CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20762

CHEMISTRY REVIEW(S)

FEB 1 4 1997

DIVISION OF PULMONARY DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-762 **CHEM. REVIEW #** 1 **REVIEW DATE:** 2/13/97

RECOMMEND ACTION: Not Approved (NA)

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	9/30/96	10/1/96	10/15/96

NAME & ADDRESS OF APPLICANT: Schering Corporation
Galloping Hill Road
Kenilworth, N.J.
07033

DRUG PRODUCT NAME

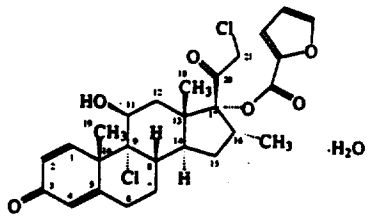
Proprietary:	NASONEX™ Nasal Spray
Nonproprietary:	mometasone furoate nasal spray
USAN:	mometasone furoate
Code Name/#:	SCH 32088 Monohydrate
Chem.Type/Ther.Class:	3S

PHARMACOL. CATEGORY/INDICATION: Anti-inflammatory corticosteroid for prophylaxis and treatment of seasonal allergic rhinitis (SAR), and treatment of perennial rhinitis (PR)

DOSAGE FORM: nasal spray
DOSE: 100 or 200 µg once daily
STRENGTHS: 50 µg mometasone furoate/actuation (100 mg formulation/actuation)

ROUTE OF ADMINISTRATION: intranasal
DISPENSED: _X_ Rx ___ OTC

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



Mometasone Furoate Monohydrate

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

Molecular Formula: $C_{27}H_{30}Cl_2O_6 \cdot H_2O$
Molecular Weight: 539.458

SUPPORTING DOCUMENTS:

DMFs:

DMF No.	Holder Name	Subject	Status	Date Reviewed	Reference in CR#1 review

RELATED DOCUMENTS (if applicable):

NDA 19-543 Elocon (Mometasone Furoate) Ointment (Schering, approved 30-Apr-87)*
NDA 19-625 Elocon (Mometasone Furoate) Emulsion, Cream (Schering, approved 06-May-87)*
NDA 19-796 Elocon (Mometasone Furoate) Lotion (Schering, approved 30-Mar-89)*

*Note: These products are for topical application.

CONSULTS:

Consult	Date Forwarded	Status	Comments
EER	11/6/96	Pending	
Microbiology	11/25/96	Pending	Evaluation of preservative effectiveness test validation and specification limits for preservatives and microbial limits tests and specs. for the drug substance and drug product
Biometrics (Stability)	Not forwarded.		Will be forwarded once updated stability data are submitted by the firm.
Pharmacology	11/6/96 informal consult forwarded on impurities and specifications (ds and dp)	Pending	
Methods Validation	Not requested.		Will not be forwarded until deficiencies addressed by firm.
Environmental Assessment	Not forwarded for concurrence (see comment).		Will not be forwarded until deficiencies addressed by firm.
Labeling & Nomenclature	11/13/96	Recommendations received dated 1/7/97.	

REMARKS/COMMENTS:

CONCLUSIONS & RECOMMENDATIONS: The application as submitted is not approvable from the standpoint of chemistry, manufacturing, and controls.

cc:
Orig. NDA 20-762
HFD-570/Division File
HFD-570/CBertha/2/13/97
HFD-570/DToyer
HFD-570/GPoochikian
HFD-570/AWorobec
HFD-570/TDu
R/D Init by GPoochikian: 2/14/97

filename: 96-09-30.rev

Craig M. Bertha, Ph.D.
Review Chemist

JUL -9 1997

DIVISION OF PULMONARY DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-762 **CHEM. REVIEW #** 2 **REVIEW DATE:** 7/8/97

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	9/30/96	10/1/96	10/15/96
AMENDMENT (BC)*	3/24/97	3/25/97	3/25/97
AMENDMENT (BC)*	4/4/97	4/7/97	4/7/97
AMENDMENT (BC)*	5/8/97	5/9/97	5/9/97
AMENDMENT (BC)*	5/14/97	5/15/97	5/19/97
AMENDMENT (AC)*	6/17/97	6/18/97	6/20/97

*Subject of this review.

NAME & ADDRESS OF APPLICANT: Schering Corporation
Galloping Hill Road
Kenilworth, N.J.
07033

DRUG PRODUCT NAME:

Proprietary:	NASONEX™ Nasal Spray
Nonproprietary:	mometasone furoate nasal spray
USAN:	mometasone furoate
Code Name/#:	SCH 32088 Monohydrate
Chem.Type/Ther.Class:	3S

PHARMACOL. CATEGORY/INDICATION: Anti-inflammatory corticosteroid for prophylaxis and treatment of seasonal allergic rhinitis (SAR), and treatment of perennial rhinitis (PR)

DOSAGE FORM: nasal spray

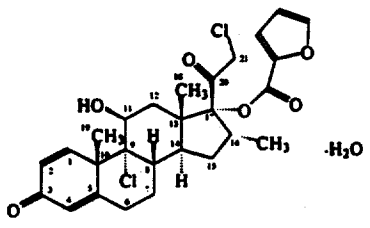
DOSE: 100 or 200 µg once daily

STRENGTHS: 50 µg mometasone furoate/actuation (100 mg formulation/actuation), 120 actuations (trade size)

ROUTE OF ADMINISTRATION: intranasal

DISPENSED: _X_ Rx ___ OTC

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



Mometasone Furoate Monohydrate

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

Molecular Formula: $C_{27}H_{30}Cl_2O_6 \cdot H_2O$ Molecular Weight: 539.458

SUPPORTING DOCUMENTS:

Drug Master Files:

DMF No.	Holder Name	Subject	Status	Date Reviewed	Reference in CR#1 review

RELATED DOCUMENTS (if applicable):

NDA 19-543 Elocon (Mometasone Furoate) Ointment (Schering, approved 30-Apr-87)*
NDA 19-625 Elocon (Mometasone Furoate) Emulsion, Cream (Schering, approved 06-May-87)[2]
NDA 19-796 Elocon (Mometasone Furoate) Lotion (Schering, approved 30-Mar-89)*

[2]Note: These products are for topical application.

CONSULTS:

Consult	Date Forwarded	Status	Comments
EER	11/6/96	Withhold Approval	See remark on p. 6.
Microbiology	11/25/96	Complete	The microbiologist recommends approval of the application in terms of microbiology (1/13/97).
Biometrics (Stability)	6/30/97	Pending	
Pharmacology	11/6/96 informal consult forwarded on impurities and specifications (ds and dp)	Pending	
Methods Validation	Not requested.		Will not be forwarded until method/specification deficiencies addressed by firm and an updated package is received.
Environmental Assessment	Forwarded for concurrence on 5/27/97.	Concurrence pending.	Revised EA from the 5/14/97 amendment was reviewed separately.
Labeling & Nomenclature	11/13/96	Complete	Recommendations received dated 1/7/97 (see remark section).

REMARKS/COMMENTS:

CONCLUSIONS & RECOMMENDATIONS: The amendments dated 4/4/97 and 6/17/97 provide a full response to the IR letter dated 2/28/97. The application as amended is not approvable from the standpoint of chemistry, manufacturing, and controls.

cc:
Orig. NDA 20-762
HFD-570/Division File
HFD-570/CBertha/7/8/97
HFD-570/DToyer
HFD-570/GPoochikian
HFD-570/AWorobec
HFD-570/TDu
R/D Init. by GPoochikian: 7/9/97

filename: 97-06-17.rev

Craig M. Bertha, Ph.D.
Review Chemist

AUG 6 1997

DIVISION OF PULMONARY DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-762 **CHEM. REVIEW #** 3 **REVIEW DATE:** 8/1/97

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	9/30/96	10/1/96	10/15/96
AMENDMENT (BC)	3/24/97	3/25/97	3/25/97
AMENDMENT (BC)	4/4/97	4/7/97	4/7/97
AMENDMENT (BC)	5/8/97	5/9/97	5/9/97
AMENDMENT (BC)	5/14/97	5/15/97	5/19/97
AMENDMENT (AC)	6/17/97	6/18/97	6/20/97
AMENDMENT (BC)*	7/21/97	7/22/97	7/23/97

*Subject of this review.

NAME & ADDRESS OF APPLICANT: Schering Corporation
Galloping Hill Road
Kenilworth, N.J.
07033

DRUG PRODUCT NAME:

Proprietary:	NASONEX™ Nasal Spray
Nonproprietary:	mometasone furoate nasal spray
USAN:	mometasone furoate
Code Name/#:	SCH 32088 Monohydrate
Chem.Type/Ther.Class:	3S

PHARMACOL. CATEGORY/INDICATION: Anti-inflammatory corticosteroid for prophylaxis and treatment of seasonal allergic rhinitis (SAR), and treatment of perennial rhinitis (PR)

DOSAGE FORM: nasal spray

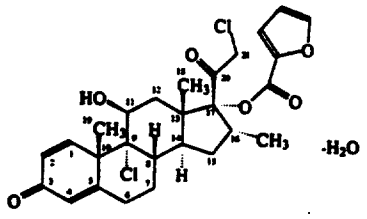
DOSE: 100 or 200 µg once daily

STRENGTHS: 50 µg mometasone furoate/actuation (100 mg formulation/actuation), 120 actuations (trade size)

ROUTE OF ADMINISTRATION: intranasal

DISPENSED: _X_ Rx ___ OTC

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



Mometasone Furoate Monohydrate

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

Molecular Formula: $C_{27}H_{30}Cl_2O_6 \cdot H_2O$ Molecular Weight: 539.458

SUPPORTING DOCUMENTS:

Drug Master Files:

DMF No.	Holder Name	Subject	Status	Date Reviewed	Reference in CR#1 review

RELATED DOCUMENTS (If applicable):

NDA 19-543 Elocon (Mometasone Furoate) Ointment (Schering, approved 30-Apr-87)*

NDA 19-625 Elocon (Mometasone Furoate) Emulsion, Cream (Schering, approved 06-May-87)[2]

NDA 19-796 Elocon (Mometasone Furoate) Lotion (Schering, approved 30-Mar-89)*

[2]Note: These products are for topical application.

CONSULTS:

Consult	Date Forwarded	Status	Comments
EER	11/6/96	Withhold Approval	See remark on p. 6.
Microbiology	11/25/96	Complete	The microbiologist recommends approval of the application in terms of microbiology (1/13/97).
Biometrics (Stability)	6/30/97	Pending	
Pharmacology	11/6/96 informal consult forwarded on impurities and specifications (ds and dp)	Pending	
Methods Validation	Not requested.		Will not be forwarded until an updated MV package is received from firm.
Environmental Assessment	Forwarded for concurrence on 7/28/97.	Concurrence pending.	Revised EA from the 5/14/97 amendment was reviewed separately.
Labeling & Nomenclature	11/13/96	Complete	Recommendations received dated 1/7/97 (see remark section).

REMARKS/COMMENTS:

CONCLUSIONS & RECOMMENDATIONS: The amendment dated 7/21/97 provides a response to our facsimile of 7/10/97 and is the subject of this review. The application as amended is not approvable from the standpoint of chemistry, manufacturing, and controls.

cc:
Orig. NDA 20-762
HFD-570/Division File
HFD-570/CBertha/8/1/97
HFD-570/DToyer
HFD-570/GPoochikian
HFD-570/AWorobec
HFD-570/TDu
R/D Init. by GPoochikian: 8/6/97
filename: 97-07-21.rev.doc

Craig M. Bertha, Ph.D.
Review Chemist

n:\nda\20762\chem\97-08-22.rev.doc

DIVISION OF PULMONARY DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-762 **CHEM. REVIEW #** 4 **REVIEW DATE:** 8/27/97

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	9/30/96	10/1/96	10/15/96
AMENDMENT (BC)	3/24/97	3/25/97	3/25/97
AMENDMENT (BC)	4/4/97	4/7/97	4/7/97
AMENDMENT (BC)	5/8/97	5/9/97	5/9/97
AMENDMENT (BC)	5/14/97	5/15/97	5/19/97
AMENDMENT (AC)	6/17/97	6/18/97	6/20/97
AMENDMENT (BC)	7/21/97	7/22/97	7/23/97
AMENDMENT (BL)*	8/14/97	8/15/97	8/25/97
AMENDMENT (BC)*	8/22/97	8/25/97	8/26/97

*Subject of this review.

NAME & ADDRESS OF APPLICANT: Schering Corporation
Galloping Hill Road
Kenilworth, N.J.
07033

DRUG PRODUCT NAME:

Proprietary:	NASONEX™ Nasal Spray
Nonproprietary:	mometasone furoate nasal spray
USAN:	mometasone furoate
Code Name/#:	SCH 32088 Monohydrate
Chem.Type/Ther.Class:	3S

PHARMACOL. CATEGORY/INDICATION: Anti-inflammatory corticosteroid for prophylaxis and treatment of seasonal allergic rhinitis (SAR), and treatment of perennial rhinitis (PR)

DOSAGE FORM: nasal spray

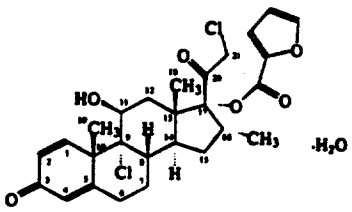
DOSE: 100 or 200 µg once daily

STRENGTHS: 50 µg mometasone furoate/actuation (100 mg formulation/actuation), 120 actuations (trade size)

ROUTE OF ADMINISTRATION: intranasal

DISPENSED: X Rx ___ OTC

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



Mometasone Furoate Monohydrate

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

Molecular Formula: $C_{27}H_{30}Cl_2O_6 \cdot H_2O$ Molecular Weight: 539.458

SUPPORTING DOCUMENTS:

Drug Master Files:

DMF No.	Holder Name	Subject	Status	Date Reviewed	Reference in CR#1 review

RELATED DOCUMENTS (if applicable):

NDA 19-543 Elocon (Mometasone Furoate) Ointment (Schering, approved 30-Apr-87)[1]

NDA 19-625 Elocon (Mometasone Furoate) Emulsion, Cream (Schering, approved 06-May-87)[1]

NDA 19-796 Elocon (Mometasone Furoate) Lotion (Schering, approved 30-Mar-89)[1]

[1]Note: These products are for topical application.

CONSULTS:

Consult	Date Forwarded	Status	Comments
EER	11/6/96	Withhold Approval	See remark on p. 6.
Microbiology	11/25/96	Complete	The microbiologist recommends approval of the application in terms of microbiology (1/13/97).
Biometrics (Stability)	6/30/97	Pending	
Pharmacology	11/6/96 informal consult forwarded on impurities and specifications (ds and dp)	Pending	
Methods Validation	Not requested.		Will not be forwarded until an updated MV package is received from firm.
Environmental Assessment	Forwarded for concurrence on 7/28/97.	Concurrence pending.	Revised EA from the 5/14/97 amendment was reviewed separately.
Labeling & Nomenclature	11/13/96	Complete	Recommendations received dated 1/7/97 (see remark section).

REMARKS/COMMENTS:

CONCLUSIONS & RECOMMENDATIONS: The amendment dated 8/22/97 provides a response to our letter of 8/11/97 and is the subject of this review. Additionally, the draft labeling and labels in the 8/14/97 amendment are reviewed herein. The application as amended is not approvable from the standpoint of chemistry, manufacturing, and controls.

cc:
Orig. NDA 20-762
HFD-570/Division File
HFD-570/CBertha/8/27/97
HFD-570/DToyer
HFD-570/GPoochikian
HFD-570/AWorobec
HFD-570/TDu
R/D Init. by GPoochikian: 8/28/97
filename: 97-08-22.rev.doc

Craig M. Bertha, Ph.D.
Review Chemist

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20762

ENVIRONMENTAL ASSESSMENT AND/OR FONSI

ENVIRONMENTAL ASSESSMENT

AND

FINDING OF NO SIGNIFICANT IMPACT

FOR

NASONEX™

(Mometasone Furoate Monohydrate)

Nasal Spray

NDA 20-762

FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

DIVISION OF PULMONARY DRUG PRODUCTS

(HFD-570)

FINDING OF NO SIGNIFICANT IMPACT

NDA 20-762

NASONEX™
(Mometasone Furoate Monohydrate)
Nasal Spray

The National Environmental Policy Act of 1969 (NEPA) requires all Federal agencies to assess the environmental impact of their actions. FDA is required under NEPA to consider the environmental impact of approving certain drug product applications as an integral part of its regulatory process.

The Food and Drug Administration, Center for Drug Evaluation and Research has carefully considered the potential environmental impact of this action and has concluded that this action will not have a significant effect on the quality of the human environment and that an environmental impact statement therefore will not be prepared.

In support of their new drug application for NASONEX Nasal Spray, Schering-Plough Corporation has ~~conducted a number of environmental studies and~~ prepared an environmental assessment (EA, attached) in accordance with 21 CFR 25.31a (a), which evaluates the potential environmental impacts of the manufacture, use and disposal of the product. Based on the predicted market volume, the fifth year production estimate for all of the applicant's products containing Mometasone Furoate was used to calculate the Expected Introduction Concentration (EIC) of Mometasone Furoate, which is less than one (1) ppb. Thus, following the Tier 0 approach, the applicant has provided an abbreviated EA that does not contain items 7, 8, 9, 10, and 11.

Mometasone Furoate is a chemically synthesized drug which is administered as a nasal spray for the prophylaxis and treatment of symptoms of seasonal allergic rhinitis and the treatment of symptoms of perennial rhinitis in adults and adolescents 12 years of age and older. The mometasone furoate drug substance will be manufactured by Schering Plough Products, Inc. (synthesis of the crude drug substance) and Schering Corporation (purification) at their facilities in Manati, Puerto Rico and Union, NJ, respectively. The drug product will be manufactured by Schering Plough Products, Inc. and Schering Corporation at their facilities in Manati, PR and Kenilworth, NJ, respectively. The finished drug product will be used in hospitals, clinics and/or patients in their homes.

The drug substance will enter the environment through wastewater emissions at the drug substance manufacturing site in Union, NJ and through air, wastewater and solid waste from the drug product manufacturing facilities.

Disposal of the drug may result from out of specification lots, discarding of unused or expired product, and user disposal of empty or partly used product and packaging. Returned or out-of-specification drug substance and rejected or returned drug product will be disposed of at licensed incineration facilities. At U.S. hospitals and clinics, empty or partially empty packages will be disposed according to hospital/clinic regulations. From home use, empty or partially empty containers will typically be disposed of by a community's solid waste management system which may include landfills, incineration and recycling, while minimal quantities of unused drug may be disposed of in the sewer system.

The Center for Drug Evaluation and Research has concluded that the product can be manufactured, used and disposed of without any expected adverse environmental effects. Precautions taken at the sites of manufacture of the bulk product and its final formulation are expected to minimize occupational exposures and environmental release. Adverse effects are not anticipated upon endangered or threatened species or upon property listed in or eligible for listing in the National Register of Historic Places.

7/21/97
Date

Craig M. Bertha, Ph.D.
Review Chemist
Division of Pulmonary Drug Products
Center for Drug Evaluation and Research

7/24/97
Date

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

7/22/97
Date

Tao Du, Ph.D.
Review Pharmacologist/Toxicologist
Division of Pulmonary Drug Products
Center for Drug Evaluation and Research

7/28/97
Date

Hilary Sheevers, Ph.D.
Pharmacology/Toxicology Team Leader
Division of Pulmonary Drug Products (HFD-570)
Office of Drug Evaluation II
Center for Drug Evaluation and Research

8/7/97
Date

CONCURRED
Nancy B. Sager
Environmental Scientist
Center for Drug Evaluation and Research

Attachment: Releasable Environmental Assessment (not including *confidential* appendix 1)

ENVIRONMENTAL ASSESSMENT
Pursuant to 21 CFR Part 25.31a(a)

NASONEX™ NASAL SPRAY
(Mometasone Furoate Aqueous Nasal Spray)
NDA 20-762

1. DATE: May 13, 1997

2. NAME OF APPLICANT: Schering Corporation

3. ADDRESS: 2000 Galloping Hill Road
Kenilworth, New Jersey 07033
Contact: Dr. Tobias Massa
Telephone: 908-298-5711

4. DESCRIPTION OF THE PROPOSED ACTION:

a. Request for Approval

Schering Corporation is submitting this environmental assessment (EA) pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mometasone Furoate Aqueous Nasal Spray. Each spray delivers Nasonex™ Nasal Spray equivalent to 50 micrograms of Mometasone Furoate.

b. Need for Action

The proposed indications for Mometasone Furoate Aqueous Nasal Spray are prophylaxis and treatment of symptoms of seasonal allergic rhinitis and treatment of symptoms of perennial rhinitis in adults and adolescents 12 years of age and older.

c. Production Locations

Mometasone furoate will be produced at Schering-Plough Products, Inc. in Manati, Puerto Rico. This material will then be sent to Schering Corporation in Union, New Jersey where it will be purified, converted to mometasone fuorate monohydrate, and micronized. The final drug product will be manufactured (mixing, filling, packaging, and labeling) at the applicant's facility in Kenilworth, New Jersey and at the Manati facility.

The Manati facility is located at Highway 686, Km. 0.5 in Manati, Puerto Rico 00674. This is in the northern coastal region of Puerto Rico, about 2 miles from the Atlantic Ocean. The climate in the region is tropical.

The Union facility is located at 1011 Morris Avenue in Union, New Jersey 07083. The area is characterized by industrial and commercial uses and is bordered by the Elizabeth River. The terrain is flat and the climate is temperate.

The Kenilworth facility is located at 2000 Galloping Hill Road in Kenilworth, New Jersey 07033. The terrain is flat and the climate temperate. The area is characterized by industrial and commercial uses.

d. Location of Use

Through the approval of this action, Mometasone Fuorate Aqueous Nasal Suspension will be used by consumers throughout the United States.

e. Disposal Sites

Any rejected drug product or waste drug intermediate from the Manati facility which is not reprocessed will be sent off-site for incineration. The facility currently used for this purpose is:

Ogden Martin Systems of Lake, Inc.
3830 Rogers Industrial Park Road
Okahumpka, Florida 34762
USEPA ID No. FLD984258731
Permitting Authority: Florida Dept. of Env. Protection
Permit No. A035-193817
Expiration date: Indefinite extension

Any rejected drug product or waste drug substance from the applicant's facilities in Union and Kenilworth, New Jersey which is not reprocessed will be sent off-site for incineration. The facility currently used for this purpose is:

Environmental Waste Incineration, Inc.
70 Water Street
Long Beach, New York 11561
State ID No. 30-E-03
USEPA ID No. NYN100000052
Permitting Authority: New York State Dept. of Env. Conservation
Facility Permit No.1-2809-00088/00008-0
Expiration Date: February 12, 2001

Any product not used by consumers will be disposed of by users at their homes or at hospitals, pharmacies, or clinics accoding to procedures set at those facilities. Typically, the material is disposed via community waste

management systems which may include landfills or incinerators. Minimal quantities of product may be disposed of by users through sewer systems.

5. IDENTIFICATION OF CHEMICAL SUBSTANCES THAT ARE THE SUBJECT OF THE PROPOSED ACTION:

a. Nomenclature

i. Established Name: Mometasone Furoate Monohydrate

ii. Brand/Proprietary Name: Nasonex™ Nasal Spray

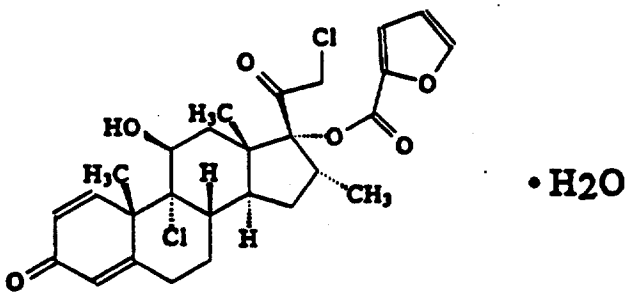
iii. Chemical Name: 9, 21-dichloro-11 beta, 17-dihydroxy-16-alpha-methylpregna-1,4-diene-3,20-dione 17-(2-furoate) monohydrate

b. Molecular Formula: $C_{27}H_{30}Cl_2O_6 \cdot H_2O$

c. Molecular Weight: 539.45

d. CAS Number: 83919-23-7 (Mometasone Furoate Anhydrous)

e. Structural Formula:



• H_2O

f. Elemental Composition:

Carbon	60.12
Hydrogen	5.93
Oxygen	20.81
Chlorine	13.14

g. **Physical Form:** White powder

h. **Melting Point:** Melts at about 220°C with decomposition.

i. **Solubility:** Practically insoluble in water (0.02 mg/mL); slightly soluble (4-8 mg/mL) in methanol, ethanol, and isopropanol; soluble (59-74 mg/mL) in acetone and chloroform; and freely soluble (>100 mg/mL) in tetrahydrofuran.

Dissociation Constant: Mometasone furoate monohydrate contains no functional groups that can be protonated or deprotonated between pH 1 and 13, and hence has no dissociation constant.

j. **Additives:**

In addition to the active substance the final dosage consists of the following ingredients:

Substance	CAS #
Microcrystalline Cellulose	9004-34-6
Carboxymethylcellulose Sodium	9004-32-4
Glycerin	56-81-5
Citric Acid Monohydrate	5949-29-1
Sodium Citrate Dihydrate	68-04-2
Polysorbate 80	9005-65-6
Benzalkonium Chloride	8001-54-5
Phenylethyl Alcohol	60-12-8
Purified Water	7732-18-5

g. **Impurities:**

There are no impurities at levels greater than 1% of the active drug substance in the product. The inactive ingredients, or additives, are all USP/NF grade materials.

6. INTRODUCTION OF SUBSTANCES INTO THE ENVIRONMENT:

The drug intermediate will be synthesized by the applicant's facility in Manati, Puerto Rico. The starting material for this synthesis will be purchased from Pharmacia & Upjohn Inc.

The drug substance, mometasone furoate monohydrate, will be produced by the applicant at its facility in Union, New Jersey. The final manufacturing of the drug product (mixing, filling, packaging, and labeling) will be performed in Manati and at the applicant's facility in Kenilworth.

The material safety data sheet for mometasone furoate monohydrate is provided in Appendix 3. Information regarding the emissions from the operations at the manufacturing facilities is provided below in sections a through d.

a. Substances Expected to be Emitted

Information on emissions from the various production locations is provided in **Confidential Appendix 1.**

b. Controls Exercised

Manati, Puerto Rico

i. Air

Air emissions will occur during synthesis of the drug intermediate, manufacture of the drug product, and cleanout of the process equipment. Emissions are controlled by condensers and carbon absorbers. The carbon absorbers are the last control before discharge and have been measured to remove 90 percent of total hydrocarbons. Removal efficiencies for specific compounds have been measured between 66 percent (methylene chloride) and 94 percent (acetone).

ii. Wastewater/Liquid Waste

Wastewater will be generated in the synthesis of the drug intermediate, manufacture of the drug product, and cleanout of the process equipment. Liquid waste is neutralized at the facility and then discharged to the Puerto Rico Aqueducts and Sewers Authority's Barceloneta Regional Wastewater Treatment Plant, located on State Road Number 684, Km. 3.8, in Barceloneta, Puerto Rico.

iii. Solid/Hazardous Waste

There are three categories of solid waste generated at this facility: hazardous waste, pharmaceutical waste, and trash. Trash, including filter cloth, fluid bed dryer bags, tray dryer papers, silica, and any discarded clothing, is sent to a licensed landfill. The landfill currently used is:

Toa Baja Municipal Landfill
State Road 866
Barrio Candelaria Arena
Toa Baja, Puerto Rico
Permitting Authority: Puerto Rico Environmental Quality Board

Hazardous waste will be generated in the synthesis of the drug intermediate and the cleanout of the process equipment. Hazardous waste is collected and transported to a licensed waste disposal firm for incineration. The facilities currently used are:

Laidlaw Environmental Services of Bartow, Inc.
170 Bartow Municipal Airport
Bartow, Florida 33830
USEPA ID No. FLD980729610
Permit No. HO53-182726A
Issuing Authority: Florida Dept. of Env. Protection
Expiration Date: 12/10/96

Safety Kleen Envirosystems Co. of Puerto Rico, Inc.
State Road No.2, Km.51.0
Manati, Puerto Rico 00701
USEPA ID No. PRD090399718
Issuing Authority: Puerto Rico Environmental Quality Board
Expiration Date: February 16, 2000

Rollins Environmental Services Inc.
13351 Scenic Highway
Baton Rouge, Louisiana 70807
USEPA ID No. LAD010395127
Issuing Authority: Louisiana Dept. of Env. Quality
Expiration Date: March 21, 2001

Marisol, Inc.
125 Factory Lane
Middlesex, New Jersey 08846
USEPA ID No. NJD002454644
Permit No. 1211B1HP04
Issuing Authority: New Jersey Dept. of Env. Protection
Expiration Date: Indefinite extension

AETS
1 Eden Lane
Flanders, New Jersey 07836

USEPA ID No. NJD980536593
Permit No: 1427G1HP07
Issuing Authority: New Jersey Dept. of Env. Protection
Expiration Date: March 31, 1999

Clean Harbors of Baltimore, Inc.
1910 Russel Street
Baltimore, Maryland 21230
USEPA ID No. MDD980555189
Permit No. A151
Issuing Authority: Maryland Dept. of the Environment
Expiration Date: Indefinite extension

Any pharmaceutical wastes, such as rejected drug intermediate, and drug product, are collected and sent off-site for incineration. The current licensed disposal facility used is listed above in Section 4.e.

Union, New Jersey

i. Air

Air emissions will occur during manufacture of the drug substance and cleanout of the process equipment. Emissions will be controlled by a packed scrubber tower and a refrigerated vent condenser. The refrigerated vent condenser is the last control before discharge and has been designed to remove 95 percent of total hydrocarbons. Removal efficiencies for specific compounds have been calculated at between 95 percent (methylene chloride) and greater than 99 percent (acetone).

ii. Wastewater/Liquid Waste

Low levels of liquid waste will be generated in the manufacture of the drug substance and subsequent cleanout of the process equipment. Any effluents, including cleaning compounds and wash water, are pretreated by neutralization prior to discharge to the Joint Meeting of Essex and Union Counties (JMEUC) Treatment Plant. Union's discharge to the JMEUC treatment plant is in accordance with the JMEUC rules and regulations and the conditions set forth in the facility discharge permit.

iii. Solid/Hazardous Waste

There are four categories of solid waste generated at the facility: hazardous waste, pharmaceutical waste, trash, and bulky waste.

Hazardous waste will be generated in the production of the drug substance and the cleanout of the process equipment. Hazardous waste is collected

and transported to a licensed waste disposal firm for incineration. The facility currently used is:

Marisol, Inc.
125 Factory Lane
Middlesex, New Jersey 08846
EPA ID No. NJD002454544
Permit No. 1211B1HP04
Issuing Authority: New Jersey Dept. of Env. Protection
Expiration Date: Indefinite extension

Pharmaceutical wastes, such as rejected drug substance are sent to a disposal firm for incineration. The licensed disposal facility currently used is listed above in Section 4.e.

Trash, including filter cloth, fluid bed dryer bags, tray dryer papers, silica, and any discarded clothing, is sent to a licensed facility for incineration. The facility currently used is:

Union County Utilities Authority
1499 Routes 1 & 9 South
Rahway, New Jersey 07065
Permitting Authority: New Jersey Department of Environmental Protection
Permit No. 2013000835
Expiration Date: 2002

Bulky waste , including construction and demolition debris and furniture, is transported to a licensed facility for disposal. The facility currently used is:

J&J Recycling Company
625 South Front Street
Elizabeth, New Jersey 07202
Permitting Authority: New Jersey Department of Environmental Protection
Permit No. 2004001179
Expiration Date: 2000

Kenilworth, New Jersey

i. Air

Air emissions may occur during mixing, filling, and packaging of the drug product. However, emissions are not of a quantity or quality that require controls.

ii. Wastewater/Liquid Waste

Wastewater will be generated from the cleanout of process equipment used in the manufacture of the final drug product. Wastewater is discharged to the sewerage system of the Rahway Valley Sewerage Authority in Union County, New Jersey.

iii. Solid/Hazardous Waste

There are four categories of solid waste generated at the facility: hazardous waste, pharmaceutical waste, trash, and bulky waste.

Hazardous waste will be generated during mixing, filling, packaging and labeling of the product and from cleanout of process equipment. Hazardous waste is disposed of off the site by:

Clean Harbors of Braintree, Inc.
385 Quincy Avenue
Braintree, Massachusetts 02184
USEPA ID No. MAD053452637
Permit No.: Hazardous Waste Interim Operating Permit #80
Issuing Authority: Mass. Dept. of Environmental Protection
Expiration Date: None

Clean Harbors of Natick, Inc.
10 Mercer Street
Natick, Massachusetts 01760
USEPA ID No. MAD980523203
Permit No.: Hazardous Waste Operating Permit #26B/94
Issuing Authority: Mass. Dept. of Environmental Protection
Expiration Date: October 24, 1999

Clean Harbors of Baltimore, Inc.
1910 Russell Street
Baltimore, Maryland 21230
USEPA ID No. MDD980555189
Permit No. A151
Issuing Authority: Maryland Dept. of the Environment
Expiration Date: Indefinite extension

Pharmaceutical wastes, such as rejected drug product, are sent to a disposal firm for incineration as described in Section 4.e.

Trash, including filter cloth, fluid bed dryer bags, tray dryer papers, silica, and any discarded clothing, is sent to a licensed facility for incineration. The facility currently used is:

Union County Utilities Authority
1499 Routes 1 & 9 South
Rahway, New Jersey 07065
Permitting Authority: New Jersey Department of Environmental Protection
Permit No. 2013000835
Expiration Date: 2002

Bulky waste , including construction and demolition debris and furniture, is transported to a licensed facility for disposal. The facility currently used is:

J&J Recycling Company
625 South Front Street
Elizabeth, New Jersey 07202
Permitting Authority: New Jersey Department of Environmental Protection
Permit No. 2004001179
Expiration Date: 2000

c. Citation of and Statement of Compliance with Applicable Emission Requirements

Manati, Puerto Rico

Listed below are the laws, rules, and regulations that cover emissions and occupational requirements that are applicable to the facility in Manati, Puerto Rico:

* National Primary and Secondary Air Quality Standards (40 CFR 50)
* National Emission Standards for Hazardous Air Pollutants (40 CFR 61)
* Puerto Rico Air Pollution Control Regulations (PREQB Regulations, August 17, 1971 et. seq.)
* U.S. EPA Pretreatment Regulations (40 CFR 403 and 439)
* Puerto Rico Water Quality Standards (PREQB Regulations, January 4, 1974 et. seq.)
* Puerto Rico Aqueduct and Sewer Authority - Facility Agreement with Schering-plough Products, Inc., Maniti, Puerto Rico
* U.S. Dept. of Labor, Occupational Safety and Health Administration (OSHA), Occupational Safety and Health Standards (29 CFR 1910)

The following permits are applicable to the control of emissions from the

manufacture of mometasone furoate at the applicant's facility in Manati, Puerto Rico:

Emission	Authorizing Agency	Permit #
Air	Puerto Rico Environmental Quality Board (EQB)	PFE-47-1290-1306-1-11-0 Expiration Date: 11/12/94 [1]
Air	Puerto Rico Environmental Quality Board (EQB)	PFE-47-0692-0853-I-0 Expiration Date: 9/8/94 [1]
Process waste-water	Puerto Rico Aqueducts and Sewer Authority (PRASA)	Pretreatment Permit GDA 91-210-026 Expiration Date: 7/13/95 [2]

[1] Letters of extension granted from The "Area Calidad de Aire" dated 6/8/94 and 8/15/95, respectively. Permits are extended under Title V of the Clean Air Act and the EQB, Rule 204 Permit to Operate, with annual payment of applicable fees.

[2] Permit has been extended by the PRASA during the renewal process.

Schering-Plough Products, Inc., Maniti, Puerto Rico is registered with the USEPA (ID No. PRD 090 139536) for the handling and control of hazardous and solid waste.

The Manati facility is in compliance with emission requirements, including occupational requirements, which are applicable to the manufacturing process.

Union, New Jersey

Listed below are the laws, rules, and regulations at the federal, state, and local levels that cover emissions, including occupational requirements, and are applicable to the facility in Union:

* National Primary and Secondary Air Quality Standards (40 CFR 50)
* National Emission Standards for Hazardous Air Pollutants (40 CFR 61)
* New Jersey Air Pollution Control Regulations (N.J.A.C. 7:27 et. seq.)
* U.S. EPA Pretreatment Regulations (40 CFR 403 and 439)
* Joint Meeting of Essex and Union Counties (JMEUC) Rules and Regulations (December 20, 1989)
* Resource Conservation and Recovery Act of 1976 PL 94-580 as amended

* New Jersey Administrative Code, Title 7, Chapters 14A, 26, and 27
* U.S. Dept. of Labor, Occupational Safety and Health Administration (OSHA), Occupational Safety and Health Standards (29 CFR 1910)

The following permits are applicable to the control of emissions from the manufacture of the drug substance at the applicant's facility in Union, New Jersey:

Emission	Authorizing Agency	Permit #	Exp. Date
Air	New Jersey Dept. of Environmental Protection (NJDEP)	095068	3/29/96[1]
		082108	2/26/98
		082109	2/02/98
		102308	7/05/96
		082106	2/26/98
		082107	2/26/98
		112320	7/02/00
		115725	3/20/96[1]
Process wastewater	Joint Meeting of Essex and Union (JMEUC)	JM7145	4/14/91[2]

[1] Permits administratively extended by the New Jersey Dept. of Environmental Protection (NJDEP)

[2] Permit extended by the Joint Meeting of Essex and Union (JMEUC) until further notification

The Union facility operates under permit number (ID number) NJD001317601 for the generation, storage, and transportation of hazardous waste. This permit is issued by the Environmental Protection Agency (EPA) and the NJDEP and expires on December 30, 1996.

The facility in Union, New Jersey is in compliance with emission requirements, including occupational requirements, which are applicable to the manufacturing process.

Kenilworth, New Jersey

Listed below are the laws, rules, and regulations at the federal, state, and local levels that cover emissions, including occupational requirements, and are applicable to the facility in Kenilworth:

* National Primary and Secondary Air Quality Standards (40 CFR 50)

- National Emission Standards for Hazardous Air Pollutants (40 CFR 61)
- New Jersey Air Pollution Control Regulations (N.J.A.C. 7:27 et. seq.)
- U.S. EPA Pretreatment Regulations (40 CFR 403 and 439)
- Rules and Regulations Concerning Discharges to the Rahway Valley Sewerage Authority, effective December 1, 1989
- Resource Conservation and Recovery Act of 1976 PL 94-580 as amended
- New Jersey Administrative Code, Title 7, Chapters 14A, 26, and 27
- U.S. Dept. of Labor, Occupational Safety and Health Administration (OSHA), Occupational Safety and Health Standards (29 CFR 1910)

The following permits are applicable to the control of emissions from the manufacture of the final drug product at the facility in Kenilworth:

Emission	Authorizing Agency	Permit #	Exp. Date
Air	New Jersey Dept. of Env. Protection	NJ0001	01/01/00
Process Wastewater	Rahway Valley Sewerage Authority	RVSA035	05/31/96*
Hazardous waste	USEPA	NJD054554290	indefinite

* Permit administratively extended.

The Kenilworth facility is in compliance with emission requirements, including occupational requirements, which are applicable to the manufacturing process.

d. Discussion of the Effect of Approval on Compliance with Current Emission Requirements

The approval of the proposed action and subsequent increase in production will not affect compliance with current emission requirements at the facilities in Manati, Union, and Kenilworth.

e. Expected Introduction Concentration

FDA regulations, 21 CFR Part 25.31a(a)6, require a prediction of the concentrations of substances entering the environment as a result of the use of the product. An estimate of the expected introduction concentration (EIC)

of the drug substance for the aquatic environment has been developed and is presented in **Confidential Appendix 1.**

7. FATE OF EMITTED SUBSTANCES IN THE ENVIRONMENT:

Based on the Tier 0 approach under the new FDA guidance (see reference 1) for the submission of EA's, format item 7 is not normally needed if the maximum expected environmental concentration is less than 1 part per billion (ppb). The expected introduction concentration (EIC) of mometasone furoate has been calculated to be less than 1 ppb, and thus, fate information has not been provided.

8. ENVIRONMENTAL EFFECTS OF RELEASED SUBSTANCES

Based on the Tier 0 approach under the new FDA guidance (see reference 1) for the submission of EA's, format item 8 is not normally needed if the maximum expected environmental concentration is less than 1 ppb. The EIC of mometasone furoate has been calculated to be less than 1 ppb, and thus, information on effects has not been provided.

9. USE OF RESOURCES AND ENERGY:

Based on the Tier 0 approach under the new FDA guidance (see reference 1) for the submission of EA's, format item 9 is not normally needed if the maximum expected environmental concentration is less than 1 ppb. The EIC of mometasone furoate has been calculated to be less than 1 ppb, and thus, information on the use of resources and energy has not been provided.

10. MITIGATION MEASURES:

Based on the Tier 0 approach under the new FDA guidance (see reference 1) for the submission of EA's, format item 10 is not normally needed if the maximum expected environmental concentration is less than 1 ppb. The EIC of mometasone furoate has been calculated to be less than 1 ppb, and thus, information regarding mitigation measures has not been provided.

11. ALTERNATIVES TO THE PROPOSED ACTION:

Based on the Tier 0 approach under the new FDA guidance (see reference 1) for the submission of EA's, format item 11 is not normally needed if the maximum expected environmental concentration is less than 1 ppb. The EIC of mometasone furoate has been calculated to be less than 1 ppb, and thus, information regarding alternatives to the proposed action has not been provided.

12. LIST OF PREPARERS

The information contained in this Environmental Assessment was provided by the following individuals:

Schering-Plough Corporation	
Joseph A. Nusser	Sr. Dir. Env. Projects & Compliance
Carol M. Fletcher	Principal Environmental Engineer
Ravi K. Chivukula	Manager, Regulatory Affairs
Philip Apruzzese	Manager Plant Services
Judith Stettner	Environmental Engineer
Andrew R. Anderson	Environmental Engineer
Schering-Plough Products, Inc.	
Samuel Laguna-Garcia	Environmental Compliance Engineer
Carlos M. Jimenez-Barber	Environmental Compliance Manager

Information on the qualifications of these individuals is presented at the end of this document in Appendix 2.

13. CERTIFICATION:

The undersigned official certifies that the information presented is true, accurate and complete to the best of the knowledge of the Schering-Plough Corporation.

Appendix 1 of this document contains information which is considered confidential in nature and is therefore not releasable to the public.

The undersigned official certifies that the EA summary document and Appendices 2 and 3 contain non-confidential information and understands that this information will be made available to the public in accordance with 40 CFR 1506.6.

Date: 5/13/97

By: for Russ Cole

Joseph A. Nusser, P.E.
Senior Director
Environmental Projects & Compliance
Schering Laboratories

14. REFERENCES:

1. *Guidance for Industry for the Submission of an Environmental Assessment in Human Drug Applications asn Supplements,*

Washington, D.C., Center for Drug Evaluation and Research (CDER) Food and Drug Administration, November 1995.

15. APPENDICES:

Appendix 1: Confidential EA Information Regarding the Manufacture and Production Estimates of Mometasone Furoate Aquous Nasal Suspension

Appendix 2: Qualifications of Preparers

Appendix 3: Material Safety Data Sheet (MSDS) for Mometasone Furoate Monohydrate

APPENDIX 2

Non-confidential Information

Qualifications of Preparers

APPENDIX 2

Qualifications of Preparers

Joseph A. Nusser, P.E.

Education: ME, Environmental Engineering, Manhattan College, 1971
MS, Civil Engineering, New York University, 1969
BCE, Civil Engineering, Manhattan College, 1967

Experience: Senior Director Environmental Affairs, Schering-Plough, 1985-present
Environmental Engineer, USEPA, 1984-1985
Principal Engineer, Joseph A. Nusser & Associates, 1980-1984
Project Manager, Hydroscience, Inc. 1970-1980

Carol M. Fletcher, P.E.

Education: ME, Environmental Engineering, Stevens Institute of Technology, 1996
BE, Chemical Engineering, Stevens Institute of Technology, 1985

Experience: Principal Environmental Engineer, Schering-Plough, 1993-present
Supervising Environmental Engineer, Sadat Associates, 1992-1993
Associate Engineer, Shell Oil Company, 1989-1992
Environmental Engineer, Mobil Chemical Company, 1988-1989
Assistant Environmental Engineer, NJDEP, 1986-1988

Ravi K. Chivukula

Education: MS, Pharmaceutics, University of Houston, 1987
B. Pharm, Andhra University, 1982

Experience: Mgr. Regulatory Affairs, Schering-Plough, 1992-present
Regulatory Affairs Associate, Warner Lambert/Parke-Davis, 1987-1992

Philip Apruzzese

Education: MS, Technology Management, Stevens Institute of Technology, 1993
BS, Chemical Engineering, Stevens Institute of Technology, 1970

Experience: Manager Plant Services, Schering-Plough, 1991-present
Operations Manager, Schering-Plough, 1987-1991
Engineering Manager, Schering-Plough, 1985-1987

Judith Stettner

Education: BS, Environmental Engineering, Rensselaer Polytechnic Institute, 1990

Experience: Environmental Engineer, Schering-Plough, 1993-present
Associate Engineer, Ebasco Environmental, 1990-1993

Andrew R. Anderson, P.E.

Education: ME, Environmental Engineering, Manhattan College, 1976
BS, Mechanical Engineering, Union College, 1970

Experience: Senior Associate, Malcolm Pirnie, Inc., 1990-1996
Principal Engineer, Geraghty &Miller, Inc., 1988-1990
Associate, Malcolm Pirnie, Inc., 1980-1988
Environmental Engineer, Hydroscience, Inc., 1978-1980

Samuel Laguna-Garcia, P.E.

Education: BS, Chemical Engineering, University of Puerto Rico, 1981

Experience: Env. Compliance Engineer, Schering-Plough Products, 1992-present
Environmental Engineer, Pedro Panzardi and Assoc., 1990-1992
Engineer, Puerto Rico Env. Quality Board, 1989-1990
Env. Specialist, Solid Waste Management Authority, 1987-1989

Carlos M. Jimenez-Barber

Education: MS, Physics, Unversity of Rochester
BS, Physics, University of Puerto Rico

Experience: Env. Compliance Manager, Schering-Plough Products, 1987-present
Vice President, Puerto Rico Env. Quality Board, 1985-1987
Environmental Manager, Squibb, 1976-1978
President, Puerto Rico Env. Quality Board, 1973-1976

APPENDIX 3

Non-confidential Business Information

Material Safety Data Sheet (MSDS) for Mometasone Furoate Monohydrate

Material Safety Data Sheet

MOMETASONE FUROATE

Page: 1
Rev. Date 05/14/96

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

COMPANY CONTACT: Safety & Industrial Hygiene
TELEPHONE NUMBER: (908)298-5044

EMERGENCY TELEPHONE NUMBER
Safety and Industrial Hygiene (908)298-5044

PRODUCT NAME: MOMETASONE FUROATE
PRODUCT CODE: SCH 32088
CAS NUMBER: 83919-23-7
CHEMICAL FAMILY: Steroid
CHEMICAL FORMULA: C27 H30 C12 O6

SYNONYMS: 9-ALPHA,21-DICHLORO-11 BETA,17-DIHYDROXY-16 ALPHA-METHYLPREGNA-1,4-DIENE-3,20 DIONE 17-(2-FUROATE)
ELOCON
SCH 32088

2. COMPOSITION/INFORMATION ON INGREDIENTS

INGREDIENT NAME	EXPOSURE LIMITS	CONCENTRATION PERCENT BY WEIGHT
Mometasone Furoate	PEL	
CAS NUMBER: 83919-23-7	TLV	
	None	
	None	

3. HAZARDS IDENTIFICATION

POTENTIAL HEALTH EFFECTS

EYES
Although mometasone furoate was not irritating to the eyes in laboratory studies, it may produce eye irritation or an allergic reaction in sensitive individuals.

SKIN
May produce skin irritation in sensitive individuals. Other symptoms include burning, itching, and dryness. Systemic absorption through the skin producing suppression of adrenal gland function or target organ effects is possible.

INGESTION
Mometasone furoate is slightly hazardous by ingestion based upon the oral LD 50 in rats of greater than 2000 mg/kg. Ingestion of sufficient quantities may produce reversible suppression of the hypothalmic/pituitary/adrenal (HPA) system, manifestations of Cushing's syndrome (redistribution of fat, often with great obesity, muscular weakness, skeletal weakness, and blood pressure. The face often assumes a rounded shape, the characteristic "moon face". Other symptoms associated with HPA suppression include high blood glucose levels often concurrent with the presence of sugar in the urine.

INHALATION
The exact effects of inhalation of mometasone furoate in humans are unknown, Acute inhalation studies using laboratory animals indicate a slight hazard. Other studies indicate that systemic absorption occurs producing effects in the thymus, adrenal and mammary glands, as well as liver, spleen, and blood changes consistent with exposure to glucocoticoids.

Material Safety Data Sheet MOMETASONE FUROATE	Page: 2 Rev. Date 05/14/96

4. FIRST AID MEASURES

EYES
Flush with water for at least 15 minutes. Obtain medical attention.

SKIN
Remove contaminated clothing. Wash exposed area with soap and water. Obtain medical attention.

INGESTION
Give copious amounts of water and induce vomiting, if conscious. Obtain medical attention.

INHALATION
Remove from exposure. If not breathing, give artificial respiration. Obtain medical attention.

5. FIRE FIGHTING MEASURES

FLAMMABLE PROPERTIES
FLASH POINT: n/a°F

FIRE AND EXPLOSION HAZARDS
Under normal conditions of use this material does not pose a significant fire or explosion hazard. However, like most organic compounds, it is combustible and may form a dust explosion hazard if widely dispersed in air.

EXTINGUISHING MEDIA
Water,CO2, Dry Chemical

FIRE FIGHTING INSTRUCTIONS
Fight fire from a safe distance or protected location. Use water spray to keepcontainers and equipment cool. Wear full protective equipment including self-contained breathing apparatus (SCBA).

6. ACCIDENTAL RELEASE MEASURES

Sweep, scoop, or vacuum up spill. Minimize contact with spilled material. Keep other personnel away from the clean-up area. Wear appropriate respiratory protection and protective clothing in the spill area. Notify your supervisor immediately. Clean area with a wet mop. Dispose of spilled material and clean up materials as given in Waste Disposal Methods below.

7. HANDLING AND STORAGE

HANDLING AND STORAGE PRECAUTIONS
Store in double lined plastic in fiberboard or other appropriate container, Store in a cool, dry, well ventilated area.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

ENGINEERING CONTROLS
Provide adequate local exhaust ventilation.

EYE/FACE PROTECTION
Safety glasses/side shields.

SKIN PROTECTION
Lab Coat or uniform
Gloves- Latex.

RESPIRATORY PROTECTION
Minimum of half facepiece respirator with high efficiency cartridges.

Material Safety Data Sheet MOMETASONE FUROATE	Page: 3 Rev. Date 05/14/96

9. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE
White to off-white powder.

BASIC PHYSICAL PROPERTIES
MELTING POINT: 215-228°C
MOLECULAR WEIGHT: 521.40
SOLUBILITY (H2O): Insoluble

10. STABILITY AND REACTIVITY

STABILITY: Stable

HAZARDOUS DECOMPOSITION PRODUCTS
Hydrogen chloride

11. TOXICOLOGICAL INFORMATION

MISCELLANEOUS TOXICOLOGICAL INFORMATION
LD 50 oral (rats)> 2000 mg/kg. Mometasone furoate is classified as slightly hazardous via the oral route. In animal studies it was non-irritating to the skin and eyes. Acute inhalation toxicity studies at a maximum dust concentration of 0.68 mg/L did not produce any mortality although there were persistant signs of exposure during the 14 day observation period. These signs included rales, ano-genital staining, emaciation and body weight losses. Long term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility. Genetic toxicity tests with mometasone furoate (Ames test, Mouse lymphoma assay, and Micronucleus test) did not show any mutagenic potential. Corticosteroids are generally teratogenic in test animals when administered systemically at relatively low dosage levels. They have also been shown to be teratogenic after dermal application in laboratory animals. There are no adequately controlled studies in pregnant women. Since risk cannot be ruled out, exposure of pregnant women to mometasone furoate should be controlled to the lowest levels possible.

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE
Hypersensitivity to mometasone furoate or other corticosteroids.

12. ECOLOGICAL INFORMATION

NO DATA GIVEN

13. DISPOSAL CONSIDERATIONS

While not hazardous waste, material should be disposed in an environmentally sound manner. Incineration is the preferred disposal method.

14. TRANSPORT INFORMATION

PROPER SHIPPING NAME: N/A

15. REGULATORY INFORMATION

NO DATA GIVEN

16. OTHER INFORMATION

Hazard Rating - HEALTH: 1 Slight
- FIRE: 1 Slight
- REACTIVITY: 0 Negligible

Material Safety Data Sheet MOMETASONE FUROATE	Page: 4 Rev. Date 05/14/96

16. OTHER INFORMATION - Continued

REFERENCE DOCUMENTATION
Schering Toxicology Sourcing Document.
Physician's Desk Reference (1988)

OTHER SOLUBILITIES: Slightly soluble in octanol, very soluble in ethanol; soluble in acetone, DMF, dioxane, methanol, methylene chloride.

DISCLAIMER OF EXPRESSED AND IMPLIED WARRANTIES
Although reasonable care has been taken in the preparation of this document, we extend no warranties and make no representations as to the accuracy or completeness of the information contained therein, and assume no responsibility regarding the suitability of this information for the user's intended purposes or for the consequences of its use. Each individual should make a determination as to the suitability of the information for their particular purpose(s).