CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 020762/S-049

Trade Name: NASONEX®

Generic Name: mometasone furoate monohydrate

Sponsor: Merck Sharp Dohme

Approval Date: 04/18/2014

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:

NDA 020762/S-049

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 020762/S-049

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20762/S-049

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 07033-1310

Dear Ms. Sikorski:

Please refer to your Supplemental New Drug Application (sNDA) dated and received December 19, 2013, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for NASONEX® (Mometasone furoate monohydrate) Nasal Spray

This Prior Approval supplemental new drug application provides for the following changes:

1. Addition of [redacted] (b) (4) as an alternate supplier for the device components (pumps, actuators, bottles and caps)
2. Additional packaging specification for shot weight (mg) of pumps manufactured by [redacted] (b) (4), using water as the test medium

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,

{See appended electronic signature page}

Ramesh Raghavachari, Ph.D.
Branch Chief, Branch IX,
Division of New Drug Quality Assessment III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

RAMESH RAGHAVACHARI
04/18/2014

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 020762/S-049

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 K6-1, 1620 Kenliworth, NJ, 07033-1310		**4. Supplement(s):** PAS **Number:** 49 **Date(s):** 12/19/2013	
5. Name of Drug: Nasonex nasal spray		**6. Nonproprietary name:** Mometasone furoate	
7. Supplement Provides for: Registration of alternate supplier and packaging specification			**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); $C_{27}H_{30}Cl_2O_6 \bullet H_2O$: MW = 539.45

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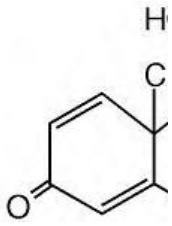

15. Comments:

- Carol M. Rivera-López, Ph.D. reviewed the leachables/extractables data on 03/21/2014 and did not identify a safety concern with the changes.
- DMF (b) (4) (LOA 27-AUG-2013) and DMF (b) (4) (LOA 2-MAY-2013) were referenced in this supplement. Sufficient information was contained in the application and a full review of the DMFs was not necessary.

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

The 17 g presentation of Nasonex is manufactured at MSD–Singapore. (b) (4) is the current supplier of the bottles and caps and (b) (4) is the current supplier of the metered dose spray pumps and actuators. This supplement provides for the registration of (b) (4) as an alternate supplier for the pumps, actuators, bottles and caps for 17 g fill size. An LOA from (b) (4) for DMF (b) (4) (LOA 27-AUG-2013) and (b) (4) for pump (b) (4) in DMF (b) (4) (LOA 5-2-2013) were submitted. Sufficient information was contained within the application and a separate full review of these DMFs was not performed.

This supplement also provides for water as the test medium in the pump specification for shot weight (mg) for pumps manufactured by (b) (4). The current method with a water/alcohol mixture as the test medium will remain as an alternative method. The pumps from (b) (4) only list water as the test medium for the shot weight specification. There were no changes to the finished product release and shelf-life specifications.

Quality Information Amendment 1:

Justification of Shot Weight Specification Change for Nasonex Pumps

There were no changes to the final drug product specifications in this supplement. The change in shot weight specification only applies to the specification for the pump components. The pumps from (b) (4) will only have the shot weight specification listed with water, whereas the pumps

from (b) (4) will have the shot weight specifications listed with either water or the previously approved water/ethanol test medium.

Table 1 Shot Weight Release Specifications for Incoming Pump Component and Finished Drug Product at Merck

Shot Weight Test Media	Incoming Pump Component Shot Weight Release† (Current)	Incoming Pump Component Shot Weight Release† (Proposed)	Finished Drug Product Shot Weight Release‡ (Current)
Water/Alcohol	(b) (4)		
Water		(b) (4)	
Product			(b) (4)

† representing overall mean shot weight of 50 pumps (filled bottles) per batch

‡ representing average shot weight of 10 bottles per batch

Data for the new specifications were collected from Merck Singapore (20 batches of (b) (4) pump) (b) (4) (103 batches of the (b) (4) pump) and (b) (4) (30 batches of the (b) (4) pump). As can be seen above, the number of pumps to be tested with both test media is the same, the only difference is the final shot weight. The use of water results in an upward shift by close to 5 mg for the acceptance criteria. However, both sets of specifications for the pumps were narrower that the shot release specification for the final product.

Figure 4 Singapore Shot Weight Results for (b) (4) Pump (20 Lots)

(b) (4)

Figure 5 (b) (4) Shot Weight Results for (b) (4) Pump (103 lots)

Figure 6 (b) (4) Shot Weight Results for (b) (4) Pump (30 Lots)

The tables above show the shot weights for the test with water with pumps from both (b) (4) and (b) (4). There were some differences between the pumps. The mean delivery was lower with the (b) (4) pumps than the (b) (4) pumps (b) (4). The sponsor states that the final proposed specification took into account the performance of both suppliers. Except for 1 of the (b) (4) batches shown in Figure 5, every other batch was within specification.

Evaluation: Adequate

The shot weight measured with water as the test medium was evaluated in pumps from both (b) (4) and (b) (4) and the proposed specification is (b) (4) mg. This range is narrower than the shot weight for the finished drug product which is (b) (4) mg and is adequate.

Quality Information Amendment 2: *Dimensional Comparability Primary Components*
Quality Information Amendment 2 compared the dimensions for the components from the approved and proposed suppliers. Most of the dimensions are the same for the bottles and dust caps from both suppliers, as shown below. The differences in dimension ranges are attributed to process capability. The maximum difference in dimensions was (b) (4) mm (neck width) for the bottles and (b) (4) mm (overall height) for the dust cap. Most of the differences were due to process capabilities.

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8	Bottle Heig
9	Wall Thickness

APPEARS THIS WAY ON ORIGINAL

	Dust Cap Dim (b) (4) – *Critical Dimension*
1	Resin
2	Weight
3	Overall He

The pump design is different from both suppliers, but the dose delivery and performance requirements are the same. The (b) (4) pump is crimped onto bottles from (b) (4) or (b) (4) (b) (4) The diagrams for (b) (4) pump (left) and (b) (4) pump (right) are provided below for comparison.

(b) (4)

The different pump designs resulted in a number of different dimensions between the pumps. The parameter for outside (b) (4) diameter is not critical for the (b) (4) pump because the (b) (4) The largest difference was for the distance from the end of (b) (4) (b) (4) compared to end of (b) (4) (b) (4). The (b) (4) would therefore extend further into the bottle with the new pump. The bottle height is unchanged and is (b) (4) mm. Therefore, there is a much less space between the end of the (b) (4) and the bottle in the components from (b) (4). Refer to the pump performance evaluation in section 3.2.P.2.

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1	Pump Ste Outside Diameter
2	End of (b) (4) to (b) (4)
3	(b) (4)

APPEARS THIS WAY ON ORIGINAL

7	(b) (4) (b) (4) Thickness
8	Overall M Shot Weig (Water)

A comparison of the actuator dimensions are provided below. All of the parameters are similar and the largest difference was in overall height. The difference in this parameter was (b) (4) vs. (b) (4)

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3	Height to Shoulder

Actuator – Dimensional Comparability

(b) (4)

Evaluation: Adequate
The actuator, bottle and dust caps all had very similar dimensions between the suppliers. The largest difference was in the pump dimensions, which was a result of the new design of the pump. The described dimensions are adequate.

Quality Information Amendment 3 and 4:
MMD Packaging Technology Memo
A leachables study (Quality Information Amendment 3) and extractables study (Quality Information Amendment 4) were performed with the new (b) (4) pump and bottle for Nasonex. The only leachable identified above the LOQ was the (b) (4) isomer. Carol M. Rivera-López, Ph.D. reviewed the leachables/extractables data on 03/21/2014 and did not identify any safety concerns. The sponsor stated that the tox. limits were below those allowed in USP <232>. This is adequate.

Evaluation: Adequate
Only one leachable was identified above the LOQ in the leachables study. Carol M. Rivera-López evaluated this data and did not identify a safety concern. This is adequate.

3.2.P.2 Pharmaceutical Development

Container Closure System

The currently approved container consists of (b) (4) or (b) (4) HDPE bottles and caps from (b) (4) and the (b) (4) pump. The proposed container consists of (b) (4) HDPE bottles and the (b) (4) pump from (b) (4). The (b) (4) components and bottle material also met USP <661>, <387>, and <87> .

(b) (4)

The resins are similar between the systems, but the fundamental design differences reside in the pump assembly. The resins used are listed below. The (b) (4) pump provides a (b) (4), as opposed to the (b) (4) in the (b) (4) design. In addition, the (b) (4) in the (b) (4) pump is replaced by a (b) (4) in the (b) (4) pump design. The sponsor states that the other pump components have similar design features for both systems.

Table 3 Bottle & Cap Comparison of Materials

	(b) (4)	(b) (4)
Component	Resin	Resin
Bottle (b)	High Density Polyethylene (HDPE) (b) (4)	High Density Polyethylene (HDPE) (b) (4)
Dustcap	(b) (4)	(b) (4)

Table 2 Comparability Container Closure Component Materials

(b) (4) versus (b) (4) Pump and Actuator Delivery Systems	
	(b) (4)

The label instructs patients prime the pump 10 times before the first dose. Five different bottles were tested and reached the target weight/dose by the 3rd actuation and delivered a consistent weight/dose for the remaining 17 measured actuations. The label also states that if the pump has not been used in 1 week, it will be necessary to reprime the pump. The new pumps were tested to verify that the prime was held. Three bottles were stored upright and 3 bottles were stored inverted and tested at day 1 and day 8. The spray weight and assay/spray were within specification for every value. The label states that each bottle of Nasonex should deliver 120 sprays. 18 units were tested for all 120 sprays and were within specification for the entire duration (shown below). These studies showed the the new pumps perform comparably to the approved pumps in the initial prime, hold of a prime, and delivery of a consistent spray over 120 actuations.

Table 10 Weight per Dose: Labeled Dose Statistical Summary – Batch: AT/NRP/351

(b) (4)					
Unit	**N**	**Mean**	**SD**	**Min**	**Max**
1	120				(b) (4)
2	120				
3	120				
4	120				
5	120				
6	120				
7	120				
8	120				
9	120				
10	120				
11	120				
12	120				
13	120				
14	120				
15	120				
16	120				
17	120				
18	120				

In addition to weight/dose, content uniformity, and particle size measurement were compared, as shown below. The ranges for all of these values were within specification. The mean for the content uniformity was slightly higher with the (b) (4) pumps, but the standard deviation was lower. Greater variability was observed in the particle size distribution. For example, the mean of (b) (4). Although there was greater variability, all values were still within specification. Ovality was also measured and these values were within specification for both pumps.

Table 11 Comparability Analysis ((b) (4) Device and (b) (4)

(b) (4)						(b) (4)
Parameter	**Component System**	**N**	**Mean**	**SD**	**SE Mean**	**Range**
(b) (4)						

An in-use study was also performed with the weight/dose measured over 60 days to mimic the patient's use. The pumps were stored upright at ambient conditions and 2 sprays were actuated daily. As can be seen below, the behavior of the pump at day 1 and 60 for assay/ spray and weight/ dose was consistent.

Table 17 Patient In-Use Study Statistical Summary – Batch AT/NRP/351

Parameter	Specification	N	Mean	St Dev	SE Mean
Day 1 Assay per Spray (mcg)	(b) (4)	10	(b) (4)	(b) (4)	(b) (4)
Day 60 Assay per Spray (mcg)		10			
Day 1 Wt per Dose (mg)		10			
Day 60 Wt per Dose (mg)		10			

A discussion of the extractable/ leachable data was provided and the only leachable found above the LOQ were the (b) (4) isomers. Carol M. Rivera-López, Ph.D. reviewed the leachables/extractables data on 03/21/2014 and did not identify a safety concern with the changes.

Evaluation: Adequate
The performance of the (b) (4) pumps were compared to the (b) (4) pumps. There were minor differences, but both pumps were within specification for every test.

3.2.P.7 Container Closure System
The USP testing of packaging components was performed on a development basis. All of the packaging components met the USP criteria, but these will not be incorporated into the specifications. This was the same approach that was taken with the approved packaging components. The list of packaging components was updated with the material from (b) (4). The information in this section contains information for both the approved components and the proposed components from (b) (4). There were no changes described to the drawings and specifications for the approved presentation.

The pumps had similar functional tests, but otherwise differed in the extractables and dimensions. As discussed above the only difference in the functional tests was the use of water instead of water/ethanol as the test medium for the (b) (4) pump mean shot weight specification. The only difference in the actuator were the difference in dimensions and the extractables, which were based on the incoming product specifications. The only difference in the dust cap was that the dust cap from (b) (4) does not have a push-off test of (b) (4) This difference would not be expected to impact the performance of the pump and is adequate.

Evaluation: Adequate
The drawings and specifications for the new components from (b) (4) were included in this section. The specifications were also updated for the (b) (4) pump to include measurement of the shot weight with either water or a water/alcohol mixture. There were differences in the dimensions, as discussed above. The other difference between these components was the change in extractables.

3.2.P.8.1 Stability Summary and Conclusion

Table 19 Stability Batch: AT/NRP/351 Primary Component Lot Summary

Components – Nasonex Batch AT/NRP/351	Batch / Lot Numbers Used
Nasonex® (b) (4) HDPE (b) (4) Material Number: (b) (4)	120601099
Pump with (b) (4) Material Number: (b) (4)	120701459
Actuator (b) (4) White (b) (4), Material Number: (b) (4)	120701460
Nasonex® Dust Cap (b) (4) Material Number: (b) (4)	120400849

Batch AT/NRP/351 is a non-commercial registration batch of 17 g Nasonex® which was manufactured at MSD-Singapore. The container for this batch consisted of the new components from (b) (4), as shown above. It was placed on long-term and accelerated stability studies to support the drug product expiry of 24 months. 6 months of accelerated stability data and 9 months of long-term stability data were submitted in this supplement, and the sponsor stated that this study will continue for 24 months.

There was 1 investigation due to equipment failure, but reanalysis found this sample within specification. This is adequate.

Evaluation: Adequate
One batch of drug product in the new container was placed on stability and stability testing will continue to the expiry date of 24 months. This is adequate.

3.2.P.8.2 Post-approval Stability Protocol and Stability Commitment
The sponsor committed to placing the first three batches in the new package on stability at 25°C ± 2°C/40% ± 5% RH and 40°C ± 2°C /15% ± 5% RH. The long-term stability batches will be tested at 0, 3, 6, 9, 12, 18, 24 months, and annually thereafter to a maximum of 60 months. The accelerated stability batches will be tested at 1, 3 and 6 months. After the initial stability protocol conditions are met, one batch for every fifty batches in a production year (minimum one batch per calendar year), will be placed on stability and stored inverted at 25°C ± 2°C/40% ± 5% RH.

Evaluation: Adequate
The sponsor provided a post-approval commitment to place the first three batches of drug product manufactured with this change on stability and continue monitoring for the duration of the shelf life. This is adequate.

3.2.P.8.3 Stability Data
Batch AT/NRP/351 was tested for 9 months at 25 °C, 40% RH and 6 months at 40 °C, 15% RH. The container, closure, pump and actuator were all supplied by (b) (4) in this batch. All values were within specification at all time points and only one trend was observed. The weight loss of the container increased to 0.3 g over 6 months at accelerated conditions, and 0.1 g over 9 months at long term conditions. This loss in weight is comparable to trends observed in the approved container. There were no other stability trends observed and all parameters were within specification. This is adequate.

Evaluation: Adequate
6 months of accelerated and 9 months of long term stability data were submitted for one batch of drug product manufactured in the new container from (b) (4) All values were within specification for the entire stability study and the only trend observed was that there was a 0.3 g loss in weight at accelerated conditions, which is comparable to the weight loss observed in the approved container. This is adequate.

Overall Evaluation: Adequate
Supporting data was submitted to compare the approved and proposed pump performances. There were some differences, but both pumps were within specification for all of the tests. Stability data was submitted for the drug product in the new container from (b) (4). All values were within specification and the only trend observed was a 0.3 g loss in weight at accelerated conditions.

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/s/

ERIKA E ENGLUND
04/15/2014

RAMESH RAGHAVACHARI
04/15/2014

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 020762/S-049

PHARMACOLOGY REVIEW(S)

PHARMACOLOGY/TOXICOLOGY REVIEW
CHEMISTRY CONSULT REQUEST

NDA number:	20762/S-050
Applicant:	Merck Sharp & Dohme Corp.
Date of submission:	December 19, 2013
Date of consult:	February 24, 2014
Reviewer Name:	Carol M. Rivera-López, Ph.D.
Supervisor:	Marcie Wood, Ph.D.
Review Division:	Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)
Review Completion Date:	March 21, 2014

Drug:	Nasonex® (mometasone furoate) nasal spray
Generic Name:	Mometasone furoate monohydrate
Trade Name:	Nasonex® nasal spray, 50mcg
Route of Administration:	Intranasal

Subject: Nonclinical evaluation of (b) (4) isomers identified as a leachable in Nasonex® nasal spray.

Safety Assessment

This review evaluates the safety of (b) (4) isomers (CAS number (b) (4)) as a leachable in Nasonex® nasal spray (CMC request for consultation dated February 24, 2014; Attachment 1). The chemical structure of (b) (4) is presented below in Figure 1 (excerpted from the sponsor's submission).

Figure 1: (b) (4) (isomers) Chemical Structure

(b) (4)

The maximum daily exposure of (b) (4) was determined based on the results of a stability batch test (3 month upright position 40°C/15%RH) that found a concentration of (b) (4) of this compound. The maximum daily dose for Nasonex® based on the approved label is 4 sprays/day (2 sprays/nostril/day). Each spray contains 100 µL. Therefore, the maximum daily exposure of (b) (4) is (b) (4) for a 60 kg individual (Table 1).

Table 1: Potential Maximum Daily Dose of (b) (4) in Humans

Compound	Concentration	µg/day*	µg/kg/day**
(b) (4) CAS No. (b) (4)	(b) (4)	(b) (4)	(b) (4)

* = based on a total of 4 sprays/day (100 µL/spray)
** = for a 60 kg individual

Merck submitted a brief toxicological assessment for (b) (4) at this maximum daily concentration. According to Merck, because (b) (4) is below the Toxicological Threshold of Toxicological Concern (TTC) level of (b) (4) (ICH Guidance for Industry), it is considered safe when the drug product is administered in the prescribed manner (maximum of 4 sprays/day). The levels of (b) (4) will be tested in longer-term stability samples and will be reviewed again when projections for end shelf-life become available.

This reviewer agrees that current levels of this leachable are acceptable. In addition to the relatively low levels found (below the TTC), this is also supported by data from a number of published toxicity studies. The US Environmental Protection Agency (EPA) completed an action plan for (b) (4) and (b) (4) in August of 2010[1]. In this action plan, potential human health effects of (b) (4) (based on the data from toxicity studies) were discussed. A brief summary of the EPA's findings follows.

Potential Human Health Effects

The oral and dermal acute toxicity of (b) (4) is considered to be low. (b) (4) is highly irritating and corrosive to the skin and eyes but does not have significant skin sensitizing effects. The No Observed Adverse Effect Levels (NOAELs) for systemic toxicity in repeat dose rat oral toxicity studies up to 90-days in duration were identified at the (b) (4) level range based on decreased body weights. The NOAELs for reproductive toxicity in rat range from (b) (4) based on decreases in epididymal sperm density or testicular sperm head counts, increases in estrous cycle length, and decreases in ovarian weights. The developmental NOAELs for offspring range from (b) (4) based on accelerated vaginal opening in rat pups. Finally, the NOAEL for rat maternal toxicity in the embryo-fetal developmental rat study range from (b) (4) based on decreased terminal body weight.

In addition, (b) (4) tested negative in a full battery of genetic toxicity studies (Ames assay, *in vitro* chromosomal aberration assay, and *in vivo* micronucleus assay).

There are no US Occupational Health and Safety Administration (OSHA) Permissible Exposure Limits (PELs) or National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limits (RELs) for (b) (4) Additional literature search found that ingested (b) (4) is rapidly metabolized into compounds that are not estrogenic and are eliminated within 24 hours (data from an ADME study in rats). In

[1] US EPA Action Plan on (b) (4)

addition, this study also found no (b) (4) accumulation in any organ or tissue following a (b) (4) [2].

In conclusion, based on all the aforementioned, the maximum daily levels of (b) (4) for a 60 kg patient) are considered safe because they are below the TTC of (b) (4). In addition, the maximum daily levels are well below the NOAEL identified in a 90-day oral toxicology study in rats (b) (4)

[2] (b) (4) *Regulatory Toxicology and Pharmacology* (b) (4).

Attachment 1: CMC Consult Request – DARRTS version

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

REQUEST FOR CONSULTATION

TO *(Office/Division)*:	FROM (*Name, Office/Division, and Phone Number of Requestor)*:
Marcie Wood Division Of Pulmonary, Allergy, And Rheumatology Products	Youbang Liu, ONDQA/Division III, 301-796-1926

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
2/24/14		20762/S-049	Prior Approval Supplement	12/19/13

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
NASONEX® Nasal Spray			3/24/14

NAME OF FIRM: Merck Sharp & Dohme Corp

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 2a MEETING
- ☐ END-OF-PHASE 2 MEETING
- ☐ RESUBMISSION
- ☒ SAFETY / EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
- ☐ END-OF-PHASE 2 MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):
- ☐ CHEMISTRY REVIEW
- ☒ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 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
- ☒ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS:

Pharm/Tox consult for the leachables data described in 1.11.1 Quality Information Amendment 3 and 3.2.P.2 Pharmaceutical Development (NDA20762 S049). The only leachable identified above the identification threshold were the (b) (4) isomers.

SIGNATURE OF REQUESTOR	METHOD OF DELIVERY (Check one)
Youbang Liu	☐ DFS ☒ EMAIL ☐ MAIL ☐ HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

YOUBANG LIU
02/24/2014

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/s/

CAROL M RIVERA-LOPEZ
03/21/2014

MARCIE L WOOD
03/21/2014
I concur

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 020762/S-049

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20762/S-049

ACKNOWLEDGEMENT --
PRIOR APPROVAL SUPPLEMENT

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-049

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

Date of supplement: December 19, 2013

Date of receipt: December 19, 2013

This supplemental application proposes the following changes: (1) an alternate supplier for the device components (pumps, actuators, bottles and caps); (2) an additional packaging specification for shot weight (mg) of pumps manufactured by (b) (4), using water as the test medium.

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 February 18, 2014 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be April 19, 2014.

Please 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, please 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

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/s/

YOUBANG LIU
02/26/2014

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

REQUEST FOR CONSULTATION

TO *(Office/Division)*:	FROM (*Name, Office/Division, and Phone Number of Requestor)*:
Marcie Wood Division Of Pulmonary, Allergy, And Rheumatology Products	Youbang Liu, ONDQA/Division III, 301-796-1926

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
2/24/14		20762/S-049	Prior Approval Supplement	12/19/13

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
NASONEX® Nasal Spray			3/24/14

NAME OF FIRM: Merck Sharp & Dohme Corp

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 2a MEETING
- ☐ END-OF-PHASE 2 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)*:

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/s/

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02/24/2014