CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-762/S007

Trade Name: Nasonex Aqueous Nasal Spray 50mcg

Generic Name: mometasone furoate monohydrate

Sponsor: Schering Corporation

Approval Date: August 8, 2004

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APPLICATION NUMBER:
NDA 20-762/S007

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APPLICATION NUMBER:

NDA 20-762/S007

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-762/S-007

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attention: Teresa Perney, Ph.D.
Manager, Global Regulatory Affairs

Dear Dr. Perney:

Please refer to your supplemental new drug application dated July 28, 2000, received July 31, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nasonex (mometasone furoate monohydrate) Aqueous Nasal Spray, 50mcg.

We acknowledge receipt of your submissions dated October 2, November 2 and 28, 2000, January 12, and February 16, 2001, and February 10 and 24, March 10, April 19 and 23, and August 18, 2004.

Your submission of April 23, 2004, constituted a complete response to our February 2, 2001, action letter.

This supplemental new drug application provides for a new formulation of Nasonex Nasal Spray that does not include the excipient phenylethyl alcohol.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the submitted labeling (text for the package insert, text for the patient package insert, and carton labels dated August 18, 2004 and immediate container labels dated April 23, 2004).

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-762/S-007." Approval of this submission by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Pulmonary and Allergy Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

If you propose, at a future date,(b)(4)---------- ----------you will need to choose a unique proprietary name in order to distinguish that product from the phenylethyl free formulation of Nasonex approved in this supplement. The name and its use in the labels must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit any proprietary name to the Agency for our review prior to its implementation.

We remind you that the term "NEW" in the descriptor "NEW Scent-Free Mist" should only be used to describe the marketing phase of the product for the first 6 months.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Lori Garcia, Regulatory Project Manager, at (301) 827-5580.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary and Allergy Drug Products, HFD-570
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

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

/s/

Badrul Chowdhury
8/25/04 04:09:56 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-762/S007

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-762/S-007

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attention: Nicholas J. Pelliccione, Ph.D.
Vice President
CMC Worldwide Regulatory Affairs

Dear Dr. Pelliccione:

Please refer to your supplemental new drug application dated July 28, 2000, received July 31, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nasonex (mometasone furoate) Nasal Spray.

We acknowledge receipt of your submissions dated October 2, and November 2 and 28, 2000.

We also refer to your submission dated January 12, 2001. This submission has not been reviewed in the current review cycle. You may incorporate this submission by specific reference as part of your response to the deficiencies cited in this letter.

This supplement provides for a new formulation of Nasonex Nasal Spray that does not include phenylethyl alcohol.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to address the following deficiencies.

1. You have indicated that you wish to [redacted] Nasonex Nasal Spray formulation, and have proposed the tradename "Nasonex [redacted] for this new formulation. In consultation with the FDA Office of Post-Marketing Drug Risk Assessment and Division of Drug Marketing, Advertising, and Communications, we, as a Division, do not find this name to be acceptable. We suggest that you [redacted] the existing name, Nasonex Nasal Spray, for the formulation [redacted]

2. During recent inspections of the manufacturing facilities for your supplement, a number of cGMP deficiencies were noted. Satisfactory inspections will be required before this application may be approved.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed prior to approval of this supplemental application.

If you have any questions, call Mr. David Hilfiker, Regulatory Project Manager, at (301) 827-1084.

Sincerely yours,

{See appended electronic signature page}

Guirag Poochikian, Ph.D.
Chemistry Team Leader, DNDC II for
Division of Pulmonary and Allergy Drug Products (HFD-570)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

/s/

Guiragos Poochikian
2/2/01 09:40:05 AM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-762/S007

LABELING

NASONEX®

(mometasone furoate monohydrate)

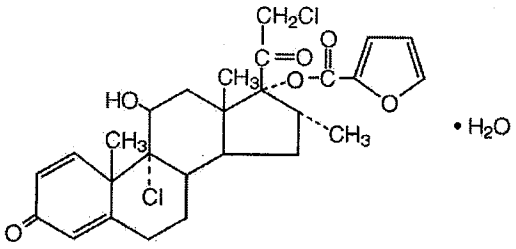
Nasal Spray, 50 mcg*

PRODUCT INFORMATION

FOR INTRANASAL USE ONLY

***calculated on the anhydrous basis**

DESCRIPTION Mometasone furoate monohydrate, the active component of NASONEX Nasal Spray, 50 mcg, is an anti-inflammatory corticosteroid having the chemical name, 9,21-Dichloro-11ß,17-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione 17-(2 furoate) monohydrate, and the following chemical structure:



Mometasone furoate monohydrate is a white powder, with an empirical formula of $C_{27}H_{30}Cl_2O_6 \cdot H_2O$, and a molecular weight of 539.45. It is practically insoluble in water; slightly soluble in methanol, ethanol, and isopropanol; soluble in acetone and chloroform; and freely soluble in tetrahydrofuran. Its partition coefficient between octanol and water is greater than 5000.

NASONEX Nasal Spray, 50 mcg is a metered-dose, manual pump spray unit containing an aqueous suspension of mometasone furoate monohydrate equivalent to 0.05% w/w mometasone furoate calculated on the anhydrous basis; in an aqueous medium containing glycerin, microcrystalline cellulose and carboxymethylcellulose sodium, sodium citrate, citric acid, benzalkonium chloride, and polysorbate 80. The pH is between 4.3 and 4.9.

After initial priming (10 actuations), each actuation of the pump delivers a metered spray containing 100 mg of suspension containing mometasone furoate monohydrate equivalent to 50 mcg of mometasone furoate calculated on the anhydrous basis. Each bottle of NASONEX Nasal Spray, 50 mcg provides 120 sprays.

CLINICAL PHARMACOLOGY NASONEX Nasal Spray, 50 mcg is a corticosteroid demonstrating anti-inflammatory properties. The precise mechanism of corticosteroid action on allergic rhinitis is not known. Corticosteroids have been shown to have a wide range of effects on multiple cell types (eg, mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (eg, histamine, eicosanoids, leukotrienes, and cytokines) involved in inflammation.

In two clinical studies utilizing nasal antigen challenge, NASONEX Nasal Spray, 50 mcg decreased some markers of the early- and late-phase allergic response. These observations included decreases (vs placebo) in histamine and eosinophil cationic protein levels, and reductions (vs baseline) in eosinophils, neutrophils, and epithelial cell adhesion proteins. The clinical significance of these findings is not known.

The effect of NASONEX Nasal Spray, 50 mcg on nasal mucosa following 12 months of treatment was examined in 46 patients with allergic rhinitis. There was no evidence of atrophy and there was a marked reduction in intraepithelial eosinophilia and inflammatory cell infiltration (eg, eosinophils, lymphocytes, monocytes, neutrophils, and plasma cells).

Pharmacokinetics: ***Absorption:*** Mometasone furoate monohydrate administered as a nasal spray is virtually undetectable in plasma from adult and pediatric subjects despite the use of a sensitive assay with a lower quantitation limit (LOQ) of 50 pcg/mL.

Distribution: The in vitro protein binding for mometasone furoate was reported to be 98% to 99% in concentration range of 5 to 500 ng/mL.

Metabolism: Studies have shown that any portion of a mometasone furoate dose which is swallowed and absorbed undergoes extensive metabolism to multiple

metabolites. There are no major metabolites detectable in plasma. Upon in vitro incubation, one of the minor metabolites formed is 6ß-hydroxy-mometasone furoate. In human liver microsomes, the formation of the metabolite is regulated by cytochrome P-450 3A4 (CYP3A4).

Elimination: Following intravenous administration, the effective plasma elimination half-life of mometasone furoate is 5.8 hours. Any absorbed drug is excreted as metabolites mostly via the bile, and to a limited extent, into the urine.

Special Populations: The effects of renal impairment, hepatic impairment, age, or gender on mometasone furoate pharmacokinetics have not been adequately investigated.

Pharmacodynamics: Three clinical pharmacology studies have been conducted in humans to assess the effect of NASONEX Nasal Spray, 50 mcg at various doses on adrenal function. In one study, daily doses of 200 and 400 mcg of NASONEX Nasal Spray, 50 mcg and 10 mg of prednisone were compared to placebo in 64 patients with allergic rhinitis. Adrenal function before and after 36 consecutive days of treatment was assessed by measuring plasma cortisol levels following a 6-hour Cortrosyn (ACTH) infusion and by measuring 24-hour urinary-free cortisol levels. NASONEX Nasal Spray, 50 mcg, at both the 200- and 400-mcg dose, was not associated with a statistically significant decrease in mean plasma cortisol levels post-Cortrosyn infusion or a statistically significant decrease in the 24-hour urinary-free cortisol levels compared to placebo. A statistically significant decrease in the mean plasma cortisol levels post-Cortrosyn infusion and 24-hour urinary-free cortisol levels was detected in the prednisone treatment group compared to placebo.

A second study assessed adrenal response to NASONEX Nasal Spray, 50 mcg (400 and 1600 mcg/day), prednisone (10 mg/day), and placebo, administered for 29 days in 48 male volunteers. The 24-hour plasma cortisol area under the curve (AUC_{0-24}), during and after an 8-hour Cortrosyn infusion and 24-hour urinary-free cortisol levels were determined at baseline and after 29 days of treatment. No statistically significant differences of adrenal function were observed with NASONEX Nasal Spray, 50 mcg compared to placebo.

A third study evaluated single, rising doses of NASONEX Nasal Spray, 50 mcg (1000, 2000, and 4000 mcg/day), orally administered mometasone furoate (2000, 4000, and 8000 mcg/day), orally administered dexamethasone (200, 400, and 800 mcg/day), and placebo (administered at the end of each series of doses) in 24 male volunteers. Dose administrations were separated by at least 72 hours. Determination of serial plasma cortisol levels at 8 AM and for the 24-hour period following each treatment were used to calculate the plasma cortisol area under the curve (AUC_{0-24}). In addition, 24-hour urinary-free cortisol levels were collected prior to initial treatment administration and during the period immediately following each dose. No statistically significant decreases in the plasma cortisol AUC, 8 AM cortisol levels, or 24-hour urinary-free cortisol levels were observed in volunteers treated with either NASONEX Nasal Spray, 50 mcg or oral mometasone, as compared with placebo treatment. Conversely, nearly all volunteers treated with the three doses of dexamethasone demonstrated abnormal 8 AM cortisol levels (defined as a cortisol level <10 mcg/dL), reduced 24-hour plasma AUC values, and decreased 24-hour urinary-free cortisol levels, as compared to placebo treatment.

Three clinical pharmacology studies have been conducted in pediatric patients to assess the effect of mometasone furoate nasal spray, on the adrenal function at daily doses of 50, 100, and 200 mcg vs placebo. In one study, adrenal function before and after 7 consecutive days of treatment was assessed in 48 pediatric patients with allergic rhinitis (ages 6 to 11 years) by measuring morning plasma cortisol and 24-hour urinary-free cortisol levels. Mometasone furoate nasal spray, at all three doses, was not associated with a statistically significant decrease in mean plasma cortisol levels or a statistically significant decrease in the 24-hour urinary-free cortisol levels compared to placebo. In the second study, adrenal function before and after 14 consecutive days of treatment was assessed in 48 pediatric patients (ages 3 to 5 years) with allergic rhinitis by measuring plasma cortisol levels following a 30-minute Cortrosyn infusion. Mometasone furoate nasal spray, 50 mcg, at all three doses (50, 100, and 200 mcg/day), was not associated with a statistically significant decrease in mean plasma cortisol levels post-Cortrosyn infusion compared to placebo. All patients had a normal response to Cortrosyn. In

the third study, adrenal function before and after up to 42 consecutive days of once-daily treatment was assessed in 52 patients with allergic rhinitis (ages 2 to 5 years), 28 of whom received mometasone furoate nasal spray, 50 mcg per nostril (total daily dose 100 mcg), by measuring morning plasma cortisol and 24-hour urinary-free cortisol levels. Mometasone furoate nasal spray was not associated with a statistically significant decrease in mean plasma cortisol levels or a statistically significant decrease in the 24-hour urinary-free cortisol levels compared to placebo.

Clinical Studies: The efficacy and safety of NASONEX Nasal Spray, 50 mcg in the prophylaxis and treatment of seasonal allergic rhinitis and the treatment of perennial allergic rhinitis have been evaluated in 18 controlled trials, and one uncontrolled clinical trial, in approximately 3000 adults (ages 17 to 85 years) and adolescents (ages 12 to 16 years). This included 1757 males and 1453 females, including a total of 283 adolescents (182 boys and 101 girls) with seasonal allergic or perennial allergic rhinitis, treated with NASONEX Nasal Spray, 50 mcg at doses ranging from 50 to 800 mcg/day. The majority of patients were treated with 200 mcg/day. These trials evaluated the total nasal symptom scores that included stuffiness, rhinorrhea, itching, and sneezing. Patients treated with NASONEX Nasal Spray, 50 mcg, 200 mcg/day had a significant decrease in total nasal symptom scores compared to placebo-treated patients. No additional benefit was observed for mometasone furoate doses greater than 200 mcg/day. A total of 350 patients have been treated with NASONEX Nasal Spray, 50 mcg for 1 year or longer.

The efficacy and safety of NASONEX Nasal Spray, 50 mcg in the treatment of seasonal allergic and perennial allergic rhinitis in pediatric patients (ages 3 to 11 years) have been evaluated in four controlled trials. This included approximately 990 pediatric patients ages 3 to 11 years (606 males and 384 females) with seasonal allergic or perennial allergic rhinitis treated with mometasone furoate nasal spray at doses ranging from 25 to 200 mcg/day. Pediatric patients treated with NASONEX Nasal Spray, 50 mcg (100 mcg total daily dose, 374 patients) had a significant decrease in total nasal symptom (congestion, rhinorrhea, itching, and sneezing) scores, compared to placebo-treated patients. No additional benefit was observed

for the 200-mcg mometasone furoate total daily dose in pediatric patients (ages 3 to 11 years). A total of 163 pediatric patients have been treated for 1 year.

In patients with seasonal allergic rhinitis, NASONEX Nasal Spray, 50 mcg, demonstrated improvement in nasal symptoms (vs placebo) within 11 hours after the first dose based on one single-dose, parallel-group study of patients in an outdoor "park" setting (park study) and one environmental exposure unit (EEU) study, and within 2 days in two randomized, double-blind, placebo-controlled, parallel-group seasonal allergic rhinitis studies. Maximum benefit is usually achieved within 1 to 2 weeks after initiation of dosing.

Prophylaxis of seasonal allergic rhinitis for patients 12 years of age and older with NASONEX Nasal Spray, 50 mcg, given at a dose of 200 mcg/day, was evaluated in two clinical studies in 284 patients. These studies were designed such that patients received 4 weeks of prophylaxis with NASONEX Nasal Spray, 50 mcg prior to the anticipated onset of the pollen season; however, some patients received only 2 to 3 weeks of prophylaxis. Patients receiving 2 to 4 weeks of prophylaxis with NASONEX Nasal Spray, 50 mcg demonstrated a statistically significantly smaller mean increase in total nasal symptom scores with onset of the pollen season as compared to placebo patients.

INDICATIONS AND USAGE NASONEX Nasal Spray, 50 mcg is indicated for the treatment of the nasal symptoms of seasonal allergic and perennial allergic rhinitis, in adults and pediatric patients 2 years of age and older. NASONEX Nasal Spray, 50 mcg is indicated for the prophylaxis of the nasal symptoms of seasonal allergic rhinitis in adult and adolescent patients 12 years and older. In patients with a known seasonal allergen that precipitates nasal symptoms of seasonal allergic rhinitis, initiation of prophylaxis with NASONEX Nasal Spray, 50 mcg is recommended 2 to 4 weeks prior to the anticipated start of the pollen season. Safety and effectiveness of NASONEX Nasal Spray, 50 mcg in pediatric patients less than 2 years of age have not been established.

CONTRAINDICATIONS Hypersensitivity to any of the ingredients of this preparation contraindicates its use.

WARNINGS The replacement of a systemic corticosteroid with a topical corticosteroid can be accompanied by signs of adrenal insufficiency and, in addition, some patients may experience symptoms of withdrawal; ie, joint and/or muscular pain, lassitude, and depression. Careful attention must be given when patients previously treated for prolonged periods with systemic corticosteroids are transferred to topical corticosteroids, with careful monitoring for acute adrenal insufficiency in response to stress. This is particularly important in those patients who have associated asthma or other clinical conditions where too rapid a decrease in systemic corticosteroid dosing may cause a severe exacerbation of their symptoms.

If recommended doses of intranasal corticosteroids are exceeded or if individuals are particularly sensitive or predisposed by virtue of recent systemic steroid therapy, symptoms of hypercorticism may occur, including very rare cases of menstrual irregularities, acneiform lesions, and cushingoid features. If such changes occur, topical corticosteroids should be discontinued slowly, consistent with accepted procedures for discontinuing oral steroid therapy.

Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in nonimmune children or adults on corticosteroids. In such children or adults who have not had these diseases, particular care should be taken to avoid exposure. How the dose, route, and duration of corticosteroid administration affects the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chickenpox, prophylaxis with varicella zoster immune globin (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information.) If chickenpox develops, treatment with antiviral agents may be considered.

PRECAUTIONS General: Intranasal corticosteroids may cause a reduction in growth velocity when administered to pediatric patients (see **PRECAUTIONS, Pediatric Use** section). In clinical studies with NASONEX Nasal Spray, 50 mcg, the development of localized infections of the nose and pharynx with *Candida albicans* has occurred only rarely. When such an infection develops, use of NASONEX Nasal Spray, 50 mcg_should be discontinued and appropriate local or systemic therapy instituted, if needed.

Nasal corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculous infection of the respiratory tract, or in untreated fungal, bacterial, systemic viral infections, or ocular herpes simplex.

Rarely, immediate hypersensitivity reactions may occur after the intranasal administration of mometasone furoate monohydrate. Extremely rare instances of wheezing have been reported.

Rare instances of nasal septum perforation and increased intraocular pressure have also been reported following the intranasal application of aerosolized corticosteroids. As with any long-term topical treatment of the nasal cavity, patients using NASONEX Nasal Spray, 50 mcg over several months or longer should be examined periodically for possible changes in the nasal mucosa.

Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal septum ulcers, nasal surgery, or nasal trauma should not use a nasal corticosteroid until healing has occurred.

Glaucoma and cataract formation was evaluated in one controlled study of 12 weeks' duration and one uncontrolled study of 12 months' duration in patients treated with NASONEX Nasal Spray, 50 mcg at 200 mcg/day, using intraocular pressure measurements and slit lamp examination. No significant change from baseline was noted in the mean intraocular pressure measurements for the 141 NASONEX-treated patients in the 12-week study, as compared with 141 placebo-treated patients. No individual NASONEX-treated patient was noted to have developed a significant elevation in intraocular pressure or cataracts in this 12-week study. Likewise, no significant change from baseline was noted in the mean

intraocular pressure measurements for the 139 NASONEX-treated patients in the 12-month study and again, no cataracts were detected in these patients. Nonetheless, nasal and inhaled corticosteroids have been associated with the development of glaucoma and/or cataracts. Therefore, close follow-up is warranted in patients with a change in vision and with a history of glaucoma and/or cataracts.

When nasal corticosteroids are used at excessive doses, systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, NASONEX Nasal Spray, 50 mcg should be discontinued slowly, consistent with accepted procedures for discontinuing oral steroid therapy.

Information for Patients: Patients being treated with NASONEX Nasal Spray, 50 mcg should be given the following information and instructions. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all intended or possible adverse effects. Patients should use NASONEX Nasal Spray, 50 mcg at regular intervals (once daily) since its effectiveness depends on regular use. Improvement in nasal symptoms of allergic rhinitis has been shown to occur within 11 hours after the first dose based on one single-dose, parallel-group study of patients in an outdoor "park" setting (park study) and one environmental exposure unit (EEU) study and within 2 days after the first dose in two randomized, double-blind, placebo-controlled, parallel-group seasonal allergic rhinitis studies. Maximum benefit is usually achieved within 1 to 2 weeks after initiation of dosing. Patients should take the medication as directed and should not increase the prescribed dosage by using it more than once a day in an attempt to increase its effectiveness. Patients should contact their physician if symptoms do not improve, or if the condition worsens. To assure proper use of this nasal spray, and to attain maximum benefit, patients should read and follow the accompanying Patient's Instructions for Use carefully. Administration to young children should be aided by an adult.

Patients should be cautioned not to spray NASONEX Nasal Spray, 50 mcg into the eyes or directly onto the nasal septum.

Persons who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles, and patients should also be advised that if they are exposed, medical advice should be sought without delay.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 2-year carcinogenicity study in Sprague Dawley rats, mometasone furoate demonstrated no statistically significant increase in the incidence of tumors at inhalation doses up to 67 mcg/kg (approximately 3 and 2 times the maximum recommended daily intranasal dose in adults and children, respectively, on a mcg/m^2 basis). In a 19-month carcinogenicity study in Swiss CD-1 mice, mometasone furoate demonstrated no statistically significant increase in the incidence of tumors at inhalation doses up to 160 mcg/kg (approximately 3 and 2 times the maximum recommended daily intranasal dose in adults and children, respectively, on a mcg/m^2 basis).

Mometasone furoate increased chromosomal aberrations in an *in vitro* Chinese hamster ovary-cell assay, but did not increase chromosomal aberrations in an *in vitro* Chinese hamster lung cell assay. Mometasone furoate was not mutagenic in the Ames test or mouse-lymphoma assay, and was not clastogenic in an *in vivo* mouse micronucleus assay and a rat bone marrow chromosomal aberration assay or a mouse male germ-cell chromosomal aberration assay. Mometasone furoate also did not induce unscheduled DNA synthesis *in vivo* in rat hepatocytes.

In reproductive studies in rats, impairment of fertility was not produced by subcutaneous doses up to 15 mcg/kg (less than the maximum recommended daily intranasal dose in adults on a mcg/m^2 basis).

Pregnancy: ***Teratogenic Effects: Pregnancy Category C:*** When administered to pregnant mice, rats, and rabbits, mometasone furoate increased fetal malformations. The doses that produced malformations also decreased fetal growth, as measured by lower fetal weights and/or delayed ossification. Mometasone furoate also caused dystocia and related complications when administered to rats during the end of pregnancy.

In mice, mometasone furoate caused cleft palate at subcutaneous doses of 60 mcg/kg and above (approximately equivalent to the maximum recommended

daily intranasal dose in adults on a mcg/m^2 basis). Fetal survival was reduced at 180 mcg/kg (approximately 4 times the maximum recommended daily intranasal dose in adults on a mcg/m^2 basis). No toxicity was observed at 20 mcg/kg (less than the maximum recommended daily intranasal dose in adults on a mcg/m^2 basis).

In rats, mometasone furoate produced umbilical hernia at topical dermal doses of 600 mcg/kg and above (approximately 25 times the maximum recommended daily intranasal dose in adults on a mcg/m^2 basis). A dose of 300 mcg/kg (approximately 10 times the maximum recommended daily intranasal dose in adults on a mcg/m^2 basis) produced delays in ossification, but no malformations.

In rabbits, mometasone furoate caused multiple malformations (e.g., flexed front paws, gallbladder agenesis, umbilical hernia, hydrocephaly at topical dermal doses of 150 mcg/kg and above (approximately 10 times the maximum recommended daily intranasal dose in adults on a mcg/m^2 basis). In an oral study, mometasone furoate increased resorptions and caused cleft palate and/or head malformations (hydrocephaly or domed head) at 700 mcg/kg (approximately 55 times the maximum recommended daily intranasal dose in adults on a mcg/m^2 basis. At 2800 mcg/kg (approximately 230 times the maximum recommended daily intranasal dose in adults on a mcg/m^2 basis), most litters were aborted or resorbed. No toxicity was observed at 140 mcg/kg (approximately 10 times the maximum recommended daily intranasal dose in adults on a mcg/m^2 basis).

When rats received subcutaneous doses of mometasone furoate throughout pregnancy or during the later stages of pregnancy, 15 mcg/kg (less than the maximum recommended daily intranasal dose in adults on a mcg/m^2 basis) caused prolonged and difficult labor and reduced the number of live births, birth weight, and early pup survival. Similar effects were not observed at 7.5 mcg/kg (less than the maximum recommended daily intranasal dose in adults on a mcg/m^2 basis).

There are no adequate and well-controlled studies in pregnant women. NASONEX Nasal Spray, 50 mcg, like other corticosteroids, should be used during pregnancy only if the potential benefits justify the potential risk to the fetus. Experience with oral corticosteroids since their introduction in pharmacologic, as opposed to physiologic, doses suggests that rodents are more prone to teratogenic

effects from corticosteroids than humans. In addition, because there is a natural increase in corticosteroid production during pregnancy, most women will require a lower exogenous corticosteroid dose and many will not need corticosteroid treatment during pregnancy.

Nonteratogenic Effects: Hypoadrenalism may occur in infants born to women receiving corticosteroids during pregnancy. Such infants should be carefully monitored.

Nursing Mothers: It is not known if mometasone furoate is excreted in human milk. Because other corticosteroids are excreted in human milk, caution should be used when NASONEX Nasal Spray, 50 mcg is administered to nursing women.

Pediatric Use: Controlled clinical studies have shown intranasal corticosteroids may cause a reduction in growth velocity in pediatric patients. This effect has been observed in the absence of laboratory evidence of hypothalamic-pituitary-adrenal (HPA) axis suppression, suggesting that growth velocity is a more sensitive indicator of systemic corticosteroid exposure in pediatric patients than some commonly used tests of HPA axis function. The long-term effects of this reduction in growth velocity associated with intranasal corticosteroids, including the impact on final adult height, are unknown. The potential for "catch up" growth following discontinuation of treatment with intranasal corticosteroids has not been adequately studied. The growth of pediatric patients receiving intranasal corticosteroids, including NASONEX Nasal Spray, 50 mcg, should be monitored routinely (eg, via stadiometry). The potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the availability of safe and effective noncorticosteroid treatment alternatives. To minimize the systemic effects of intranasal corticosteroids, including NASONEX Nasal Spray, 50 mcg, each patient should be titrated to his/her lowest effective dose.

Seven hundred and twenty (720) patients 3 to 11 years of age were treated with mometasone furoate nasal spray, 50 mcg (100 mcg total daily dose) in controlled clinical trials (see **CLINICAL PHARMACOLOGY, Clinical Studies** section). Twenty-eight (28) patients 2 to 5 years of age were treated with mometasone furoate

nasal spray, 50 mcg (100 mcg total daily dose) in a controlled trial to evaluate safety (see **CLINICAL PHARMACOLOGY, Pharmacokinetics** section). Safety and effectiveness in children less than 2 years of age have not been established.

A clinical study has been conducted for 1 year in pediatric patients (ages 3 to 9 years) to assess the effect of NASONEX Nasal Spray, 50 mcg (100 mcg total daily dose) on growth velocity. No statistically significant effect on growth velocity was observed for NASONEX Nasal Spray, 50 mcg compared to placebo. No evidence of clinically relevant HPA axis suppression was observed following a 30-minute cosyntropin infusion.

The potential of NASONEX Nasal Spray, 50 mcg to cause growth suppression in susceptible patients or when given at higher doses cannot be ruled out.

Geriatric Use: A total of 203 patients above 64 years of age (age range 64 to 85 years) have been treated with NASONEX Nasal Spray, 50 mcg for up to 3 months. The adverse reactions reported in this population were similar in type and incidence to those reported by younger patients.

ADVERSE REACTIONS In controlled US and international clinical studies, a total of 3210 adult and adolescent patients ages 12 years and older received treatment with NASONEX Nasal Spray, 50 mcg at doses of 50 to 800 mcg/day. The majority of patients (n = 2103) were treated with 200 mcg/day. In controlled US and international studies, a total of 990 pediatric patients (ages 3 to 11 years) received treatment with NASONEX Nasal Spray, 50 mcg, at doses of 25 to 200 mcg/day. The majority of pediatric patients (720) were treated with 100 mcg/day. A total of 513 adult, adolescent, and pediatric patients have been treated for 1 year or longer. The overall incidence of adverse events for patients treated with NASONEX Nasal Spray, 50 mcg was comparable to patients treated with the vehicle placebo. Also, adverse events did not differ significantly based on age, sex, or race. Three percent or less of patients in clinical trials discontinued treatment because of adverse events; this rate was similar for the vehicle and active comparators.

All adverse events (regardless of relationship to treatment) reported by 5% or more of adult and adolescent patients ages 12 years and older who received NASONEX Nasal Spray, 50 mcg, 200 mcg/day and by pediatric patients ages 3 to 11 years who received NASONEX Nasal Spray, 50 mcg, 100 mcg/day in clinical trials vs placebo and that were more common with NASONEX Nasal Spray, 50 mcg than placebo, are displayed in the table below.

ADVERSE EVENTS FROM CONTROLLED CLINICAL TRIALS IN SEASONAL ALLERGIC AND PERENNIAL ALLERGIC RHINITIS

(PERCENT OF PATIENTS REPORTING)

	Adult and Adolescent Patients 12 years and older		Pediatric Patients Ages 3 to 11 years	
	NASONEX 200 mcg (n = 2103)	VEHICLE PLACEBO (n = 1671)	NASONEX 100 mcg (n = 374)	VEHICLE PLACEBO (n = 376)
Headache	26	22	17	18
Viral Infection	14	11	8	9
Pharyngitis	12	10	10	10
Epistaxis/Blood-Tinged Mucus	11	6	8	9
Coughing	7	6	13	15
Upper Respiratory Tract Infection	6	2	5	4
Dysmenorrhea	5	3	1	0
Musculoskeletal Pain	5	3	1	1
Sinusitis	5	3	4	4
Vomiting	1	1	5	4

Other adverse events which occurred in less than 5% but greater than or equal to 2% of mometasone furoate adult and adolescent patients (ages 12 years and older) treated with 200-mcg doses (regardless of relationship to treatment), and more frequently than in the placebo group included: arthralgia, asthma, bronchitis, chest pain, conjunctivitis, diarrhea, dyspepsia, earache, flu-like symptoms, myalgia, nausea, and rhinitis.

Other adverse events which occurred in less than 5% but greater than or equal to 2% of mometasone furoate pediatric patients ages 3 to 11 years treated with 100-mcg doses vs placebo (regardless of relationship to treatment) and more

frequently than in the placebo group included: diarrhea, nasal irritation, otitis media, and wheezing.

The adverse event (regardless of relationship to treatment) reported by 5% of pediatric patients ages 2 to 5 years who received NASONEX Nasal Spray, 50 mcg, 100 mcg/day in a clinical trial vs placebo including 56 subjects (28 each NASONEX Nasal Spray, 50 mcg and placebo) and that was more common with NASONEX Nasal Spray, 50 mcg than placebo, included: upper respiratory tract infection (7% vs 0%, respectively). The other adverse event which occurred in less than 5% but greater than or equal to 2% of mometasone furoate pediatric patients ages 2 to 5 years treated with 100-mcg doses vs placebo (regardless of relationship to treatment) and more frequently than in the placebo group included: skin trauma.

Rare cases of nasal ulcers and nasal and oral candidiasis were also reported in patients treated with NASONEX Nasal Spray, 50 mcg, primarily in patients treated for longer than 4 weeks.

In postmarketing surveillance of this product, cases of nasal burning and irritation, anaphylaxis and angioedema, and rare cases of nasal septal perforation have been reported. Disturbances of taste and smell have been reported very rarely.

OVERDOSAGE There are no data available on the effects of acute or chronic overdosage with NASONEX Nasal Spray, 50 mcg. Because of low systemic bioavailability, and an absence of acute drug-related systemic findings in clinical studies, overdose is unlikely to require any therapy other than observation. Intranasal administration of 1600 mcg (8 times the recommended dose of NASONEX Nasal Spray, 50 mcg) daily for 29 days, to healthy human volunteers, was well tolerated with no increased incidence of adverse events. Single intranasal doses up to 4000 mcg have been studied in human volunteers with no adverse effects reported. Single oral doses up to 8000 mcg have been studied in human volunteers with no adverse effects reported. Chronic overdosage with any corticosteroid may result in signs or symptoms of hypercorticism (see **PRECAUTIONS**). Acute overdosage with this dosage form is unlikely since one

bottle of NASONEX Nasal Spray, 50 mcg contains approximately 8500 mcg of mometasone furoate.

DOSAGE AND ADMINISTRATION Adults and Children 12 Years of Age and Older: The usual recommended dose for prophylaxis and treatment of the nasal symptoms of seasonal allergic rhinitis and treatment of the nasal symptoms of perennial allergic rhinitis is two sprays (50 mcg of mometasone furoate in each spray) in each nostril once daily (total daily dose of 200 mcg).

In patients with a known seasonal allergen that precipitates nasal symptoms of seasonal allergic rhinitis, prophylaxis with NASONEX Nasal Spray, 50 mcg (200 mcg/day) is recommended 2 to 4 weeks prior to the anticipated start of the pollen season.

Children 2 to 11 Years of Age: The usual recommended dose for treatment of the nasal symptoms of seasonal allergic and perennial allergic rhinitis is one spray (50 mcg of mometasone furoate in each spray) in each nostril once daily (total daily dose of 100 mcg).

Improvement in nasal symptoms of allergic rhinitis has been shown to occur within 11 hours after the first dose based on one single-dose, parallel-group study of patients in an outdoor "park" setting (park study) and one environmental exposure unit (EEU) study and within 2 days after the first dose in two randomized, double-blind, placebo-controlled, parallel-group seasonal allergic rhinitis studies. Maximum benefit is usually achieved within 1 to 2 weeks. Patients should use NASONEX Nasal Spray, 50 mcg only once daily at a regular interval.

Prior to initial use of NASONEX Nasal Spray, 50 mcg, the pump must be primed by actuating ten times or until a fine spray appears. The pump may be stored unused for up to 1 week without repriming. If unused for more than 1 week, reprime by actuating two times, or until a fine spray appears.

Directions for Use: Illustrated **Patient's Instructions for Use** accompany each package of NASONEX Nasal Spray, 50 mcg.

Directions for Cleaning: Illustrated **Applicator Cleaning Instructions** accompany each package of NASONEX Nasal Spray, 50 mcg.

HOW SUPPLIED NASONEX (mometasone furoate monohydrate) Nasal Spray, 50 mcg is supplied in a white, high-density, polyethylene bottle fitted with a white metered-dose, manual spray pump, and blue cap. It contains 17 g of product formulation, 120 sprays, each delivering 50 mcg of mometasone furoate per actuation. Supplied with **Patient's Instructions for Use** (NDC 0085-1197-01).

Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature]. Protect from light.

When NASONEX Nasal Spray, 50 mcg is removed from its cardboard container, prolonged exposure of the product to direct light should be avoided. Brief exposure to light, as with normal use, is acceptable.

SHAKE WELL BEFORE EACH USE.

Schering®

Schering Corporation

Kenilworth, NJ 07033 USA

XXXXXXXXT

PHARMACIST

Pull to Remove

GIVE TO PATIENT

Patient's Instructions for Use

SHAKE WELL BEFORE EACH USE

NASONEX®

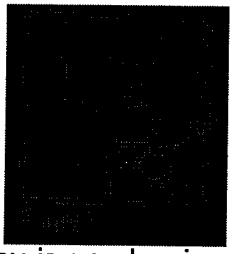
(mometasone furoate monohydrate)

Nasal Spray, 50 mcg*

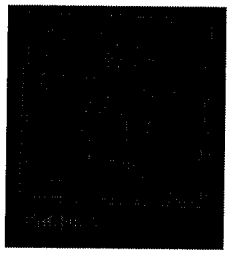
*calculated on the anhydrous basis

Shake the bottle well before each use. Read complete instructions carefully and use only as directed.

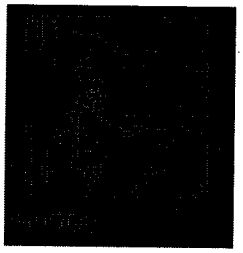
1. Remove the plastic cap (Figure 1).



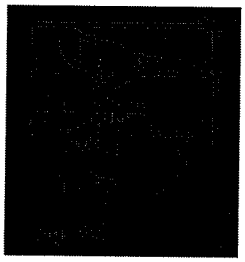
2. The very first time the spray is used, prime the pump by pressing downward on the shoulders of the white applicator using your forefinger and middle finger while supporting the base of the bottle with your thumb (Figure 2). Press down and release the pump ten times or until a fine spray appears. DO NOT spray into eyes. The pump is now ready to use. The pump may be stored unused for up to 1 week without repriming. If unused for more than 1 week, reprime by spraying two times or until a fine spray appears.



3. Gently blow your nose to clear the nostrils. Close one nostril. Tilt your head forward slightly and, keeping the bottle upright, carefully insert the nasal applicator into the other nostril (Figure 3). DO NOT spray directly onto nasal septum, the wall between the two nostrils.



4. For each spray, press firmly downward once on the shoulders of the white applicator using your forefinger and middle finger while supporting the base of the bottle with your thumb. Breathe gently inward through the nostril (Figure 4).



5. Then breathe out through the mouth.

6. Repeat in the other nostril.

7. Wipe the nasal applicator with a clean tissue and replace the plastic cap.

Pediatric Use: Administration to young children should be aided by an adult. The **Patient's Instructions for Use**, Steps 1 to 7 should be followed.

The correct amount of medication in each spray can only be assured up to 120 sprays from the bottle even though the bottle is not completely empty. You should keep track of the number of sprays used from each bottle of NASONEX Nasal Spray, 50 mcg and discard the bottle after using 120 sprays.

Cleaning: Please see **Applicator Cleaning Instructions** on reverse.

Caution: NASONEX Nasal Spray, 50 mcg is formulated for once-daily dosing. You should use NASONEX Nasal Spray, 50 mcg only once daily at a regular interval. Since NASONEX Nasal Spray, 50 mcg is not intended to give rapid relief of your nasal symptoms, the prescribed dosage should not be increased by using more often than once daily in an attempt to increase its effectiveness. NASONEX Nasal Spray, 50 mcg, controls the underlying disorders responsible for your attacks so it is important that you use it regularly at the time recommended by your physician.

Based on single-day studies, done in a park, during pollen season or in a controlled pollen exposure room, improvement in nasal symptoms of allergic rhinitis has been shown to occur within 11 hours after the first dose. In other studies that lasted up to 2 weeks, improvement in nasal symptoms of seasonal allergic rhinitis was shown to occur within 2 days after the first dose. The full benefit of NASONEX Nasal Spray, 50 mcg is usually achieved within 1 to 2 weeks.

NASONEX Nasal Spray, 50 mcg should not be sprayed into the eyes.
Spraying NASONEX Nasal Spray, 50 mcg directly onto the nasal septum should be avoided.

Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature]. Protect from light.

When NASONEX Nasal Spray, 50 mcg is removed from its cardboard container, prolonged exposure of the product to direct light should be avoided. Brief exposure to light, as with normal use, is acceptable.

SHAKE WELL BEFORE EACH USE.

Schering®

Schering Corporation

Kenilworth, NJ 07033 USA

U.S. Patent No. D355,844

Rev. XX/XX

PHARMACIST

GIVE TO PATIENT

APPLICATOR CLEANING INSTRUCTIONS

Please see reverse for Patient's Instructions for Use

NASONEX®

(mometasone furoate monohydrate)

Nasal Spray, 50 mcg*

*calculated on the anhydrous basis

1. To clean the nasal applicator, remove the plastic cap (Figure 1).

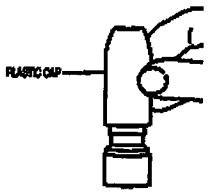


Figure 1

2. Pull gently upward on the white nasal applicator so that it comes free (Figure 2).

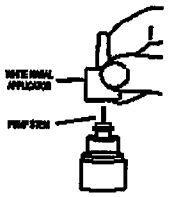


Figure 2

3. Soak the nasal applicator in cold tap water and/or rinse both ends of the nasal applicator under cold tap water and dry. (Figure 3).

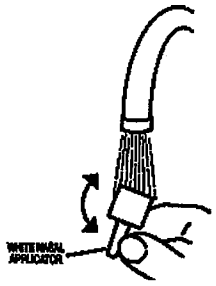


Figure 3

4. Rinse the plastic cap under cold water and dry (Figure 4).

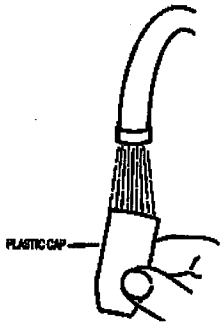


Figure 4

5. Reassemble the nasal applicator being certain the pump stem is reinserted into the applicator's center hole (Figure 5).

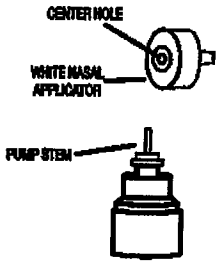


Figure 5

6. Reprime the pump by pressing downward on the shoulders of the white applicator using your forefinger and middle finger while supporting the base of the bottle with your thumb. Press down and release the pump two times or until a fine spray appears. DO NOT spray into eyes. The pump is now ready to use. The pump may be stored unused for up to 1 week without repriming. If unused for more than 1 week, reprime by spraying two times or until a fine spray appears (Figure 6).

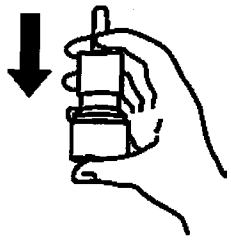


Figure 6

7. Replace the plastic cap (Figure 7).

Figure 7

Schering®

Schering Corporation

Kenilworth, NJ 07033 USA

U.S. Patent No. D355,844

Rev. XX/XX

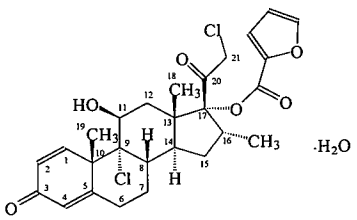
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-762/S007

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW #5

	1. ORGANIZATION HFD-570 DPDP	2. NDA NUMBER 20-762
3. NAME AND ADDRESS OF APPLICANT *(City and State)* Schering Corporation 2000 Galloping Hill Road Kenilworth, NJ 07033		4. AF NUMBER 5. SUPPLEMENT(S) NUMBER(S) DATES(S) SCF-007 7/28/00
6. NAME OF DRUG Nasonex® Nasal Spray	7. NONPROPRIETARY NAME mometasone furoate nasal spray	
8. SUPPLEMENT PROVIDES FOR: CMC information supporting a new formulation of the drug product which does not include the preservative phenylethyl alcohol (PEA) for use with the crimped-on pump presentations only (10 g sample and 17 g trade size bottles).		9. AMENDMENT(S), REPORT(S), ETC. SCF-007 (BC) 10/2/00 SCF-007 (BC) 11/2/00 SCF-007 (BL) 11/28/00 SCF-007 (BC) 2/24/04* *Subject of this review.
10. PHARMACOLOGICAL CATEGORY anti-inflammatory corticosteroid	11. HOW DISPENSED RX X OTC __	12. RELATED IND/NDA/DMF
13. DOSAGE FORM(S) aqueous nasal spray	14. POTENCY 50 mcg/act (100 or 200 mcg/day)	
15. CHEMICAL NAME AND STRUCTURE 9,21-Dichloro-17-[(2-furanylcarbonyl)oxy]-11-hydroxy-16-methylpregna-1,4-diene-3,20-dione Monohydrate  Mometasone Furoate Monohydrate		16. RECORDS AND REPORTS CURRENT YES X NO___ REVIEWED YES X NO___

17. COMMENTS: See attached review notes.

cc:
Orig. NDA 20-762
HFD-570/div. File
HFD-570/CBertha/3/4/04
HFD-570/RLostritto
HFD-570/LGarcia
R/D Init. by:_____
F/T by: CBertha/3/4/04
doc # 04-02-24.rev.doc

CONCLUSIONS AND RECOMMENDATIONS: CMC recommends approval of the supplement contingent on the following: **a).** a satisfactory EES for the sites involved in the manufacture of the drug product; **b).** a satisfactory response to the labeling issues outlined in the telephone facsimile of 6/19/01 from D. Hilfiker (PM to the firm). A complete response to the 2/2/01 AE letter is pending.

19. REVIEWER NAME:	SIGNATURE	DATE COMPLETED
Craig M. Bertha, Ph.D.		3/4/04

7 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry-26-762 5007

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

/s/

Craig Bertha
3/8/04 06:31:35 AM
CHEMIST

Richard Lostritto
3/10/04 10:05:58 AM
CHEMIST

CHEMIST'S REVIEW #4

1. ORGANIZATION	2. NDA NUMBER
HFD-570 DPDP	20-762

3. NAME AND ADDRESS OF APPLICANT *(City and State)*	4. AF NUMBER
Schering Corporation 2000 Galloping Hill Road Kenilworth, NJ 07033	
	5. SUPPLEMENT(S) NUMBER(S) DATES(S) SCF-007 7/28/00

6. NAME OF DRUG	7. NONPROPRIETARY NAME
Nasonex® Nasal Spray	mometasone furoate nasal spray

8. SUPPLEMENT PROVIDES FOR: CMC information supporting a new formulation of the drug product ~~—~~ which does not include the preservative phenylethyl alcohol (PEA) for use with the crimped-on pump presentations only (10 g sample and 17 g trade size bottles).

9. AMENDMENT(S), REPORT(S), ETC.

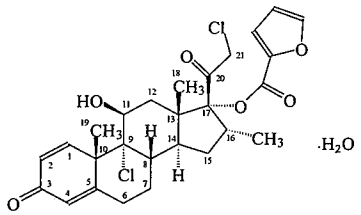
SCF-007 (BC) 10/2/00
SCF-007 (BC) 11/2/00
SCF-007 (BL) 11/28/00*

*Subject of this review.

10. PHARMACOLOGICAL CATEGORY	11. HOW DISPENSED	12. RELATED IND/NDA/DMF
anti-inflammatory corticosteroid	RX X OTC __	
13. DOSAGE FORM(S)	14. POTENCY	
aqueous nasal spray	50 mcg/act (100 or 200 mcg/day)	

15. CHEMICAL NAME AND STRUCTURE

9,21-Dichloro-17-[(2-furanylcarbonyl)oxy]-11•-hydroxy-16•-methylpregna-1,4-diene-3,20-dione Monohydrate



Mometasone Furoate Monohydrate

16. RECORDS AND REPORTS
CURRENT YES X NO___
REVIEWED YES X NO___

17. COMMENTS: See attached review notes.
cc:
Orig. NDA 20-762
HFD-570/div. File
HFD-570/CBertha/12/6/00
HFD-570/GPoochikian
HFD-570/DHilfiker
R/D Init. by:_____
F/T by: CBertha/12/6/00
doc # 00-11-28.rev.doc

18. CONCLUSIONS AND RECOMMENDATIONS: CMC concurs with the recommendations from OPDRA, i.e. ~~—~~ If the Division decides to ~~—~~, CMC concurs with the OPDRA recommendation to include the ~~—~~ n the name of the originally formulated product (containing phenylethyl alcohol). In summary, approval of the supplement is contingent on:

a). a satisfactory EES response;
b). a satisfactory evaluation from microbiology; and
c). a satisfactory resolution to the naming issue (see review notes).

19. REVIEWER NAME:	SIGNATURE	DATE COMPLETED
Craig M. Bertha, Ph.D.		12/6/00

1 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-762

S007
Chem Review
#4

/s/

Craig Bertha
12/15/00 12:04:53 PM
CHEMIST

Guiragos Poochikian
12/15/00 04:30:12 PM
CHEMIST

CHEMIST'S REVIEW #3

1. ORGANIZATION	2. NDA NUMBER
HFD-570 DPDP	20-762

3. NAME AND ADDRESS OF APPLICANT *(City and State)*	4. AF NUMBER
Schering Corporation 2000 Galloping Hill Road Kenilworth, NJ 07033	
	5. SUPPLEMENT(S) NUMBER(S) DATES(S) SCF-007 7/28/00

6. NAME OF DRUG	7. NONPROPRIETARY NAME
Nasonex® Nasal Spray	mometasone furoate nasal spray

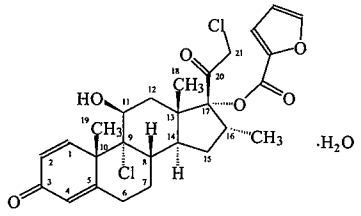
8. SUPPLEMENT PROVIDES FOR: CMC information supporting a new formulation of the drug product which does not include the preservative phenylethyl alcohol (PEA) for use with the crimped-on pump presentations only (10 g sample and 17 g trade size bottles).	9. AMENDMENT(S), REPORT(S), ETC. SCF-007 (BC) 10/2/00 SCF-007 (BC) 11/2/00* *Subject of this review.

10. PHARMACOLOGICAL CATEGORY	11. HOW DISPENSED	12. RELATED IND/NDA/DMF
anti-inflammatory corticosteroid	RX X OTC __	

13. DOSAGE FORM(S)	14. POTENCY
aqueous nasal spray	50 mcg/act (100 or 200 mcg/day)

15. CHEMICAL NAME AND STRUCTURE

9,21-Dichloro-17-[(2-furanylcarbonyl)oxy]-11β-hydroxy-16α-methylpregna-1,4-diene-3,20-dione Monohydrate



Mometasone Furoate Monohydrate

16. RECORDS AND REPORTS
CURRENT YES X NO___
REVIEWED YES X NO___

17. COMMENTS: Amendment of 11/2/00 corrects an error in the particle size specifications for the DS. The acceptance criterion is corrected to read that 90% of the drug substance is < 50 µm as per the original approval. See the reproduced pages 4, 5, and 6 of the DS specifications attached below.

cc:
Orig. NDA 20-762
HFD-570/div. File
HFD-570/CBertha/11/6/00
HFD-570/GPoochikian
HFD-570/DHilfiker
R/D Init. by:_____
F/T by: CBertha/11/6/00
doc # 00-11-02.rev.doc

18. CONCLUSIONS AND RECOMMENDATIONS: The supplement is recommended for **approval (AP)** from the CMC perspective. However, approval is contingent on a satisfactory EES response, and three satisfactory consult evaluations from biometrics, microbiology, and OPDRA/LNC.

19. REVIEWER NAME:	SIGNATURE	DATE COMPLETED
Craig M. Bertha, Ph.D.		11/6/00

3 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-762
5007
Chem Review
#3

/s/

Craig Bertha
11/13/00 02:56:58 PM
CHEMIST

Guiragos Poochikian
11/13/00 03:53:57 PM
CHEMIST

CHEMIST'S REVIEW #2

1. ORGANIZATION	2. NDA NUMBER
HFD-570 DPDP	20-762

3. NAME AND ADDRESS OF APPLICANT *(City and State)*
Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

OCT 10 2000

4. AF NUMBER

5. SUPPLEMENT(S)
NUMBER(S) DATES(S)
SCF-007 7/28/00

6. NAME OF DRUG	7. NONPROPRIETARY NAME
Nasonex® Nasal Spray	mometasone furoate nasal spray

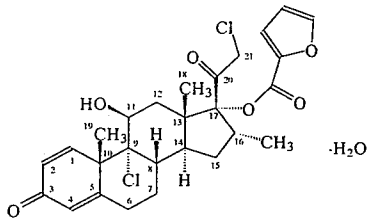
8. SUPPLEMENT PROVIDES FOR: CMC information supporting a new formulation of the drug product ( ) which does not include the preservative phenylethyl alcohol (PEA) for use with the crimped-on pump presentations only (10 g sample and 17 g trade size bottles).

9. AMENDMENT(S), REPORT(S), ETC.
SCF-007 (BC) 10/2/00*

*Subject of this review.

10. PHARMACOLOGICAL CATEGORY	11. HOW DISPENSED	12. RELATED IND/NDA/DMF
anti-inflammatory corticosteroid	RX X OTC __	
13. DOSAGE FORM(S)	14. POTENCY	
aqueous nasal spray	50 mcg/act (100 or 200 mcg/day)	

15. CHEMICAL NAME AND STRUCTURE
9,21-Dichloro-17-[(2-furanylcarbonyl)oxy]-11β-hydroxy-16α-methylpregna-1,4-diene-3,20-dione Monohydrate



Mometasone Furoate Monohydrate

16. RECORDS AND REPORTS
CURRENT YES X NO___
REVIEWED YES X NO___

17. COMMENTS: See review notes attached. Note that due to stability issues associated with the original application, which resulted in a 15 month expiry and extension by PAS only, a biometrics consult for evaluation of the proposed expiry period of 15 months for the newly formulated product was forwarded to the biometrics team and the results are pending.

cc:
Orig. NDA 20-762
HFD-570/div. File
HFD-570/CBertha/10/6/00
HFD-570/GPoochikian
HFD-570/DHilfiker
R/D Init. by: 10/10/00
F/T by: CBertha/10/6/00
doc # 00-10-02.rev.doc

18. CONCLUSIONS AND RECOMMENDATIONS: The supplement is recommended for **approval (AP)** from the CMC perspective. However, approval is contingent on a satisfactory EES response, and three satisfactory consult evaluations from biometrics, microbiology, and OPDRA/LNC.

REVIEWER NAME:	SIGNATURE	DATE COMPLETED
Craig M. Bertha, Ph.D.		10/6/00

24 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-762
SOP Chem Reviews #2

CHEMIST'S REVIEW #1

1. ORGANIZATION	2. NDA NUMBER
HFD-570 DPDP	20-762

3. NAME AND ADDRESS OF APPLICANT *(City and State)*
Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

4. AF NUMBER

5. SUPPLEMENT(S)
NUMBER(S) DATES(S)
SCF-007 7/28/00

6. NAME OF DRUG	7. NONPROPRIETARY NAME
Nasonex® Nasal Spray	mometasone furoate nasal spray

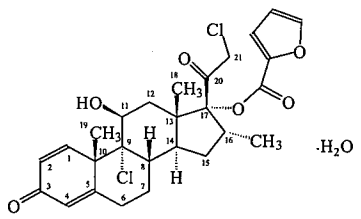
8. SUPPLEMENT PROVIDES FOR: CMC information supporting a new formulation of the drug product which does not include the preservative phenylethyl alcohol (PEA) for use with the crimped-on pump presentations only (10 g sample and 17 g trade size bottles).

9. AMENDMENT(S), REPORT(S), ETC.

10. PHARMACOLOGICAL CATEGORY	11. HOW DISPENSED
anti-inflammatory corticosteroid	RX X OTC __
13. DOSAGE FORM(S)	**14. POTENCY**
aqueous nasal spray	50 mcg/act (100 or 200 mcg/day)

12. RELATED IND/NDA/DMF

15. CHEMICAL NAME AND STRUCTURE
9,21-Dichloro-17-[(2-furanylcarbonyl)oxy]-11β-hydroxy-16α-methylpregna-1,4-diene-3,20-dione Monohydrate



Mometasone Furoate Monohydrate

16. RECORDS AND REPORTS
CURRENT YES X NO___
REVIEWED YES X NO___

17. COMMENTS: See review notes attached. Note that due to stability issues associated with the original application, which resulted in a 15 month expiry and extension by PAS only, a biometrics consult for evaluation of the proposed expiry period of 15 months for the newly formulated product was forwarded to the biometrics team.

cc:
Orig. NDA 20-762
HFD-570/div. File
HFD-570/CBertha/8/18/00
HFD-570/GPoochikian
HFD-570/DHilfiker
R/D Init. by:_____
F/T by: CBertha/8/18/00
doc # 00-07-28.rev.doc

18. CONCLUSIONS AND RECOMMENDATIONS: The supplement is **not approvable (NA)** from the CMC perspective. The comments contained in the draft letter should be forwarded to the applicant by the PM. It is noted that approval is also contingent on a satisfactory EES response, and three satisfactory consult evaluations from biometrics, microbiology, and OPDRA/LNC.

19. REVIEWER NAME:	SIGNATURE	DATE COMPLETED
Craig M. Bertha, Ph.D.		8/18/00

10 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-762
5007
Chem Review
#1

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-762/S007

STATISTICAL REVIEW(S)

STATISTICAL REVIEW AND EVALUATION
STABILITY STUDY

NDA Number:	**20-762/S-007**
Applicant:	**Schering Corporation**
Name of Drug:	**Nasonex™ [redacted] Nasal Spray, 50 mcg**
Statistical Reviewer:	**Feng Zhou, HFD-715**
Chemistry Reviewer:	**Craig Bertha, Ph.D., HFD-570**
Document Reviewed:	**Stability Report, Volume1-2 dated February 24, 2004**

I. Introduction

The sponsor submitted additional stability data for the newly formulated product of Nasonex™ [redacted] Nasal Spray, 50 mcg. The data were from two manufacturing sites, Kenilworth, NJ and Manati, PR and two packaging configurations: crimped-on pump, trade size (17-g fill) and crimped-on pump, sample size (10-g fill). The sponsor proposed a 24-month shelf life for its product (volume 1).

II. Stability Parameters

The following is a list of stability parameters and specifications the sponsor used to establish the stability for Nasonex [redacted] Nasal Spray, 50 mcg and the chemistry reviewer agreed with it.

Assay for Mometasone Furoate	90.0 – 110% of LS (0.45–0.55 mg/g)
Assay for Benzalkonium Chloride	90.0 – 110% of LS (0.18-0.22 mg/g)
Uniformity of Spray Content	
– Beginning Portion of Container	[redacted]
– Middle Portion of Container	
– End Portion of Container	
PH	4.3 – 4.9
Average Weight per Actuation	
– Beginning Portion of Container	[redacted]
– Middle Portion of Container	
– End Portion of Container	
Osmolality	

III. Sponsor's Stability Analysis

Table 1 summarized the electronic data, which the sponsor submitted on April 19, 2004.

Table 1. Summary of all stability data submitted by sponsor

°C/%RH	Manuf. Site	Size	Batch	Time Point (month) 0	3	6	9	12	15	18	24	36

The sponsor performed separate statistical analyses based on data for each package size across manufacturing sites under 25°C/35%RH storage condition. The expiration dates were estimated for all parameters. Table 2 summarizes the sponsor's statistical results.

The sponsor claimed that the statistical methods used were in accordance with FDA's "Guidelines for Submitting Documentation for the Stability of Human Drugs Biologics." The sponsor also claimed that it used the Agency's SAS Stability Analysis Program (STAB) to perform the statistical analysis. The sponsor's analyses results appear to support a 24-month shelf life for the product.

Table 2. The Sponsor's Statistical Results

Table 1 Summary of Results

Test	Package Type	Number of Batches	Model	Batch	Estimated Expiration Period
Osmolality	Trade				
	Sample				
pH	Trade				
	Sample				

Note: Batch refers to the ordered batch numbers used in analyses. The corresponding batch identification can be found in the analyses output.

KEY: Model 1 - common slope and common intercepts
Model 2 - common slope and separate intercepts
Model 3 - separate slopes and separate intercepts

Table 2 continues to next page.

Table 1 Summary of Results

Test	Package Type	Number of Batches	Model	Batch	Estimated Expiration Period
Assay for Mometasone Furoat					
Assay for Benzalkonium Chlori					
Individual Dose Uniformity Beginning					
Individual Dose Uniformity Middle					
Individual Dose Uniformity End					
Average Dose Uniformity Beginning					
Average Dose Uniformity Middle					
Average Dose Uniformity End					

IV. Reviewer's Stability Analysis

This reviewer requested the electronic stability data on February 2, 2004. In response, the sponsor submitted the electronic data on April 19, 2004. The data set included data up to [redacted] months from [redacted] batches for trade package of two manufacturing sites and [redacted] batches for sample package of two manufacturing sites under 25°C/35%RH storage condition, [redacted] in total (See Table 1 for details).

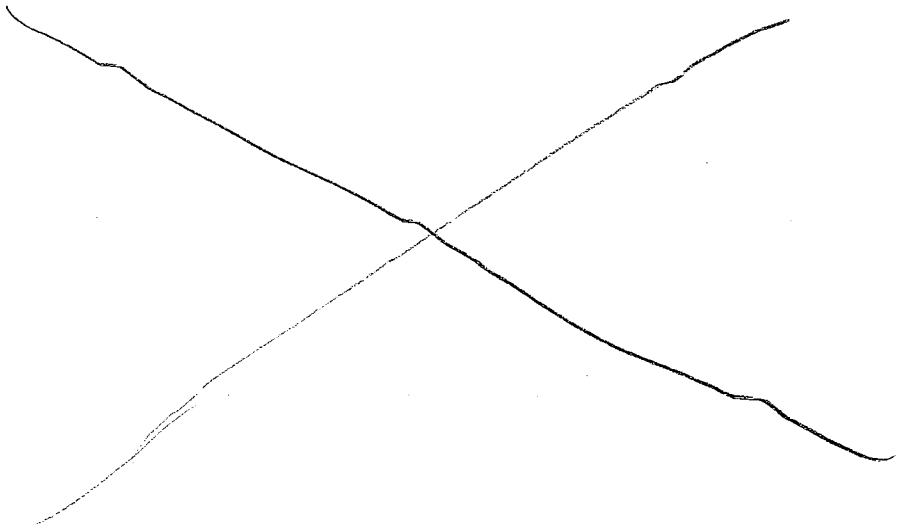
There were [redacted] batches [redacted] manufactured at Kenilworth site and [redacted] batches [redacted] manufactured at Manati site. It is noted that, FDA guidance[1] recommends that at least three batches be tested for each manufacturing site and package size combination. Since the sponsor's study failed to meet the above FDA minimum requirement of three batches, the reviewer performed separate statistical analyses based on data for each manufacturing site across [redacted] package sizes under 25°C/35%RH storage condition. The results of this reviewer's analysis presented in Table 3 appear to support a 24-month expiration date.

Table 3. Expiry date analysis for Nasonex [redacted] Nasal Spray, 50 mcg by Manufacturing Sites

Test	*Specification*	*Package Size*	*Manufacturer Site*	*Batch*	*Model*	*Fitted Line*	*Minimum Expiry Date*
Assay Benzalkonium Chloride	90 - 110% (0.18–0.22mg/g)						
Assay Mometasone Furoate	90 - 110% (0.45-0.55mg/g)						
PH	4.3 - 4.9						
Osmolality	[redacted] Milliosmoles						
Uniformity of Spray Content (Initial)	[redacted]						
Uniformity of Spray Content (Middle)	[redacted]						

[1] *Guideline for Submitting Documentation for the Stability of Human Drugs and Biologics, FDA.*

Test	*Specification*	*Package Size*	*Manufacturer Site*	*Batch*	*Model*	*Fitted Line*	*Minimum Expiry Date*
Uniformity of Spray Content (End)							
Average Weight per Actuation (Initial)							
Average Weight per Actuation (Middle)							
Average Weight per Actuation (End)							

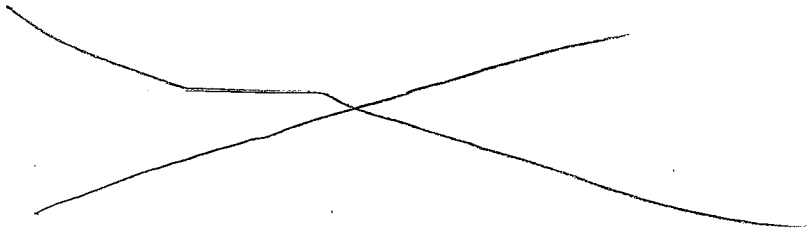


Note: Model = 1 – common slope and common intercepts
Model = 2 – common slope and separate intercepts
Model = 3 – separate slopes and separate intercepts

Table 4 shows results of an additional statistical analysis using the data of batches package sizes and the two individual manufacturing sites. The shortest estimated expiration dating period of is based on the Osmolality data of the size manufactured at Manati, PR site. The estimated expiration dating periods based on the data of other parameters of batches are greater than months. Therefore the analysis results based on combined data of batches of two manufacturing sites and the package sizes under 25°C/35%RH storage condition appear to support a 24-month expiration period.

Table 4. Expiry date analysis for Nasonex Nasal Spray, 50 mcg

Test	*Specification*	*Package Size*	*Manufacturer Site*	*Batch*	*Model*	*Fitted Line*	*Minimum Expiry Date*
Assay Benzalkonium Chloride	90 - 110% (0.18–0.22mg/g)						
Assay Mometasone Furoate	90 - 110% (0.45-0.55mg/g)						



Test	*Specification*	*Package Size*	*Manufacturer Site*	*Batch*	*Model*	*Fitted Line*	*Minimum Expiry Date*
PH	4.3 - 4.9						
Osmolality	[redacted] Milliosmoles						
Uniformity of Spray Content (Initial)							
Uniformity of Spray Content (Middle)							
Uniformity of Spray Content (End)							
Average Weight per Actuation (Initial)							
Average Weight per Actuation (Middle)							
Average Weight per Actuation (End)							

Note: Model = 1 – common slope and common intercepts
Model = 2 – common slope and separate intercepts
Model = 3 – separate slopes and separate intercepts

V. Conclusion

The sponsor's study did not meet the FDA requirement of testing at least three batches each manufacturing site and package size combination.

The results of this reviewer's analyses using data of [redacted] batches and data for each manufacturing site across package sizes show that the sponsor's stability data support a 24 month expiration date for two the package types of Nasonex [redacted] Nasal Spray, 50 mcg manufactured at Kenilworth, NJ and Manati, PR sites.

The results of the sponsor's analyses based on data for [redacted] package size across manufacturing sites also reach the same conclusion as that reached by this reviewer's analysis results.

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File name: stab20_762_Mar10_04.doc

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

/s/

Feng Zhou
4/29/04 01:22:33 PM
BIOMETRICS

Karl Lin
4/29/04 01:52:24 PM
BIOMETRICS
Concur with review

STATISTICAL REVIEW AND EVALUATION
STABILITY STUDY

NDA Number:	20-762
Applicant:	Schering Corporation
Name of Drug:	Nasonex™ [redacted] Nasal Spray, 50 mcg
Statistical Reviewer:	Feng Zhou, HFD-715
Chemistry Reviewer:	Craig Bertha, Ph.D., HFD-570
Document Reviewed:	Stability Report, Volume1-3 dated July 28, 2000

I. Introduction

The sponsor submitted the stability data for Nasonex™ [redacted] Nasal Spray, 50 mcg. The data from two manufacturing sites, Kenilworth, NJ and Manati, PR, included two packaging configurations: 1) crimped-on pump, trade size (17-g fill), 2) crimped-on pump, sample size (10-g fill) (p20-26, v1). The sponsor proposed a 15-month shelf life for its product (p150, v2).

II. Stability Parameters

The following is a list of stability parameters and specifications the sponsor used to establish the stability for Nasonex [redacted] Nasal Spray, 50 mcg.

Assay for Mometasone	90.0 – 110% of LS
Assay for Benzalkonium	90.0 – 110% of LS
Uniformity of Spray Content	
– Beginning Portion of Container	[redacted]
– Middle Portion of Container	
– End Portion of Container	
PH	4.3 – 4.9
Average Weight per Actuation	
– Beginning Portion of Container	[redacted]
– Middle Portion of Container	
– End Portion of Container	
Osmolality	

III. Sponsor's Stability Analysis

The data submitted by the sponsor were summarized in Table A below. The electronic data, not included in the original NDA submission, were submitted in a subsequent amendment.

Table A. Summary of all stability data submitted by sponsor

°C/%RH	Manuf. Site	Size	Batch	Time Point (M) 0	1	3	6	9	12
[redacted]									

S = Submitted in paper copy
E = Submitted in electronic copy

The sponsor performed statistical analyses based on only [redacted] batches collapsed across manufacturing sites for the two package sizes under 25°C/35%RH storage condition. The expiration dates were estimated for all parameters.

Tables 1 and 2 summarize the sponsor's statistical results.

In Table 2, data for the Assay for Benzalkonium Chloride from [redacted] batches were used in the selection of degradation model. The data from the [redacted] batches were pooled to obtain a [redacted] month estimated expiration dating period. This is the shortest estimated period among those for all the tested parameters. The sponsor's analyses appear to support a 15-month shelf life for the product.

The sponsor claimed that the statistical methods used were in accordance with FDA's "Guidelines for Submitting Documentation for the Stability of Human Drugs Biologics." The sponsor also claimed that it used the Agency's SAS Stability Analysis Program (STAB) to perform the statistical analysis.

Table 1 [Section 4.B.8.3.4.] Summary of the Statistical Analyses for the Stability Batches of Mometasone Furoate Aqueous ——— Nasal Spray, 0.05% - Trade Size

Test	Batch No.	Model	Predicted Expiration Period (months)
Assay for Mometasone Furoate			
Assay for Benzalkonium Chloride			
pH			
Osmolality			
Drug Delivery for the Beginning of the Can			
Drug Delivery for the Middle of the Can ——— the Labelled Number of Actuations)			
Drug Delivery for the Labelled Number of Actuations			
Average Weight Per Actuation for the Beginning of the Can			
Average Weight Per Actuation for the Middle of the Can——— the Labelled Number of Actuations)			
Average Weight Per Actuation for the Labelled Number of Actuations			

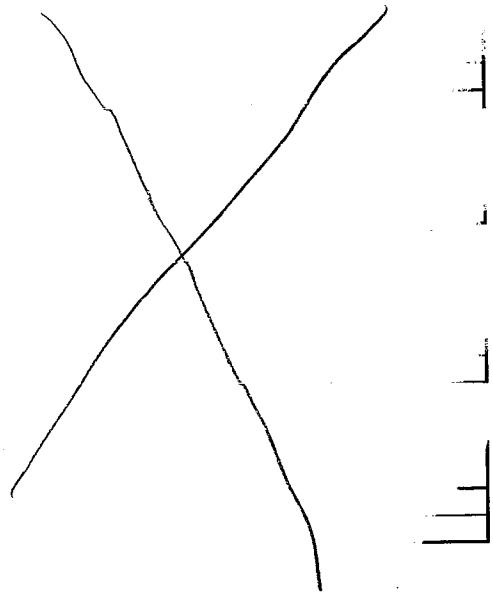
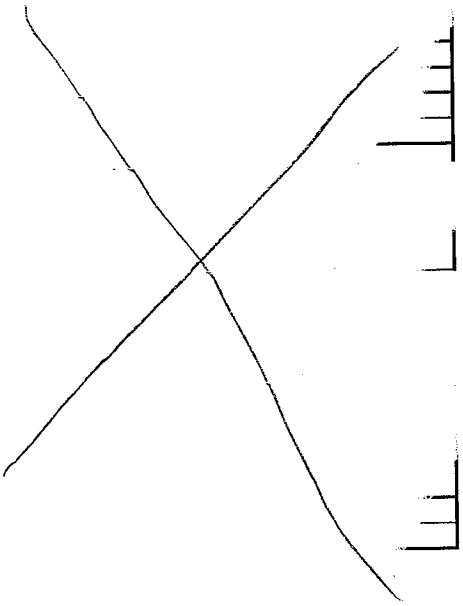


Table 2 [Section 4.B.8.3.4.] Summary of the Statistical Analyses for the Stability Batches of Mometasone Furoate Aqueous ←——→ Nasal Spray, 0.05% - Sample Size

Test	Batch No.	Model	Predicted Expiration Period (months)
Assay for Mometasone Furoate			
Assay for Benzalkonium Chloride			
pH			
Osmolality			
Drug Delivery for the Beginning of the Can			
Drug Delivery for the Middle of the Can ← of the Labelled Number of Actuations)			
Drug Delivery for the Labelled Number of Actuations			
Average Weight Per Actuation for the Beginning of the Can			
Average Weight Per Actuation for the Middle of the Can ← of the Labelled Number of Actuations)			
Average Weight Per Actuation for the Labelled Number of Actuations			



IV. Reviewer's Stability Analysis

This reviewer requested the electronic stability data on 10/3/2000. In response, the sponsor submitted the electronic data on 11/02/2000. The data set included data up to months from batch for manufacturing sites and two package sizes under 25°C/35%RH storage condition, batches in total (See Table A). There were a few discrepancies in the values of some parameters between the electronic data and paper copy of NDA in batch Five values of variable - LEVEL in the electronic data differed from those in the paper copy of NDA. This reviewer used the electronic data to evaluate the submission[1].

There were only batches at Kenilworth site and batches at Manati site with electronic data of 25°C/35%RH storage condition. Given this deficiency, the reviewer consulted with the chemistry reviewer (Dr. Bertha) and at his direction performed the statistical analysis using the combined data from the individual manufacturing sites.

Tables B-1 and B-2 summarize the results for all parameters for manufacturing sites Manati and Kenilworth, respectively.

The results of this reviewer's analysis presented in Tables B-1 and B-2 appear to support a 15-month expiration date.

It is noted that, FDA guidance[2] recommends that at least three batches be tested for each manufacturing site and package size combination. As the sponsor's study failed to meet the FDA minimum requirement of three batches, this reviewer performed an additional statistical analysis based on for each package size and manufacturing site.

Table C contains the estimated expiration dating periods based on the data from individual batches of different sizes and sites.

As shown in table C, the estimated expiration dating period based on the assay data of for sample size manufactured at Manati, PR site is months. It is the shortest estimated expiration period among those presented in Table C. The results of analysis based on batches of two manufacturing sites and the two package sizes under 25°C/35%RH storage condition appear to support a month expiration period.

[1] This reviewer obtained the similar results as shown in table 1 and 2 by using electronic data.
[2] *Guideline for Submitting Documentation for the Stability of Human Drugs and Biologics, FDA.*

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V. Conclusion

The sponsor's study did not meet the FDA requirement of testing at least three batches per manufacturing site and package size combination.

The results of this reviewer's analysis using data of / — 6 batches show that the sponsor's stability data support a /month expiration date for all the package types of Nasonex™ ——— Nasal Spray, 50 mcg manufactured at Kenilworth, NJ and Manati, PR sites.

It is noted that the 12 months estimated expiration dating period is based on data of ——— batches of the two package sizes manufactured at the two sites. It is well known that results based on testing of a/ ——— / / ————), and that results based on testing only > batches provide an unreliable estimate. Because of the lack of adequate number of batches (a minimum of three batches) in analysis, the estimated expiration-dating period may not be reliable.

3 Page(s) Withheld

1 § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Statistical- 20-762
5007
Review #1

/s/

Feng Zhou
12/6/00 04:53:13 PM
TECHNICAL

Karl Lin
12/7/00 07:45:50 AM
BIOMETRICS

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-762/S007

MICROBIOLOGY REVIEW

REVIEW FOR HFD-570
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF/HFD-805
MICROBIOLOGY REVIEW # 1 OF SUPPLEMENT

January 04, 2001

A. 1. **NDA/ANDA/IND/:** NDA 20-762/S-007

2. **TYPE OF SUPPLEMENT:** SCF

3. **SUPPLEMENT PROVIDES FOR:** Removal of Phenylethyl Alcohol as a preservative for manufacturing [redacted] nasal spray.

4. **APPLICANT/SPONSOR:** Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033.

5. **MANUFACTURING SITE:** Kenilworth, NJ

6. **PRODUCT NAME DRUG:**
Proprietary: Nasonex ® [redacted]
Nonproprietary: Mometasone furoate monohydrate.
Drug Priority Classification: S

7. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Momethasone furoate monohydrate (0.05%) in [redacted] mL plastic spray bottles.

8. **METHOD (S) OF STERILIZATION:** None (non-sterile product). The product is preserved with [redacted]; of benzalkonium chloride [BAC].

9. **PHARMACOLOGICAL CATEGORY:** Treatment of the symptoms of seasonal/perennial allergic rhinitis.

B. 1. **DOCUMENT/LETTER DATE:** July 28, 2000
2. **RECEIPT DATE:** August 15, 2000
3. **CONSULT DATE:** October 20, 2000
4. **DATE OF AMENDMENT:** NA
5. **ASSIGNED FOR REVIEW:** November 11, 2000
6. **SUPPORTING/RELATED DOCUMENTS:** None

C. REMARKS: The consult requests review of supplemental application NDA 20-762/S-007 for 0.05% Nasonex® (mometasone furoate monohydrate). The document submitted consists of pages 5 through 18 from section 4.B.9 Pharmaceutical development report. The submitted pages contain an introduction, experimental procedure, BAC assay results and the Antimicrobial Preservative Effectiveness (APE) results.

D. CONCLUSIONS: The Microbiology section of the application containing the Antimicrobial Preservative Effectiveness for Benzalkonium chloride is recommended for approval based on the information provided.

Vinnie Pawar, Ph.D.

cc:

Original NDA 20-762/S-007
HFD 570/Div. File
HFD 160/Consult
HFD 570/C. Bertha/G. Poochikian
HFD 160/Microbiologist/V.Pawar [HFD-805]

Drafted by: V. Pawar, 01/04/2001
R/D initialed by: P. Cooney

3 Page(s) Withheld

√ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Microbiology- 20-762
S007

/s/

Vinayak Pawar
1/16/01 11:53:21 AM
MICROBIOLOGIST

Peter Cooney
1/16/01 04:14:29 PM
MICROBIOLOGIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-762/S007

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Division of Pulmonary and Allergy drug Products

REGULATORY PROJECT MANAGER REVIEW

Application Number: NDA 20-762/S-007

Name of Drug: Nasonex (mometasone furoate monohydrate) Aqueous Nasal Spray

Applicant: Schering Corporation

Material Reviewed:

Submission Date(s): April 23, 2004

Receipt Date(s): April 26, 2004

Background and Summary

A complete response to the approvable letter for Supplement 007 dated February 2, 2001, was received on April 26, 2004. Supplement 007 provides for a new formulation of Nasonex Nasal Spray that does not include the excipient phenylethyl alcohol. This complete response detailed Schering's plan to Revised labeling and packaging were also provided.

Review

The last approved labeling, submitted on June 10, 2003, was compared to the proposed labeling submitted April 23, 2004, and August 18, 2004. The proposed labeling is nearly identical to the currently approved package insert except for the deletion of the excipient "phenylethyl alcohol" from the DESCRIPTION section. Also, the phrase "the wall between the two nostrils" was added to Instruction No. 3 in the Patient's Instructions for Use. The phrase now reads: DO NOT spray directly onto nasal septum, the wall between the two nostrils.
Of note, the labeling submitted on April 23, 2004, , in fact, it will be supplied with a blue dust cap. This correction was made in the revised labeling submitted to the Agency on August 18, 2004. In addition, the bottle (immediate container) labels for the 17g and 10g products submitted on April 23, 2004, contain the This was discussed with Schering, and the plan is to change the color to blue on the bottle (immediate container) labels at a future date.

Conclusions

The CMC review dated May 5, 2004, recommends this supplemental application for approval

from the CMC perspective. The immediate container label submitted on April 23, 2004, is acceptable. The carton labels, package insert, and patient instructions for use submitted on August 18, 2004, which include the revisions requested by FDA on August 16, 2004, are acceptable and therefore, should be approved.

Lori A. Garcia, R.Ph.
Regulatory Project Manager

Supervisory Comment/Concurrence:

Sandy Barnes
Chief, Project Management Staff

Drafted: LAG/August 20, 2004
Revised/Initialed:
Finalized:
Filename: Document1

CSO LABELING REVIEW

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

/s/

Lori Garcia
9/3/04 07:55:49 AM
CSO

Division of Pulmonary and Allergy Drug Products

REGULATORY PROJECT MANAGER REVIEW

Application Number: NDA 20-762/SCF 007 FA

Name of Drug: Nasonex (mometasone furoate monohydrate) Aqueous Nasal Spray, 50mcg

Applicant: Schering Corporation

Material Reviewed:

Submission Date(s): November 15, 2004

Received Date(s): November 17, 2004

Background and Summary

NDA 20-762/SCF 007 was approved on August 25, 2004, and provides for a new formulation of Nasonex Nasal Spray, 50mcg, that does not include the excipient phenylethyl alcohol. The approval letter stated that the final printed labeling should be identical to the submitted labeling (text for the package insert, text for the patient's instructions for use, and carton labels dated August 18, 2004, and immediate container labels dated April 23, 2004).

Review

I compared the final printed labeling submitted on November 15, 2004, to the approved labeling text and they are identical.

Conclusions

The final printed labeling submitted on November 15, 2004, should be acknowledged and retained.

Lori Garcia, R.Ph.
Regulatory Project Manager

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/s/

Lori Garcia
1/28/05 04:38:47 PM
CSO

Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm. 15B03
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: **April 26, 2001**

NDA NUMBER: **20-762/S-007**

NAME OF DRUG: **Nasonex** [redacted]
(Mometasone Furoate Monohydrate Nasal Spray)

NDA HOLDER: **Schering Corporation**

I. INTRODUCTION

This supplemental application provides for a new formulation of Nasonex Nasal Spray, identical in all respects to the original formulation except for the absence of the preservative phenylethyl alcohol. This modification is intended to [redacted] The sponsor intends to [redacted]

The sponsor first proposed '[redacted] the proprietary name for this new formulation. However, the Division did not find this name acceptable and the sponsor then submitted the alternative name "Nasonex [redacted] '. OPDRA completed a Proprietary Name Review on December 1, 2000 and did not recommend use of the name Nasonex [redacted]

On January 12, 2001, the sponsor requested the Division reconsider the name based on the lack of potential for any risk associated with confusion [redacted] and precedence established with other marketed products. The sponsor submitted marketing materials for other currently marketed products that do not contain phenylethyl alcohol which are being promoted as [redacted] Schering would like the opportunity to make similar claims with their new formulation. The Division is not opposed to the promotion of such information but is concerned about establishing a new precedent for the use of such a promotional description as part of the proprietary name. The Division has not allowed companies to use proprietary names that describe what they do NOT have. The Division proposed we consider the allowance of a modifier such as [redacted] on the container label and carton labeling without allowing it to be part of the tradename associated with the product.

This consult was written in response to a request from the Division for OPDRA to provide our opinion on Schering's rebuttal and whether the use of modifiers, such as ' [redacted] and [redacted] should or should not be allowed in proprietary names for products.

PRODUCT INFORMATION

Nasonex [redacted] is a metered-dose, manual pump spray unit containing an aqueous suspension of mometasone furoate monohydrate equivalent to 0.05% w/w mometasone furoate calculated on the anhydrous basis. After initial priming, each actuation of the pump delivers a metered spray containing 100 mg of suspension containing mometasone furoate monohydrate equivalent to 50 mcg of mometasone furoate. Each bottle provides 120 sprays. Nasonex is indicated for the treatment of the nasal symptoms of seasonal allergic and perennial rhinitis in adult and pediatric patients 3 years of age and older and for the prophylaxis of the nasal symptoms of seasonal allergic rhinitis in adult and adolescent patients 12 years and older. The usual recommended dose for prophylaxis and treatment of the nasal symptoms of seasonal allergic rhinitis and treatment of the nasal symptoms of perennial allergic rhinitis is two sprays in each nostril once daily.

II. RISK ASSESSMENT

A. *SPONSOR COMMENT*

We do not believe that using the tradename "Nasonex [redacted] Nasal Spray" raises any safety issues. This is not a situation where additional ingredients are being added to the new formulation. The only difference between the two formulations is the absence of phenylethyl alcohol from the new formulation. Neither the presence nor the absence of phenylethyl alcohol presents a safety issue for patients. A search of the published literature failed to identify any reports of hypersensitivity reactions due to phenylethyl alcohol.

[redacted]

OPDRA RESPONSE

OPDRA searched the FDA Adverse Event Reporting System (AERS) and MedLine for reports of hypersensitivity reactions due to phenylethyl alcohol and also failed to find any published reports on this issue. [redacted]

Therefore, OPDRA agrees with the sponsor that the tradename does not raise any safety concerns.

[i] Research Projects at the Department of Humanities, Social and Political Sciences, *Electrocortical and Autonomic Alteration by Odor Administration,* Eidgenossische Technische Hochschule Zurich; www.rereth.ethz.ch/gess/verhalten/zeier/pj.03.html

[ii] Social Issues Research Center, Clements Oxford UK, *The Smell Report*, Fox, K; www.sirc.org/publik/smell_human.html

B. *SPONSOR COMMENT*

Nasonex Nasal Spray. The term is a concise, straightforward and neutral description of one Nasonex product

A review of promotional and advertising materials for similar products illustrates that the name we are proposing

OPDRA RESPONSE

The use we have no objections to this proposal. We also acknowledge that in the intranasal corticosteroid market, there is recognition by both the drug companies and the physicians prescribing these products that certain intranasal steroids

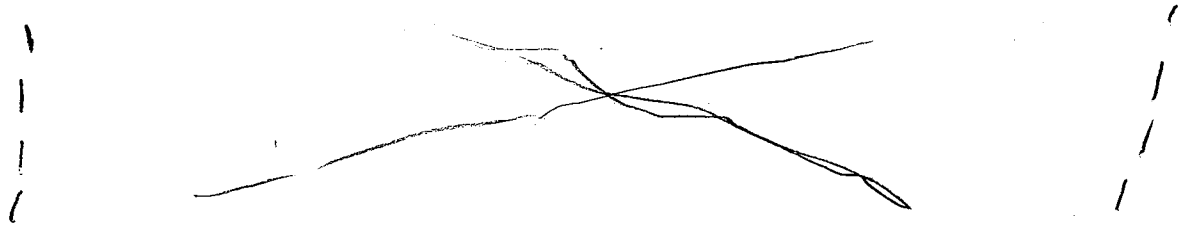
These descriptors appear only in the text of the advertisements.

In this case the product dosing is the same for both formulations.

C. *SPONSOR COMMENT*

We believe that the Division's suggestion that Schering use

OPDRA RESPONSE



III. RECOMMENDATIONS

OPDRA has no objections to the use of the proprietary name "Nasonex [redacted] Nasal Spray".

OPDRA would appreciate feedback of the final outcome of this consult. We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Carol Holquist, R.Ph. at 301-827-0915.

Carol Holquist, R.Ph.
Safety Evaluator
Office of Postmarketing Drug Risk Assessment (OPDRA)

Concur:

Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Postmarketing Drug Risk Assessment (OPDRA)

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

/s/

Carol Holquist
4/30/01 01:07:50 PM
PHARMACIST

Jerry Phillips
4/30/01 01:23:45 PM
DIRECTOR

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Parklawn Rm. 6-34
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: March 2, 2004

NDA: 20-762/S-007

NAME OF DRUG: **Nasonex**
(Mometasone Furoate Monohydrate Nasal Spray)
50 mcg/spray

NDA SPONSOR: Schering Corporation

I. INTRODUCTION

This consult was written in response to a request from the Division of Pulmonary and Allergy Drug Products, for an assessment of the proprietary name "Nasonex®" regarding potential name confusion with other proprietary or established drug names. The container labels, carton and package insert labeling were submitted for review and comment.

This supplemental application provides for a new formulation of Nasonex® Nasal Spray, identical in all respects to the original formulation except for the absence of the excipient phenylethyl alcohol. This modification is intended The sponsor intends to

The sponsor originally proposed the name "Nasonex®" as the proprietary name for the new formulation. However, the Division did not find the name acceptable. The sponsor submitted the alternative name "Nasonex". OPDRA did not recommend the use of this name in a consult dated December 1, 2000 (OPDRA Consult # 00-0313). In response to a rebuttal submitted by the sponsor dated January 12, 2001, OPDRA reversed its original decision and recommended the use of the modifier on the container label and carton labeling

II. RISK ASSESSMENT

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[i,ii] as well as several FDA databases[iii] for existing drug names which sound-alike or look-alike to "Nasonex to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S.

[i] MICROMEDEX Integrated Index, 2004, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[ii] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[iii] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support proprietary name consultation requests, New Drug Approvals 1998-2004, and the electronic online version of the FDA Orange Book.

Patent and Trademark Office's Text and Image Database[iv] and the data provided by Thomson & Thomson's SAEGIS™ Online Service[v] were also conducted. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Nasonex——— Potential concerns regarding drug marketing and promotion related to the proposed name was also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC did not have any concerns from a promotional perspective regarding the proposed name Nasonex———

2. The Expert Panel identified four proprietary names that have potential for confusion with Nasonex——— These products are listed in Table 1 (see below), along with the dosage form available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	**Dosage form(s), Established name**	**Usual adult Dose***	**Other****
Nasonex——— (Rx)	**Mometasone Nasal Spray 50 micrograms/spray**	**2 sprays in each nostril once daily. Prophylaxis: Begin 2 to 4 weeks prior to the anticipated start of the pollen season.**	
Nasonex (Rx)	Mometasone Nasal Spray 50 micrograms/spray	2 sprays in each nostril once daily. Prophylaxis: Begin 2 to 4 weeks prior to the anticipated start of the pollen season.	**L/A, S/A
Sanorex (Rx) *Discontinued*	Mazindol Tablets 1 mg and 2 mg Phenteremine Capsules 15 mg and 30 mg	1 mg to 3 mg daily with meals, up to a maximum of 3 mg/day. 15 mg to 30 mg before breakfast; or 10 to 14 hours before bedtime.	**L/A
Nasacort AQ (Rx)	Triamcinolone Nasal Spray 55 micrograms/spray	2 sprays in each nostril once daily.	**L/A
Nuromax (Rx)	Doxacurium Injection 1 mg/mL	Tracheal Intubation 0.05 mg/kg (2 x ED_{95}) Prolonged Neuromuscular Block 0.08 mg/kg (3 x ED_{95})	**L/A
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)			

[iv] WWW location http://www.uspto.gov.

[v] Data provided by Thomson & Thomson's SAEGIS(tm) Online Service, available at www.thomson-thomson.com.

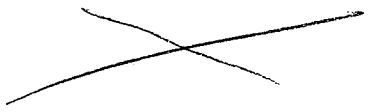
B. PHONETIC ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs though the phonetic algorithm. The phonetic search modules return a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. No additional names of concern were identified in POCA that were not discussed in EPD.

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of Nasonex with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 129 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Nasonex (see below). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: 	Nasonex use as directed, #1.
Inpatient RX: 	

2. Results:

One respondent interpreted the proposed name as Nasonex, an approved product currently marketed in the United States.

D. DQRS AND AERS DATABASE SEARCH

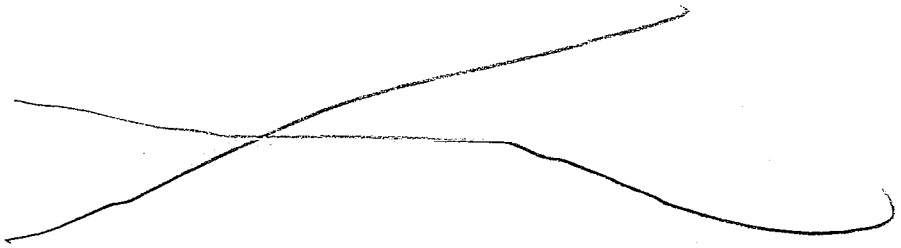
Since the drug "Nasonex", is currently approved in the U.S. market, DMETS searched the *DQRS* and *FDA Adverse Event Reporting System (AERS)* database for all postmarketing safety reports of medication errors associated with Nasonex, in order to determine the degree of name confusion with Nasonex and other approved drug products. The MedDRA Preferred Term (PT), "Medication Error" and the drug name "Nasonex%", and "mometasone" were used to perform these searches. This search strategy yielded ten (10) medication errors. One of the reports involved Nasonex being used by an unintended user; one report involved a patient who ran out of medicine, and discontinued use, thereby experiencing an under dosage; three of the reports involved cases in which the patient took the wrong dose of medicine due to misreading the prescription label; two cases involved disease contraindications; and three cases involved an incorrect route of administration, two of which were accidental, and one in which the physician wrote the prescription incorrectly. None of these reports involved errors relating to name confusion, labeling or packaging.

E. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name "Nasonex———", the primary concerns related to four look-alike and/or sound-alike names currently marketed in the United States. The products considered to have potential for name confusion with Nasonex——— were: Nasonex, Sanorex, Nasacort AQ, and Nuromax. Upon further review of the names gathered from EPD, the name Nuromax was not reviewed further due to a lack of convincing look-alike similarities with Nasonex——— in addition to numerous differentiating product characteristics such as product strength, dosage form, route of administration, dosage formulation, and indication of use.

We conducted prescription studies to simulate the prescription ordering process. In this case, there was confirmation that Nasonex——— could be confused with Nasonex. One respondent from the inpatient study misinterpreted the name as "Nasonex". Although there are limitations to the predictive value of these studies, primarily due to sample size, we have safety concerns due to the positive interpretation with this drug product. A positive finding in a study with a small sample size may indicate a high risk and potential for medication errors when extrapolated to the general U.S. population.

1. Nasonex is identical in look and sound to the proposed name, Nasonex——— if the suffix ——— is omitted. Like Nasonex———, Nasonex contains the active ingredient, mometasone, and is indicated for the treatment of nasal symptoms associated with seasonal allergic and perennial allergic rhinitis in adults and patients two years of age and older; and for the prophylaxis of nasal symptoms of seasonal allergic rhinitis in adult and adolescent patients 12 years of age and older. The recommended dose is 2 sprays in each nostril once daily. Nasonex and Nasonex——— share the same root word, Nasonex. They also contain the same active ingredient (mometasone), and have an overlapping indication of use (allergic rhinitis), route of administration (intranasal), dosage form (nasal spray), strength (50 micrograms/spray), dosing quantity (2 sprays), and dosing interval (daily). The only difference between the products is the addition of the modifier ——— Should a prescription written for Nasonex——— be misinterpreted and dispensed with Nasonex, or vice versa, it is not likely that patients would experience adverse events, since the products contain the same active ingredient. Also, because the products have the same dosing strength and regimen, patients who inadvertently received the incorrect medication would not experience side effects associated sub-therapeutic or supra-therapeutic dosing of either medication.



Nasonex will not contain phenylethyl alcohol in its formulation, and will therefore be ; usual practice would be that a descriptor, such as appear on the container label and carton labeling, and not as part of the proprietary name.

2. Sanorex was identified to have look-alike similarity to the proposed name, Nasonex if is not designated (see below). Sanorex contains mazindol, a non-amphetamine appetite suppressant indicated for the short-term treatment of obesity. Per the U.S. Patent and Trademark Office website, Sanorex containing the active ingredient mazindol has been discontinued in the United. States. However, upon further research of various on-line prescription databases (e.g. Medline Plus Drug Information, Drugs.com, and Pharmacyhealth.net), it has been determined that the name "Sanorex" is also used as a brand of phenteremine, a prescription appetite suppressant currently marketed in the United States. The recommended dose is 15 mg to 30 mg once daily, before breakfast or 10 to 14 hours before bedtime. Therefore, prescriptions could potentially be written for Sanorex, resulting in phenteremine being dispensed. Sanorex and the root name Nasonex look similar in that each name has seven letters, and end with an identical letter combination ("ex"). The preceding letters ("r" vs. "n"), also look similar when scripted. Additionally, depending on how it is scripted, the first two letters look somewhat similar ("Sa" vs. "Na"). Both products are also administered once daily. Despite these similarities, there are differences that help to distinguish Sanorex and Nasonex from one another. The products differ in route of administration (oral vs. intranasal), dosage form (capsule vs. nasal spray), strength (55 micrograms/spray vs. 15 mg and 30 mg), and indication of use (seasonal allergic rhinitis vs. appetite suppressant). Additionally, the DQRS and AERS searches did not reveal any medication errors between the currently marketed product Nasonex and Sanorex. DMETS believes that these product differences will minimize the risk of confusion and error between Sanorex and Nasonex

Sanorex	**Nasonex**
Sanorex	Nasonex

3. Nasacort AQ was identified to have look-alike similarity to the proposed name, Nasonex when the modifier "AQ" and the suffix ' are omitted from the names, respectively (see page 7). Nasacort AQ contains the active ingredient, triamcinolone, and is indicated for the treatment of seasonal and perennial allergic rhinitis symptoms in adults and children six years of age and older. The recommended dose of Nasacort AQ is 220 micrograms (2 sprays) in each nostril once daily. When the maximum benefit has been achieved, and

symptoms have been controlled in patients initially controlled at 220 micrograms/day, the dose can then be decreased to 110 micrograms/day (1 spray) in each nostril per day. Nasacort and Nasonex look similar in that each name begins with the letter combination "Nas", followed by the letters "a" vs. "o", which can look similar when written. The last letter of each name ("t" vs. "x") can also look similar, depending on the prominence of the upstroke of the letter "t" in Nasacort. Overall, however, the endings of the name are distinguishable when written ("cort" vs. "nex"). Nasacort AQ and Nasonex Clearmist share an overlapping route of administration (intranasal), dosage form (nasal spray), dosing quantity (2 sprays), dosing regimen (once daily), and indication (seasonal allergic rhinitis). The product strengths are also numerically similar (55 micrograms/spray vs. 50 micrograms/spray). Despite the product similarities, DMETS believes that the differences in the look-alike characteristics of the end of the names, in addition to the presence of the modifier "AQ" in Nasacort AQ, will minimize confusion and errors between the products. In addition, the DQRS and AERS searches did not reveal any medication errors between Nasacort AQ the currently marketed product, Nasonex.

Nasacort	**Nasonex**
Nasacort	Nasonex

III. COMMENTS TO THE SPONSOR

DMETS does not recommend the use of the proprietary name Nasonex because we believe that the modifier is misleading.

DMETS believes that the presence of the modifier could be misleading to practitioners because it implies that Nasonex somehow clinically different than the currently marketed drug product, Nasonex. This could result in a patient receiving a prescription for and administering both Nasonex and Nasonex Should a patient use both Nasonex and Nasonex, they would be at an increased risk for experiencing side effects associated with the medications, such as headache, pharyngitis, and viral and upper respiratory tract infections. Therefore, DMETS believes that the use of the modifier will be a source of confusion and increase the risk of errors between the products. Because the only difference between the products is that Nasonex will not contain phenylethyl alcohol in its formulation, and will therefore be usual practice would be that a descriptor, such as appear on the container label and carton labeling, and not as part of the proprietary name.

, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified areas of possible improvement, which might minimize potential user error.

A. CONTAINER LABEL (17 grams)

1. Revise the strength to read "50 mcg/spray".

2. The revised container label does not appear complete. Please ensure that the [redacted]

3. Please include the statement '[redacted]

B. CARTON LABELING (10 gram Professional Sample)

1. See comment A-1.

2. Please ensure that the established name is at least half the size of the proprietary name.

3. Include a usual dosage statement.

4. Please include lot number and expiration date.

C. CARTON LABELING (17 grams)

1. See comment A-1.

2. Place [redacted] statement.

D. INSERT LABELING

See comments under CONTAINER LABEL.

E. PATIENT PACKAGE INSERT

No comments.

III. RECOMMENDATIONS

1. Although DMETS has no concerns with the use of the proprietary name Nasonex from a sound-alike and look-alike perspective, we do not recommend the use of the name. DMETS believes it is misleading because the modifier implies that the new product is clinically different than the currently marketed Nasonex. The term

2. DMETS recommends implementation of the labeling revisions as outlined in Section III of this review in order to minimize potential errors with the use of this product.

3. DDMAC finds the proprietary name Nasonex acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Sammie Beam at 301-827-3242.

Tia M. Harper-Velazquez, Pharm.D.
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Alina Mahmud, R.Ph.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

1 Page(s) Withheld

1 § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

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/s/

Tia Harper-Velazquez
5/17/04 11:16:08 AM
DRUG SAFETY OFFICE REVIEWER

Alina Mahmud
5/17/04 01:49:32 PM
DRUG SAFETY OFFICE REVIEWER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: December 1, 2000

From: Jerry Phillips, Associate Director, OPDRA

To: David Hilifiker, Project Manager HFD-570

Subject: OPDRA Consult 00-0313 for Proposed Proprietary Name for NDA 20-762/S-007

OPDRA is in receipt of your August 17, 2000 consult concerning a proprosed proprietary name of Nasonex [redacted] As stated in the consult, the Division rejected Nasonex [redacted] We understand that [redacted]

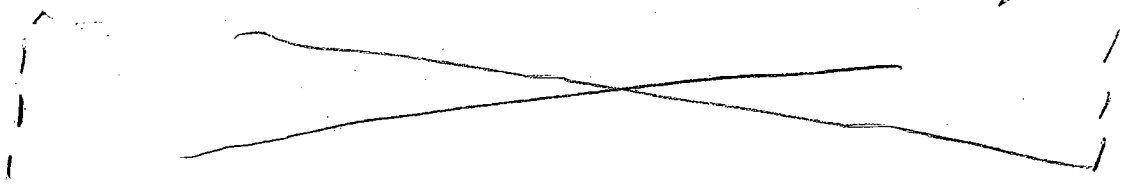
Nasonex [redacted] (does NOT have the preservative phenylethyl alcohol)

OPDRA objects to the modifier [redacted] with this formulation for several reasons:

1. There is little difference in the meaning of [redacted] vs. [redacted] in which the Division originally objected.

2. We believe that the modifier is promotional in tone and that a modifier such as [redacted] would be less promotional and more truethful.

3. We also believe that the [redacted]



If you have any questions, please feel free to contact me or Sammie Beam. Thanks.

Jerry Phillips
Associate Director, OPDRA

To:	David Hilfiker	(HILFIKERD)
CC:	Sammie Beam	(BEAMS)
CC:	Martin Himmel	(HIMMELM)

/s/

Jennifer Fan
2/9/01 04:21:26 PM
PHARMACIST

Jerry Phillips
2/12/01 07:35:28 AM
DIRECTOR

Memorandum of Telephone Facsimile Correspondence

Date: June 19, 2001

To: Joseph F. Lamendola, Schering Regulatory Affairs

Fax No.: 908-740-4131

From: David Hilfiker
Project Manager

Through: Robert Meyer, Division Director/6-18-01
Craig Bertha, CMC Reviewer/6-14-01
Guirag Poochikian, CMC Team Leader/6-16-01

Subject: Tradename Comments

# of Pages: 2

We are providing the attached information via telephone facsimile for your convenience, to expedite the progress of your drug development program. This material should be viewed as unofficial correspondence. Please feel free to contact me if you have any questions regarding the contents of this transmission.

Thank you.

June 14, 2001

Dr. Lamendola:

We refer you to your letter dated January 12, 2001, as an amendment to pending supplemental NDA 20-762/S-007. This amendment provided arguments in response to the Division's comments on the proposed tradename Nasonex [redacted] Nasal Spray.

In consultation with the Office of Post-Marketing Drug Risk Assessment, in consideration of your arguments, we consider the proposed tradename, Nasonex [redacted] Nasal Spray, acceptable.

However, the final market image carton/container labeling that you have submitted is not adequate. The entire tradename for the product, Nasonex [redacted] Nasal Spray, should be of the same [redacted] on all labeling. The generic name. [redacted] of the tradename, and prominence commensurate with the prominence of the tradename.

When you are prepared to respond to all of the deficiencies listed in the February 2, 2001, approvable letter, include revised labeling that reflects the comments above.

We remind you that in order to reopen the review of this application, a complete response should be submitted that addresses all of the deficiencies listed in the February 2 letter, including confirmation that manufacturing facilities are ready for inspections.

If you have any questions, contact me at (301) 827-1084.

David Hilfiker
Regulatory Project Manager

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/s/

David Hilfiker
6/19/01 01:40:32 PM
CSO
receipt confirmed, 6/19/01 1:27 pm

Memorandum of Telephone Facsimile Correspondence

Date: December 20, 2000

To: Mike Belman, Schering Corporation

Fax No.: 908-740-2982

From: David Hilfiker
Project Manager

Through: Robert J. Meyer, M.D.
Division Director

Subject: Proposed Tradename for Supplement 20-762/S-007

# of Pages: 2

We are providing the attached information via telephone facsimile for your convenience, to expedite the progress of your drug development program. This material should be viewed as unofficial correspondence. Please feel free to contact me if you have any questions regarding the contents of this transmission.

Thank you.

Mr. Belman:

Please refer to your pending supplemental New Drug Application 20-762/S-007, submitted on July 28, 2000. This supplement provides for a new formulation of Nasonex Nasal Spray that does not include the excipient, phenylethyl alcohol. You have indicated that you wish to [redacted] this product and the [redacted], and have proposed the tradename "Nasonex [redacted] for this new formulation.

In consultation with the FDA Office of Post-Marketing Drug Risk Assessment and Division of Drug Marketing, Advertising, and Communications, we, as a Division, do not find this name to be acceptable.

We suggest that you consider distinguishing this formulation [redacted]

Alternatively, you may choose to [redacted] retain the existing name, Nasonex Nasal Spray, for the formulation [redacted]

If you have questions, contact me at (301) 827-1084.

David Hilfiker
Regulatory Project Manager
Division of Pulmonary and Allergy Drug Products

/s/

David Hilfiker
12/20/00 11:36:11 AM
CSO

Memorandum of Telephone Facsimile Correspondence

Date: October 3, 2000

To: Nicholas Pelliccione, Schering Corporation

Fax No.: 908-740-5100

From: David Hilfiker
Project Manager

Subject: Information Request for 20-762/S-007

# of Pages: 3

We are providing the attached information via telephone facsimile for your convenience, to expedite the progress of your drug development program. This material should be viewed as unofficial correspondence. Please feel free to contact me if you have any questions regarding the contents of this transmission.

Thank you.

David Hilfiker
Project Manager
Division of Pulmonary Drug Products

Nick:

The following is a request for information to support your supplemental application, 20-762/S-007, for an formulation of Nasonex Nasal Spray.

Dave

To aid in the review of the expiration dating for 15 months (NDA 20-762), provide all of the batch record stability data for the following parameters:

Assay of Mometasone Furoate
Assay of Benzalkonium Chloride
Uniformity of Spray Content
Uniformity of Spray Content at Labeled Number of Actuations
pH
Average Weight per Actuation
    Initial
    Final
Osmolality

Please refer to the attachment entitled "Stability Data Format" for recommendations on the format and documentation of these stability data.

If you have any questions concerning this request, contact the statistical reviewer, Feng Zhou (ph. 301-827- 5581).

Suggested Stability Data Format

The evaluation of stability, in particular, the estimation of drug-expiry-dating period, requires that the sponsor supply stability data to the Agency. Table 1 illustrates a sample-stability data set with partial records. Table 2 specifies the recommended formats for the variables shown in Table 1.

Table 1. Sample Stability Data

BYVAR	TEMPER	RH	BATCH	TIME	LEVEL
ASSAY	25	40	BTCH_A	0	101.62
ASSAY	25	40	BTCH_A	0	99.52
ASSAY	25	40	BTCH_A	3	92.71
ASSAY	25	40	BTCH_A	3	94.83
ASSAY	25	40	BTCH_A	6	88.62
ASSAY	25	40	BTCH_A	6	90.15
ASSAY	25	40	BTCH_A	9	84.11
ASSAY	25	40	BTCH_A	9	86.98
IMPURITY	25	40	BTCH_A	0	0.12
IMPURITY	25	40	BTCH_A	0	0.09
IMPURITY	25	40	BTCH_A	3	0.07
More data records...					

Table 2. Description of Variables in Stability Data

Variable name	Label	Format	Valid value
BYVAR	Analysis variable	$8.	Character string
TEMPER	Temperature	3.	Numeric
RH	Relative humility	3.	Numeric
BATCH	Batch	$8.	Character string
TIME	Time in months	3.	Numeric
LEVEL	Measurement	8.4	Numeric

The above sample data set only represents the required variables. In addition, the sponsor should note the following:

- Other variables (e.g., strength and packaging type) may be included in the file(s). However, the sponsor is expected to meet the minimal requirements described above.
- The sponsor should submit a document (usually no more than 2 pages) that clearly describes the variables included in each file. A data set without appropriate documentation is not acceptable.
- In conformance with current guidance (Regulatory Submissions in Electronic Format; New Drug Applications -- issued 1/1999, posted 1/27/1999), all data should be submitted as SAS transport files.

NDA 20-762/S-007

Schering Corporation
Galloping Hill Road
Kenilworth, NJ 07033

Attention: Nicholas J. Pelliccione, Ph.D.
Vice President, CMC
Worldwide Regulatory Affairs

Dear Dr. Pelliccione:

Please refer to your supplemental new drug application dated July 28, 2000, received July 31, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nasonex (mometasone furoate monohydrate) Nasal Spray, 50 mcg.

This supplement provides for a new formulation of Nasonex Nasal Spray that does not include the preservative, phenylethyl alcohol (PEA).

We have completed our Chemistry, Manufacturing, and Controls (CMC) review of your application and have the following requests for information.

1. Tighten the drug product acceptance criterion for the osmolality of the formula [redacted] to reflect the data provided (section 4.B.6, table 6, page 122).

2. Include the acceptance limits for the drug substance process impurities in the drug product specifications as for the approved formulation. Furthermore, the specifications for the related compounds [redacted] which are controlled in the bulk drug substance, should have acceptance limits of less than [redacted], since the identity of these compounds is not known. Specifications for the bulk drug substance and the drug product should be modified to reflect this change in acceptance limits.

3. Both Agency laboratories have reported that the mometasone furoate standard for use with the method [redacted] for determination of degradation products in the drug product was of questionable purity. Provide chromatograms supporting the purity of the reference standard that was forwarded for use by the San Juan and Philadelphia Agency laboratories for assessment of this method. Indicate how it will be assured that future reference standards are also of sufficient and reliable purity. If all efforts have been exhausted, and it is not possible to further purify the reference standards, both laboratories have suggested that there be a correction factor for the purity of the reference standard of

mometasone furoate in both the assay method for the bulk drug substance and for the finished drug product. Submit your report on your efforts as well as the revised methods.

If you have any questions, call Mr. David Hilfiker, Regulatory Project Manager, at (301) 827-1084.

Sincerely yours,

Guirag Poochikian, Ph.D.
Chemistry Team Leader for
Division of Pulmonary and Allergy Drug Products (HFD-570)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:
Archival NDA 20-762
HFD-570/Div. Files
HFD-570/Hilfiker
HFD-570/Bertha
HFD-570/Poochikian/8-18-00
HFD-570/Meyer
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: HFD-570/Hilfiker/August 18, 2000
Initialed by: HFD-570/Barnes/8-18-00
Final: HFD-570/Hilfiker/8-18-00
Filename: c:\my documents\N20762\S007\000818drltr

DISCIPLINE REVIEW (DR)

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION			REQUEST FOR CONSULTATION	
TO: *(Division/Office)* Steve Wilson, Biometrics, HFD-715			FROM: Craig M. Bertha, HFD-570	
DATE 3/4/04	IND NO.	NDA NO. 20-762	TYPE OF DOCUMENT NDA Supplement (SCF-007)	DATE OF DOCUMENT 2/24/04
NAME OF DRUG NASONEX (Mometasone Furoate Anhydrous) Nasal Spray, 50 mcg		PRIORITY CONSIDERATION 3	CLASSIFICATION OF DRUG S	DESIRED COMPLETION DATE 6/4/04
NAME OF FIRM Schering Corporation				

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 X OTHER *(Specify below)*

II. BIOMETRICS

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

III. BIOPHARMACEUTICS

• •DISSOLUTION • •BIOAVAILABLITY 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 ASSESSMENT 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: See attached sheet for details.
cc: Orig NDA 20-762
HFD-570/Div File
HFD-570/CBertha
HFD-570/LGarcia/SBarnes

SIGNATURE OF REQUESTER	METHOD OF DELIVERY *(Check one)* • •MAIL X HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

N20-762/SCF-007 Biometrics Consult

COMMENTS/SPECIAL INSTRUCTIONS: Please evaluate the 25°C/35% RH stability data from the *newly formulated* product produced at the Kenilworth, NJ and Manati, PR sites in terms of the proposed expiration dating period of 24 months.

Background

This is a follow-up consult with updated stability data. Originally the supplemental application had provided [redacted] months of stability data and this was analyzed statistically by F. Zhou (see review dated 12/6/00). The firm had originally proposed a 15 month expiration dating period but now proposes 24 months based on [redacted] months of updated data for the newly formulated product.

The statistical review and evaluation dated 9/26/97 performed by Dr. G. Aras (HFD-715) for the *original formulation* of the Nasonex Nasal Spray product, in summary, concluded that a 24 month expiry could be recommended for product prepared at the Kenilworth (NJ) site but that only [redacted] months was recommended for product (depending on packaging type) prepared at the Manati, PR site. The parameters that most limited the expiration dating period recommended for the Manati product were the osmolality, the pH, and the weight of the actuations (i.e., pump delivery). Some of the difference was due, presumably to the lesser amount of stability data available for product prepared at the Manati site.

Because of the differences in the predicted stability for product prepared at the two sites, the applicant was granted 15 months of expiration dating period for the product. The product with the original formulation (containing phenylethyl alcohol preservative) was approved on 10/1/97. A letter from the Agency dated 10/3/97 expanded on the granting of the 15 month expiry period. The latter letter noted the significant differences outlined in the statistical review, asked the applicant to investigate, provide updated data and a statistical analysis, and stated that they would not be allowed to extend the expiration dating period in an annual report but would have to submit a prior approval supplement. Because of the "problems" with the stability of the original formulation, it was thought to be prudent to also request that the stability data for the newly formulated product also be scrutinized statistically, particularly with consideration given to site to site differences.

Batches and Available Stability Data

The following batches are included in the stability report:

Batch	Size	Pump Type	Manuf. Site	Available Time-points (25°C/35%RH)
[redacted]				

Parameters for Evaluation and Acceptance Criteria

Specifications parameters:	
Assay Mometasone Furoate:	**90.0 - 110% of label claim**
Assay Benzalkonium Chloride:	**90.0 - 110% of label claim**
Uniformity of Spray Content (Beginning)	**See attached two pages for specifications.**
Uniformity of Spray Content at Labeled Number of Actuations (End):	**See attached two pages for specifications.**
pH:	**4.3 - 4.9**
Average Weight per Actuation	
Initial:	[redacted]
Final:	
Osmolality:	**milliosmoles**

Data are located in the 2/24/04 submission in volume 1 (section 4.B.8, pp. 1-158) and volume 2 (section 4.B.8, pp. 125-142), and the firms statistical analysis is in volume 2 (appendix 1, pp. 1-377).

1 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Administrative- 20-762
5007

1 Page(s) Withheld

1 § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Administrative- 20-762
8007

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/s/

Richard Lostritto
3/9/04 12:35:58 PM

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: Jan. 9, 2004 **DOCUMENT DATE:** Dec. 8, 2003	**DESIRED COMPLETION DATE:** March 9, 2004	**ODS CONSULT #:** 04-0011

TO: Badrul Chowdhury, M.D., Ph.D.
Director, Division of Pulmonary and Allergy Drug Products
HFD-570

THROUGH: Lori Garcia
Project Manager
HFD-570

PRODUCT NAME: **Nasonex®** (Mometasone Furoate Monohydrate Nasal Spray) 50 micrograms/spray **NDA #:** 20-762/S-007	**SPONSOR:** Schering Corporation

SAFETY EVALUATOR: Tia M. Harper-Velazquez, Pharm.D.

RECOMMENDATIONS:

1. Although DMETS has no concerns with the use of the proprietary name Nasonex® from a sound-alike and look-alike perspective, we do not recommend the use of the name. DMETS believes it is misleading because the modifier implies that the new product is clinically different than the currently marketed Nasonex. The term
2. DMETS recommends implementation of the labeling revisions as outlined in Section III of this review in order to minimize potential errors with the use of this product.
3. DDMAC finds the proprietary name Nasonex® acceptable from a promotional perspective.

Carol Holquist, R.Ph.
Deputy Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax: (301) 443-9664

Jerry Phillips, R.Ph.
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Director, Division of Medication Errors and Technical Support (DMETS), HFD-420
PKLN Rm. 6-34

FROM:
Lori Garcia, Regulatory Project Manager
Division of Pulmonary and Allergy Drug Products, HFD-570

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
January 9, 2004		20-762	Chemistry Supplement	December 8, 2003

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Nasonex Aqueous Nasal Spray	Standard	Corticosteroid	April 7, 2004

NAME OF FIRM: IVAX Research

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)*: Trade name review

II. BIOMETRICS

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

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY 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 ASSESSMENT 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, CONCERNS, and/or SPECIAL INSTRUCTIONS:

Schering is requesting the evaluation of 3 new trade names for their product, Nasonex Aqueous Nasal Spray. Two previous consults were submitted dated July 28, 2000, and January 12, 2001. The final outcome was that the trade name NASONEX was acceptable. Schering decided not to use NASONEX and is now proposing the following 3 names: NASONEX , NASONEX AND NASONEX

PDUFA DATE:
ATTACHMENTS: December 8, 2003 submission
CC:
Archival NDA 20-762
HFD-570/Division File
HFD-570/Garcia

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one) MAIL X HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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

/s/

Lori Garcia
1/9/04 09:13:24 AM

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*: HFD-400/OPDRA/Assoc. Director for Medication Error Prevention			FROM: HFD-570/DPADP/Hilfiker	
DATE: April 3, 2001	IND NO.:	NDA NO.: 20-762/S-007	TYPE OF DOCUMENT: CMC supplement	DATE OF DOCUMENT: January 12, 2001
NAME OF DRUG: Nasonex [redacted]	PRIORITY CONSIDERATION: standard		CLASSIFICATION OF DRUG: 3S	DESIRED COMPLETION DATE: April 30, 2001

NAME OF FIRM: Schering Corporation

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)*: Tradename Consult

II. BIOMETRICS

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

III. BIOPHARMACEUTICS

- •DISSOLUTION
- •BIOAVAILABILTY 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 ASSESSMENT 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:

Please provide comments on the use of the tradename Nasonex [redacted] and previous Division precedence (see next page).

Attachment: January 12, 2001, Schering submission to NDA 20-762/S-007

SIGNATURE OF REQUESTER:	METHOD OF DELIVERY (Check one): • •MAIL • •HAND
SIGNATURE OF RECEIVER:	SIGNATURE OF DELIVERER:

response. Also, as a policy matter, we are interested on OPDRA's opinion on whether the use of modifiers, such as should or should not be allowed in tradenames for products.

CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED:	**DUE DATE:**	**OPDRA CONSULT #:**
April 5, 2001	April 30, 2001	00-0313-2

TO: Robert J. Meyer, M.D.
Director, Division of Pulmonary Drug Products
HFD-570

THROUGH: David Hilfiker, Project Manager
HFD-570

PRODUCT NAME:	**MANUFACTURER:** Schering Corporation
Nasonex Unscented (Mometasone Furoate Monohydrate Nasal Spray) **NDA #: 20-762/S-007**	

SAFETY EVALUATOR: Carol Holquist, R.Ph.

SUMMARY: In response to a consult from the Division of Pulmonary Drug Products (HFD-570), OPDRA conducted a review of the proposed proprietary name "Nasonex ——— " to determine the potential for confusion with approved proprietary and generic names as well as pending names. OPDRA concluded the proprietary name was not acceptable and the Division notified the sponsor on December 20, 2000. The sponsor responded on January 12, 2001, with a request to reconsider their proposed proprietary name.

OPDRA RECOMMENDATION: Following review of the information submitted by the sponsor, OPDRA has no objections to the use of the proprietary name "Nasonex ——— Nasal Spray".

Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment
Phone: (301) 827-3242
Fax: (301) 480-8173

Martin Himmel, M.D.
Deputy Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

/s/

David Hilfiker
4/5/01 02:16:57 PM
for R.Meyer, Division Director

RECORD OF TELEPHONE CONVERSATION

Date:	October 19, 2000
Project Manager:	Hilfiker
Subject:	**Option for 6-month Secondary Goal Date**
NDA:	20-762/S-007
Sponsor:	Schering Corporation
Product Name:	Nasonex Nasal Spray

Schering Corporation submitted a prior approval supplement on July 28, 2000, for the approval of a new formulation for Nasonex Nasal Spray. The new formulation differs from the original formulation only in that it does not include phenylethyl alcohol as an inactive ingredient.

The 4-month goal date for this supplement is November 30, 2000.

Patricia Alcock, Branch Chief in the Division of Manufacturing and Product Quality, Office of Compliance, contacted me on October 18, 2000, requesting that the Division opt for the 6-month secondary goal date on this supplement rather than the 4-month goal date. She stated that the field office is busy resolving GMP issues at Schering's manufacturing facility and would like additional time in order to complete the inspection for this supplement after other GMP issues are resolved.

After consultation with Guirag Poochikian, CMC Team Leader, I contacted Ms. Alcock to inform her that our Division agrees to defer to the secondary 6-month goal date for this supplement to give them time to complete the inspection. I informed her that the secondary goal date is January 31, 2001.

David Hilfiker
Project Manager

Concurrence: G. Poochikian, 10-20-00

Cc: Original NDA 20-762/S-007
HFD-570/Division file
HFD-570/Hilfiker
HFD-570/Bertha
HFD-570/Poochikian
HFD-570/Meyer
HFD-324/Alcock

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*: HFD-400/OPDRA/Assoc. Director for Medication Error Prevention			FROM: HFD-570/DPADP/Hilfiker	
DATE: August 17, 2000	IND NO.:	NDA NO.: 20-762/S-007	TYPE OF DOCUMENT: CMC supplement	DATE OF DOCUMENT: July 28, 2000
NAME OF DRUG: Nasonex	PRIORITY CONSIDERATION: standard		CLASSIFICATION OF DRUG: 3S	DESIRED COMPLETION DATE: November 1, 2000

NAME OF FIRM: Schering Corporation

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)*: Tradename Consult

II. BIOMETRICS

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

III. BIOPHARMACEUTICS

- DISSOLUTION
- BIOAVAILABILTY 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 ASSESSMENT 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: Schering has submitted a supplemental application to manufacture a new formulation of Nasonex Nasal Spray that does not include the preservative, phenylethyl alcohol. This modification is [redacted] from the product during use. Please note that Schering intends [redacted] Nasonex Nasal Spray, so there would be [redacted] NASONEX [redacted] if this were approved.

The Division has previously denied the tradename NASONEX [redacted] see comment 8 in attached 8-16-99 letter). Schering currently proposes NASONEX [redacted] Schering proposes to [redacted] see attached proposed labeling). The Division requests OPDRA feedback by November 1 to be able to comply with the regulatory 4-month supplement goal date of November 30, 2000.

cc: Original NDA 20-762/S-007
HFD-570/Div. Files
HFD-570/Hilfiker, Chowdhury, Bertha

SIGNATURE OF REQUESTER:	METHOD OF DELIVERY (Check one): • MAIL • HAND
SIGNATURE OF RECEIVER:	SIGNATURE OF DELIVERER:

REQUEST FOR TRADEMARK REVIEW

To: The Office of Post-Marketing Drug Risk Assessment
Attention: Associate Director for Medication Error Prevention (HFD-400)

From: **Division of Pulmonary and Allergy Drug Products**	**HFD-570**
Attention: David Hilfiker	**Phone:** (301) 827-1084
Date: August 17, 2000	
Subject: Request for Assessment of a Trademark for a Proposed New Drug Product	
Proposed Trademark: Nasonex	**NDA 20-762/S-007**
Established name, including dosage form: mometasone furoate monohydrate nasal spray, 50 mcg	
Other trademarks by the same firm for companion products: Nasonex Nasal Spray	
Indications for Use (may be a summary if proposed statement is lengthy): treatment of nasal symptoms associated with seasonal and perennial allergic rhinitis	
Initial Comments from the submitter (concerns, observations, etc.): Note that the firm plans Nasonex Nasal Sprays (see attached labeling). Also note that the carton/container labeling provided in the original supplement is a black-and-white representation.	

Attachments: (1) 8-16-99 FDA letter to Schering regarding proposed formulation
(2) Draft labeling submitted 7-28-00 (draft package insert, carton/container labeling)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-762/S-007

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attention: Yvette Henderson
Manager, Global Labeling
Global Regulatory Affairs

Dear Ms. Henderson:

We acknowledge receipt of your November 15, 2004, submission containing final printed labeling in response to our August 25, 2004, letter approving your supplemental new drug application for Nasonex (mometasone furoate monohydrate) Aqueous Nasal Spray, 50 mcg.

We have reviewed the labeling that you submitted in accordance with our August 25, 2004, letter and we find it acceptable. We note that this labeling has been superceded by the approval of supplement 023 on December 15, 2004.

If you have any questions, call Lori Garcia, Regulatory Project Manager, at 301-827-5580.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Badrul Chowdhury
1/31/05 09:37:02 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20762/S-007

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attention: Teresa Perney, Ph.D.
Manager, Global Regulatory Affairs

Dear Dr. Perney:

We acknowledge receipt on April 26, 2004, of your April 23, 2004, resubmission to your supplemental new drug application for Nasonex (mometasone furoate monohydrate) Aqueous Nasal Spray, 50mcg.

This amendment constitutes a complete response to our February 2, 2001, action letter. The user fee goal date is August 26, 2004.

If you have any questions, call Lori Garcia, Regulatory Project Manager, at (301) 827-5580.

Sincerely,

{See appended electronic signature page}

Sandy Barnes
Supervisory CSO
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Lori Garcia
5/26/04 01:32:33 PM
signed for Sandy Barnes