CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 020762/S-051

Trade Name: NASONEX®

Generic Name: mometasone furoate monohydrate

Sponsor: Merck Sharp Dohme

Approval Date: 02/24/2015

Indication: NASONEX® is a corticosteroid indicated for: 1) treatment of nasal symptoms of allergic rhinitis in patients ≥ 2 years of age; 2) treatment of nasal congestion associated with seasonal allergic rhinitis in patients ≥ 2 years of age; 3) prophylaxis of seasonal allergic rhinitis in patients ≥ 12 years of age; 4) treatment of nasal polyps in patients ≥ 18 years of age.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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APPLICATION NUMBER:

NDA 020762/S-051

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20762/S-051

APPROVAL LETTER

Merck Sharp & Dohme Corp
Attention: Wendy Sikorski
Senior Specialist, Global CMC Regulatory Affairs
2000 Galloping Hill Road, Mailstop K-6-1, 1620
Kenilworth, NJ 07033

Dear Ms. Sikorski:

Please refer to your Supplemental New Drug Application (sNDA) dated and received August 25, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Nasonex® (mometasone furoate monohydrate) Nasal Spray.

This "Changes Being Effected in 30 days" supplemental application provides for a change in the approved microbial specification of Nasonex® to comply with the official compendium.

We have completed our review of this supplemental new drug application. This supplement is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Youbang Liu, Regulatory Project Manager, at (301) 796-1926.

Sincerely,

Ramesh Raghavachari -S

Digitally signed by Ramesh Raghavachari S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300111793, cn=Ramesh Raghavachari S
Date: 2015.02.24 16:07:19 -05'00'

Ramesh Raghavachari, Ph.D.
Branch Chief, Branch I
Office of Lifecycle Drug Products
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

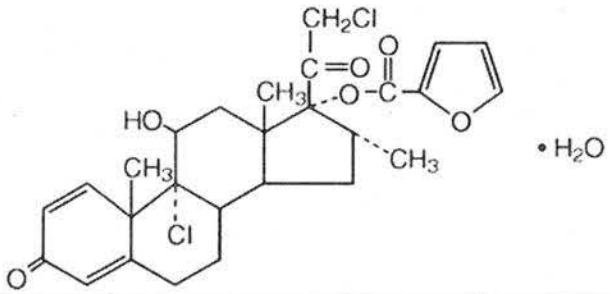
APPLICATION NUMBER:

NDA 020762/S-051

CHEMISTRY REVIEW(S)

Chemistry Review:# 1	**1. Division:** ONDQA-DPARP	**2. NDA Number:** 20-762	
3. Name and Address of Applicant: Merck Sharp and Dohme Corp. 2000 Galloping Hill Road Mailstop K23/Q50 Kenilworth, NJ, 07033-1310		**4. Supplement(s):** CBE-030 **Number:** 51 **Date(s):** 08/25/2014	
5. Name of Drug: Nasonex nasal spray		**6. Nonproprietary name:** Mometasone furoate	
7. Supplement Provides for: Change in drug product microbial specifications			**8. Amendment(s):**
9. Pharmacological Category: corticosteroid		**10. How Dispensed:** R_x	**11. Related Documents:**
12. Dosage Form: Nasal metered spray		**13. Potency:** 50 mcg/actuation	

14. Chemical Name and Structure: 21-Dichloro-11b, 17-dihydroxy-16a-methylpregna-1, 4-diene-3, 20-dione 17-(2 furoate monohydrate); $C_{27}H_{30}Cl_2O_6 \cdot H_2O$: MW = 539.45



15. Comments:

- This supplement provides for a change in drug product microbial specifications
- Vera Viehmann, Ph.D. found the proposed specifications to be consistent with USP <1111> and that no additional product quality microbiology assessment was necessary on 09/29/2014

16. Conclusion: This supplement is recommended for approval from CMC perspective

17. Name:	**Signature:**	**Date:**
Erika Englund, Ph.D., Chemist		
18. Concurrence:	**Signature:**	**Date:**
Ramesh Raghavachari, Ph.D., Branch Chief, Br., IX, ONDQA		

Drug Product Information

1. NDA 20-762 was approved October 1, 1997
2. Nasonex is indicated for:
    a. Treatment of Nasal Symptoms of Allergic Rhinitis in patients ≥2 years of age
    b. Treatment of Nasal Congestion Associated with Seasonal Allergic Rhinitis in patients ≥2 years of age
    c. Prophylaxis of Seasonal Allergic Rhinitis in patients ≥12 years of age;
    d. Treatment of Nasal Polyps in patients ≥18 years of age

3. The maximum recommended dosage is 2 sprays in each nostril twice daily
4. Nasal Spray contains 50 mcg of mometasone furoate in each 100 µL spray
5. NASONEX is a metered-dose, manual pump unit containing an aqueous suspension of mometasone furoate monohydrate (equivalent to 0.05% w/w mometasone furoate calculated on the anhydrous basis).
6. Each bottle of NASONEX provides 120 sprays.
7. Mometasone furoate is practically insoluble in water; slightly soluble in methanol, ethanol, and isopropanol; soluble in acetone and chloroform; and freely soluble in tetrahydrofuran
8. Mometasone furoate is 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.
9. NASONEX (mometasone furoate monohydrate) 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. Each bottle contains 120 sprays.
10. It is stored at 25 °C.

Chemistry Review

Current specification	Proposed harmonized specification
(b) (4)	Total Aerobic Microbial Count (cfu/mL): Not more than 100 cfu/mL
	Total Combined Yeasts and Molds Count (cfu/mL): Not more than 10 cfu/mL
	(b) (4)
	Absence of *Pseudomonas aeruginosa* (1 mL)
	Absence of *Staphylococcus aureus* (1 mL)

This supplement proposes a change to the finished drug product specification for Microbial Quality to harmonize with USP <1111> for nasal products (above). The applicant stated that based on historical data, all the batches were able to meet the acceptance criteria for the original (b) (4) specification and (b) (4) specification. The applicant stated that there would be minimal impact with the (b) (4) as both organisms would be detected through the absence of bile-tolerant and other gram-negative bacteria tests. Similarly, the (b) (4) would be monitored under the TAMC (Total Aerobic Microbial Count) and TYMC (Total Combined Yeast and Mold Count) specifications. Any microbial count reported from TAMC and TYMC is required to be identified to the species level. Vera Viehmann, Ph.D. found the

proposed specifications to be consistent with USP <1111> and that no additional product quality microbiology assessment was necessary on 09/29/2014

REV-QUALITYMICRO-02 (Review Noted (NAI))
NDA-020762
SUPPL-51
Supporting Document 3028
New/Supplement
Submit Date: 08/25/2014 - FDA Received Date: 08/25/2014

This supplement provides for changing the finished product microbial limits specification for this nasal spray drug product to comply with USP Chapter <1111> (MICROBIOLOGICAL EXAMINATION OF NONSTERILE PRODUCTS: ACCEPTANCE CRITERIA FOR PHARMACEUTICAL PREPARATIONS AND SUBSTANCES FOR PHARMACEUTICAL USE). The proposed specifications are consistent with the recommendations in USP <1111> and will help assure adequate microbial quality for the drug product. Therefore, no additional product quality microbiology assessment is necessary.

3.2.P.5.1 Specification(s)

Microbial Limits (Microbial Enumeration and Quality)	USP <61 > and <62>
Absence of Staphylococcus aureus. (1 mL)	
Absence of Pseudomonas aeruginosa (1mL)	
Total aerobic microbial count (CFU/mL): Not more than 100	
Total combined yeasts and molds count (CFU/mL): Not more than 10	
(b) (4)	

The updated microbial specifications are copied above. These are consistent with the proposed changes found acceptable by Vera Viehmann, Ph.D. on 09/29/2014. This is adequate from CMC perspective.

Overall Recommendation: Adequate
Vera Viehmann, Ph.D. found the proposed specifications to be consistent with USP <1111> and that no additional product quality microbiology assessment was necessary on 09/29/2014. The applicant updated 3.2.P.5.1 with the new specifications. This supplement is recommended for approval from CMC perspective.

Erika Elaine Englund

Digitally signed by Erika Elaine Englund
DN: cn=Erika Elaine Englund, o, ou, email=erika.englund@fda.hhs.gov, c=US
Date: 2015.01.09 13:59:33 -05'00'

Ramesh Raghavachari -S

Digitally signed by Ramesh Raghavachari -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300211793, cn=Ramesh Raghavachari -S
Date: 2015.01.11 18:55:11 -05'00'

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 020762/S-051

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20762/S-051

CBE SUPPLEMENT – ACKNOWLEDGEMENT

Merck Sharp & Dohme Corp
Attention: Wendy Sikorski
Senior Specialist, Global CMC Regulatory Affairs
2000 Galloping Hill Road, Mailstop K-6-1, 1620
Kenilworth, NJ 07033

Dear Ms. Sikorski

We have received your Supplemental New Drug Application (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

NDA Number: 20762

Supplement number: S-051

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

Date of supplement: August 25, 2014

Date of receipt: August 25, 2014

This supplemental application, submitted as a "Changes Being Effected in 30 days" supplement, proposes change in the approved microbial specification of Nasonex to comply with an official compendium.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on October 24, 2014, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be February 25, 2015.

Cite the application number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pulmonary, Allergy and Rheumatology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm.

If you have questions, call me, at (301) 796-1926.

Sincerely,

{See appended electronic signature page}

Youbang Liu
Regulatory Project Manager
Division III of New Drug Quality Assessment
Office of New Drug Quality Assessment
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/

YOUBANG LIU
09/30/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADM NISTRATION

CMC MICRO & STERILITY ASSURANCE REVIEW REQUEST

TO *(Division/Office)*: **New Drug Microbiology Staff**

E-mail to: **CDER OPS IO MICRO**

Paper mail to: **WO Bldg 51, Room 4193**

FROM: Youbang Liu, ONDQA, 301-796-1926

PROJECT MANAGER *(if other than sender):*

REQUEST DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
9/24/14		**NDA 20762/S-051**	**CBE-30 Supplement**	**08/25/14**

NAMES OF DRUG	PRIORITY CONSIDERATION	PDUFA DATE	DESIRED COMPLETION DATE
Nasonex Nasal Spray		**2/25/15**	**10/24/14**

NAME OF APPLICANT OR SPONSOR: Merck

GENERAL PROVISIONS IN APPLICATION

- ☐ 30-DAY SAFETY REVIEW NEEDED
- ☐ NDA FILING REVIEW NEEDED BY: _____
- ☐ BUNDLED
- ☐ DOCUMENT IN EDR
- ☐ CBE-0 SUPPLEMENT
- ☐ CBE-30 SUPPLEMENT
- ☐ CHANGE IN DOSAGE, STRENGTH / POTENCY

COMMENTS / SPECIAL INSTRUCTIONS:

This "CBE-30 " supplement, provides for change in the approved microbial specification of Nasonex to comply with an official compendium .

This is an e-submission and accessible in DARRTS.

SIGNATURE OF REQUESTER

Youbang Liu

REVIEW REQUEST DELIVERED BY (Check one):

☒ DARRTS ☐ EDR ☒ E-MAIL ☐ MAIL ☐ HAND

DOCUMENTS FOR REVIEW DELIVERED BY (Check one):

☒ EDR ☐ E-MAIL ☐ MAIL ☐ HAND

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/s/

YOUBANG LIU
09/24/2014