Reference is made to your letter dated May 18, 1988 regarding the subject abbreviated new drug application.

Please find enclosed a response to each of the itemized review comments. In anticipation that the information provided will be found satisfactory, we hope to hear from the Agency soon regarding the other actions required for approval of this application.

Sincerely,

Christine E. Shank

Christine E. Shank

CES/db

RECEIVED
JUN 8 1988
GENERIC DRUGS

OWEN/ALLERCREME
6201 SOUTH FREEWAY FORT WORTH, TEXAS 76134 (817) 293-0450

AN ALCON/NESTLÉ, L'ORÉAL AFFILIATE

ANDA 72-354

Owen Laboratories
Attention: Christine E. Shank
6201 South Freeway
Fort Worth, Texas 76134

JUN 8 1988

Dear Madam:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505 of the Federal Food, Drug, and Cosmetic Act for DesOwen (desonide) Lotion, 0.05%.

In order for our laboratory to validate your submitted methodology, send the following materials to the address below:

Materials to be sent:

1. Finished dosage form - Send three times the amount needed to perform the required testing. Identify the lot number of the material sent.
2. A Certificate of Analysis for the lot sent.
3. Internal and Reference standards - Send three times the amount necessary to perform the required testing. (If you do not send the standard and the District doesn't have it, the analysis will be delayed).
4. Impurity Standards - send samples of standards for any impurities for which you test the dosage form.
5. Representative chromatograms and/or spectra (if applicable).
6. Completed Material Safety Data Sheet (Form OSHA 174).

Address:
Food and Drug Administration
Attention: Jim Burkel, HFR-SW160
3032 Bryan Street
Dallas, Texas 75204

These materials must be sent within 20 days of receiving this letter. If you cannot send these materials by this date, please notify the ANDA by letter. Send copies of all correspondence regarding the samples requested to the ANDA.

We recommend that you send the samples by registered mail/return receipt requested.

Sincerely yours,

6/8/88

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drug Evaluation and Research

cc: HFN-230, HFN-234 6/6/88
RPatel/BTArnwine
R/D INITIALED BY RPatel/MSeife
mstephens: 6/3/88 (505As)
Samples
Received 6/7/88

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

Memorandum

Date 5/25/88

From Scientific Coordinator
Division of Field Science (HFC-141)

Subject Validation Assignment: ANDA # 72-354
Drug: DESONIDE LOTION
Firm: OWEN LABORATORIES FORT WORTH, TX

To

BRENDA ARNWINE (HFN-234)

The subject ANDA validation has been assigned. Please instruct the firm to send the appropriate samples, methods, and standards as soon as possible to the following laboratory(ies).

1. Laboratory: DALLAS DISTRICT (HFR- SW160)
   Tests: USP Methods:

   Firm's Methods: ASSAY & PARABENS

   Special equipment or reagents needed to be supplied by firm:

2. Laboratory: (HFR-)
   Tests: USP Methods:

   Firm's Methods:

   Special equipment or reagents needed to be supplied by firm:

Thank you for your cooperation.

Thomas S. Savage

cc: R.M. PATEL (HFN-234)
JIM BURKEL (HFR- SW160)
(HFR-)

Owen

ALLERCREME

OWEN LABORATORIES
ALLERCREME HYPO-ALLERGENIC COSMETICS

DIVISIONS OF
DERMATOLOGICAL PRODUCTS OF TEXAS, INC.

CHRISTINE E. SHANK
Manager
Regulatory Affairs

CERTIFIED MAIL P469-888-957
Return Receipt Requested

May 6, 1988

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Generic Drugs (HFN-230)
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, Maryland 20857

DRUG NEW CODES

RE: ANDA 72-354/Amendment
DesOwen® (Desonide) Lotion 0.05%
STABILITY DATA SUBMISSION

Gentlemen:

As a first order of consideration the applicant requests that, prior to initiating the review of ANDA 72-354 for DesOwen® Lotion 0.05%, the Agency give priority to completing the review of our pending application for DesOwen® (Desonide) Ointment 0.05% (ANDA 71-425). The DesOwen Ointment application was submitted on July 14, 1986 and has undergone a complete and thorough Review, Comment, and Amendment process in the intervening time. Our last amendment was submitted on January 27, 1988 which should enable completion of all the review activities and allow for final approval of this application. We greatly appreciate the Agency's consideration of this request.

With regard to ANDA 72-354 for DesOwen (Desonide) Lotion 0.05%, the applicant submits herewith in accordance with our commitment, the current available stability data from the three month accelerated studies described in the protocol found in Item 3.B.(9) of the original application submission. A summary of the studies conducted to date and a proposed expiry dating for initial production batches are provided on the following page.

Thank you for your time and consideration in review of these applications.

Sincerely,

Christine E. Shank

Christine E. Shank

CES/db
Enclosure

RECEIVED
MAY 12 1988
GENERIC DRUGS
Desk Copy: David Rosen
(HFN-230) Room 17B-25

DPT

OWEN/ALLERCREME
6201 SOUTH FREEWAY FORT WORTH, TEXAS 76134 (817) 293-0450

AN ALCON/NESTLÉ, L'ORÉAL AFFILIATE

ANDA 72-354

Owen Laboratories
Divisions of Dermatological Products of Texas, Inc.
Attention: Christine Shank
6201 South Freeway
Fort Worth, Texas 76134

MAY 18 1988

Dear Madam:

Please refer to your abbreviated new drug application dated November 25, 1987, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for DesOwen (desonide) Lotion, 0.05%.

We acknowledge receipt of your communication dated December 11, 1987 amending the application.

The application is deficient and therefore not approvable under Section 505 of the Act for the following reasons:

1. It fails to define the "suitable" equipment used in the manufacturing instructions. Please identify each piece of equipment used throughout the manufacturing process in lieu of stating suitable.

2. It fails to include Certificates of Analysis for each of the raw materials used in the drug product. Please submit the Certificates of Analysis from either the vendor or the Quality Control laboratory.

3. We await the submission of the challenge condition stability data and data from cycling studies.

4. We also await the evaluation of the vasoconstrictor study to show the bioequivalence to the reference product.

5. It is recommended that the potency of the drug product be expressed as a percent weight/volume rather that weight/weight. Please comment.

6. It fails to include in the labeling the following:

   Carton: Not Satisfactory

   1. fl oz (rather than "Fl. Oz.")

   2. Usual dosage - 2 or 3 times (rather than "2 to 3 times")

   3. Professional Samples Carton

      "...86°F (30°C). Avoid Freezing."
      (not (b) (4) °F")

Container: Not Satisfactory
(2 fl oz, 4 fl oz, 8 mL Sample)

1. See A. 1. (2 fl oz, 4 fl oz)

2. See A. 2.

Insert: Not Satisfactory

1. CLINICAL PHARMACOLOGY (Pharmacokinetics)
Paragraph 3, line 4 - Corticosteroids...

2. HOW SUPPLIED

Revise "Storage" statement to read, "Store below 86°F (30°C). Avoid Freezing."

Please revise the labels and labeling as above. We cannot request final printed copy until the question regarding expression of potency has been resolved.

The file is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application, or if you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

Rent C Johnston for 5-18-88

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drug Evaluation and Research

cc: HFN-230, HFN-234 BJ 5/17/88
GJohnston/RPatel/BTArnwine
R/D INITIALED BY RPatel/MSeife
mstephens: 5/17/88 (4966s)
Not approvable

GJohnston 5/17/88

RPatel 5/17/88

Owen

ALLERCREME

OWEN LABORATORIES
ALLERCREME HYPO-ALLERGENIC COSMETICS

DIVISIONS OF
DERMATOLOGICAL PRODUCTS OF TEXAS, INC.

CHRISTINE E. SHANK
Manager
Regulatory Affairs

CERTIFIED MAIL P-555-982-209
Return Receipt Requested

ORIG NEW CORRES

December 11, 1987

Food and Drug Administration
Center for Drugs and Biologics
Division of Generic Drugs
Attention: Document Control Room
HFN-230, Room 17B-20
5600 Fishers Lane
Rockville, Maryland 20857

RE: ANDA 72-354/Amendment
DesOwen® (Desonide) Lotion 0.05%

Gentlemen:

Reference is made to a recent (December 2, 1987) telephone conversation with Mr. Robert Pollock, CSO, Generic Drugs Division, regarding the subject Abbreviated New Drug Application submitted on November 25, 1987.

In accordance with Mr. Pollock's request, we are amending our application to delete references to the Type I Drug Master File #1229 for Dermatological Products of Texas, Inc. In place of the DMF reference, a revised "Manufacturer" section (Item 3.B.(4), page 03-0088) is provided with this submission. The revised section provides a general description of the manufacturing and laboratory facilities, identifies major equipment and lists the qualifications of the key management personnel.

Also provided are a new listing of all document references (addendum to Form 356h) and a new page 03-0090 which have been revised to delete the DMF 1229 reference.

Sincerely yours,

Christine Shank

Christine Shank

CES/db
Enclosure

DPT

OWEN/ALLERCREME
6201 SOUTH FREEWAY FORT WORTH, TEXAS 76134 (817) 293-0450

AN ALCON/NESTLÉ, L'ORÉAL AFFILIATE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Memorandum

DATE: 12-2-87

TO : Division of Manufacturing & Product Quality (HFN-320)

FROM: Division of Generic Drugs HFN- 230

Requester's Name Margo Bennett Phone 443-0193

ESTABLISHMENT EVALUATION REQUEST

Sterile Product _____ Non Sterile Product XX

Application and Supplement No. 72-354

Brand Name *(if any)* DesOwen

Establishment Name, Dosage Form and Strength Desonide Lotion, 0.05%

Profile Class Code: LIQ

Priority Classification: _____ *(See SMG BD-4820.3)*

Applicant's Name: Owen Laboratories, Div of Dermatological Products of Texas, Inc.

Address: 6201 South Freeway, Fort Worth, TX 76134

Facilities to be Evaluated: *(Name, full Address, DMF No., and responsibility)*

DPTS now Dermatological Products of Texas

1. applicant at 307 E. Josephine St., San Antonio, TX 78296 or 5303 Distribution Drive,
2. San Antonio, TX

For HFN-320 Use
Status & Date of Inspection:

AC 10/14/87

(b) (4) (b) (4)

[redacted]

Other Information or Special Requests: Inspection requested *1, [redacted] (b) (4)

****

For HFN-320 Use Only:

Date Received 12/8/87 1/4/88 DS

CGMP Compliance Status of Facilities Evaluated: acceptable

TO: Diane Sylvia

Date Completed January 6, 1988

Distribution: Original and First Copy: HFN-320
Remaining Copies: Requesting Office Use

FORM FDA 3274 (6/86)

ANDA 72-354

Owen Laboratories
Division of Dermatological Products of Texas, Inc.
Attention: Ms. Christine Shank
6201 South Freeway
Fort Worth, TX 76134

DEC 4 1987

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 for the following:

NAME OF DRUG: DesOwen (Desonide) Lotion, 0.05%

DATE OF APPLICATION: November 25, 1987

DATE OF RECEIPT: November 27, 1987

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.

Sincerely yours,

Kenneth C. Johnson /BR 12-4-87

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drug Evaluation and Research

cc:
DUP HFN-230
Rosen/Patel
kl/12-03-87
Ack 1165b

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO (Division/Office): DIV of Anti-Infective Drugs HFN 815			FROM: Div of Generic Drugs HFN 230	
DATE: 12/3/87	IND NO.	NDA NO. 72-354	TYPE OF DOCUMENT: VASOCONSTRICTOR / Clinical Study	DATE OF DOCUMENT: 11/25/87
NAME OF DRUG: Des Owen (Desonide) Lotion 0.05%		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE: ASAP
NAME OF FIRM: Owen LABS				

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY _____
- ☐ PRE-NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(Specify below)*

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW	☐ CHEMISTRY
☐ END OF PHASE II MEETING	☐ PHARMACOLOGY
☐ CONTROLLED STUDIES	☐ BIOPHARMACEUTICS
☐ PROTOCOL REVIEW	☐ OTHER
☐ OTHER	

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILITY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL– BIOPHARMACEUTICS
- ☐ IN–VIVO WAIVER REQUEST

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/SPECIAL INSTRUCTIONS *(Attach additional sheets if necessary)*

Please provide comments on the VASOCONSTRICTOR Assay protocol and clinical protocol to establish the BIOEQUIVALENCE of the product.

NOTE: This Application was found eligible for submission VIA the ANDA PETITION PROCESS.

SIGNATURE OF REQUESTER: David L Rosen 443-0193 Room 17B25	METHOD OF DELIVERY *(Check one)* ☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

FORM FDA 3291 (7/83)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Memorandum

DATE: 12-2-87

TO : Division of Manufacturing & Product Quality (HFN-320)

FROM: Division of Generic Drugs HFN- 230

Requester's Name Margo Bennett Phone 443-0193

ESTABLISHMENT EVALUATION REQUEST

Sterile Product _____ Non Sterile Product XX

Application and Supplement No. 72-354

Brand Name *(if any)* DesOwen

Establishment Name, Dosage Form and Strength Desonide Lotion, 0.05%

Profile Class Code: LIQ

Priority Classification: _____ *(See SMG BD-4820.3)*

Applicant's Name: Owen Laboratories, Div of Dermatological Products of Texas, Inc.

Address: 6201 South Freeway, Fort Worth, TX 76134

Facilities to be Evaluated: ***(Name, full Address, DMF No., and responsibility)*** For HFN-320 Use Status & Date of Inspection:

1. applicant at 307 E. Josephine St., San Antonio, TX 78296 or 5303 Distribution Drive,
2. San Antonio, TX

(b) (4)

[redacted]

Other Information or Special Requests: _____

****

For HFN-320 Use Only: Date Received _____

CGMP Compliance Status of Facilities Evaluated: _____

CSO: _____ Date Completed _____

istribution: Original and First Copy: HFN-320
Remaining Copies: Requesting Office Use

FORM FDA 3274 (6/86)

505(j)2A info is acceptable DGR

Owen

ALLERCREME

OWEN LABORATORIES
ALLERCREME HYPO-ALLERGENIC COSMETICS

DIVISIONS OF
DERMATOLOGICAL PRODUCTS OF TEXAS, INC.

CHRISTINE E. SHANK
Manager
Regulatory Affairs

CERTIFIED MAIL P-555-982-161
Return Receipt Requested

November 25, 1987

Food and Drug Administration
Center for Drugs and Biologics
Division of Generic Drugs
Attention: Document Control Room
HFN-230, Room 17B-20
5600 Fishers Lane
Rockville, Maryland 20857

RE: Abbreviated New Drug Application Submission for
DesOwen® (Desonide) Lotion 0.05%

Gentlemen:

Pursuant to the provisions of 21 CFR 314.55(c)(1) the applicant, Owen Laboratories Division of Dermatological Products of Texas, Inc., is pleased to submit herewith an abbreviated new drug application for DesOwen® (Desonide) Lotion 0.05%.

In accordance with the provisions of 21 CFR 314.55(d)(2), the applicant filed a Citizen Petition requesting a determination of ANDA suitability for the drug product. The petition was reviewed by the Agency and approved on September 10, 1987 thus satisfying the requirement under 21 CFR 314.55(c)(1) that an ANDA will be accepted if the Agency has made a separate finding of suitability. Copies of the Petition approval letter are provided in this application immediately following this cover letter and in the Human Pharmacokinetics and Bioavailability Section.

The application provides a complete description of the subject drug product and adequate information with respect to the manufacturing and control operations to assure that the product meets all applicable standards for identity, strength, quality and purity. The applicant provides a protocol for conducting three month accelerated stability studies and a commitment to report the data as soon as it becomes available.

DPT

OWEN/ALLERCREME
6201 SOUTH FREEWAY FORT WORTH, TEXAS 76134 (817) 293-0450

AN ALCON/NESTLÉ, L'ORÉAL AFFILIATE

In addition, the applicant will perform two bioequivalency studies in accordance with the conditions of the Petition approval letter. The applicant submits for review the protocols for a vasoconstrictor assay and a bio study in patients which compare the subject drug product, DesOwen Lotion 0.05%, with the listed drug product, DesOwen® (Desonide) Cream 0.05%.

The applicant extends appreciation for the time and consideration spent in review of this application and hopes to hear from the Agency soon with regard to the bioequivalency protocols.

Sincerely yours,

Christine Shank

Christine Shank

CES/db
Enclosure

ANDA ADMINISTRATIVE CONTROL RECORD

Applicant Owen Laboratories ANDA # 72-354

Date Recd. 11/27/87

Trade Name DesOwen RX ✓ OTC ___

Generic Name/Dosage Form/Strength: Desonide Lotion 0.05%

DESI Drug ___

Similar or Related Petition

Applicant Manufacturer: Yes ✓ No ___

If No: Name of Manufacturer ___

ANDA # ___ Approved: ___ Pending ___ Same Formulation ___

Application Complete: YES ✓ NO ___

Application Acceptable: YES ✓ NO ___

has been listed drug

Letter to Firm: Acknowledgement: ___ Not-acceptable ___ Date 12/4/87

CSO/CST: M. Hugo-Bennett Date 12-2-87

BIO Review Required: YES X NO ___ IN VITRO ___ IN VIVO X

Medical Officer G Johnston

Chemist Arnwine

11-425

Inspection Request to HFD 320 (Date): 12-2-87

7899e/mlb

12-354

ANDA CHECKLIST FOR COMPLETENESS AND ACCEPTABILITY OF THE APPLICATION

	Yes	No
Cover Letter	✓	
356H Signed	✓	
Table of Contents	✓	
Information to show proposed product is same as listed product: (i) indications (ii) active ingredients (iii) (a) route (b) dosage form (c) strength (iv) labeling	✓	
Patent Certification	✓	
Exclusivity Addressed (If Applicable)		
Labeling	draft	
Statement re Rx/OTC Status	✓	
Components & Composition (Unit Composition)	✓	
Manufacturing Controls	✓	
Batch Formulation	✓	
Certification of GMP	✓	
Description of Facilities		
Manufacturing Procedures (Batch Records)	✓	
Specs & Tests for Active Ingredient and Finished Dosage Form	✓	
Stability Profile Including Stability Data (Use of Stability Indicating Method)	✓	
Samples Statement Plus Data		
Bioavailability/Bioequivalence Protocol	Clinical and Vasoconstrictor	
Study		
In vivo study/waiver request		
Dissolution Data		
Environmental Impact Analysis	✓	

GGK:jmp:1/3/85:Wang 4528a