

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205641Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

Department of Health and Human Services
Food and Drug Administration

**PATENT INFORMATION SUBMITTED WITH THE FILING
OF AN NDA, AMENDMENT OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and Composition)
and/or Method of Use*

NDA NUMBER

205-641

NAME OF APPLICANT / NDA HOLDER

Merck Sharp & Dohme Corp.

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

ASMANEX® HFA 100 mcg Inhalation Aerosol; ASMANEX® HFA 200 mcg Inhalation Aerosol

ACTIVE INGREDIENT(S)

Mometasone Furoate

STRENGTH(S)

mometasone furoate 100 mcg

mometasone furoate 200 mcg

DOSAGE FORM

Inhalation Aerosol

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4).

Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the *only* information relied upon by FDA for listing a patent in the Orange Book.

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FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

6,068,832

b. Issue Date of Patent

May 30, 2000

c. Expiration Date of Patent

August 27, 2017

d. Name of Patent Owner

Merck Sharp & Dohme Corp.

Address (of Patent Owner)

Office of General Counsel
One Merck Drive - WS3B-70A, P.O. Box 100

City/State

Whitehouse Station, NJ

ZIP Code

08889

FAX Number (if available)

(908) 735-1249

Telephone Number

(908) 423-3761

E-Mail Address (if available)

paul_matukaitis@merck.com

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

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Telephone Number

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E-Mail Address (if available)

* Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment or supplement? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) 8-14 Does (Do) the patent claim(s) referenced in 4.2 claim a Pending method of use for which approval is being sought in the pending NDA, amendment or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with specific reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the proposed labeling.)
Indication and Usage: ASMANEX HFA is a corticosteroid indicated for: Maintenance treatment of asthma as prophylactic therapy in patients 12 years of age or older.

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.

Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.
Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below) **Date Signed**

Matthew A. Leff 6/20/2013

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

☐ NDA Applicant/Holder	☒ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☒ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Matthew A. Leff, Director – Patents	
Address Merck, P.O. Box 2000, RY 86-2011A	City/State Rahway, NJ
ZIP Code 07065-0907	Telephone Number 732-594-1404
FAX Number (if available) 732-594-4720	E-Mail Address (if available) matthew_leff@merck.com

The public reporting burden for this collection of information has been estimated to average 20 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

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CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

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1. GENERAL

a. United States Patent Number
6,057,307

b. Issue Date of Patent
May 2, 2000

c. Expiration Date of Patent
January 27, 2014

d. Name of Patent Owner
Merck Sharp & Dohme Corp.

Address (of Patent Owner)
Office of General Counsel
One Merck Drive - WS3B-70A, P.O. Box 100

City/State
Whitehouse Station, NJ

ZIP Code
08889

FAX Number (if available)
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Telephone Number
(908) 423-3761

E-Mail Address (if available)
paul_matukaitis@merck.com

e. **Name of agent or representative** who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

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f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment or supplement? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) 1-3, 10-12, 14-15, 17-20, 22-23	Does (Do) the patent claim(s) referenced in 4.2 claim a Pending method of use for which approval is being sought in the pending NDA, amendment or supplement? ☒ Yes ☐ No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with specific reference to the proposed labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the proposed labeling.)
Indications and Usage: ASMANEX HFA is a corticosteroid indicated for: Maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older.

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.

Yes

6. Declaration Certification

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6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed

Matthew A. Leff

6/20/2015

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Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Matthew A. Leff, Director - Patents

Address

Merck, P.O. Box 2000, RY 86-2011A

City/State

Rahway, NJ

ZIP Code

07065-0907

Telephone Number

732-594-1404

FAX Number (if available)

732-594-4720

E-Mail Address (if available)

matthew_leff@merck.com

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ACTIVE INGREDIENT(S)

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DOSAGE FORM

Inhalation Aerosol

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1. GENERAL

a. United States Patent Number
5,889,015

b. Issue Date of Patent
March 30, 1999

c. Expiration Date of Patent
January 27, 2014

d. Name of Patent Owner
Merck Sharp & Dohme Corp.

Address (of Patent Owner)
Office of General Counsel
One Merck Drive - WS3B-70A, P.O. Box 100

City/State
Whitehouse Station, NJ

ZIP Code
08889

FAX Number (if available)
(908) 735-1249

Telephone Number
(908) 423-3761

E-Mail Address (if available)
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Address (of agent or representative named in 1.e.)

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ZIP Code

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Telephone Number

E-Mail Address (if available)

* Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

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2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment or supplement? Yes No

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2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

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4. Method of Use

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4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) 1-5, 31-33, 35 Does (Do) the patent claim(s) referenced in 4.2 claim a Pending method of use for which approval is being sought in the pending NDA, amendment or supplement? Yes No

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6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed

M. A. Leff

6/26/2013

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NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Matthew A. Leff, Director - Patents

Address

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City/State

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a. United States Patent Number
6,677,323

b. Issue Date of Patent
January 13, 2004

c. Expiration Date of Patent
January 27, 2014

d. Name of Patent Owner
Merck Sharp & Dohme Corp.

Address (of Patent Owner)
Office of General Counsel
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Yes

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- 1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment or supplement? Yes No
- 2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment or supplement? Yes No
- 2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No
- 2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.
- 2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No
- 2.6 Does the patent claim only an intermediate? Yes No
- 2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

- 1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No
- 3.2 Does the patent claim only an intermediate? Yes No
- 3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:

- 4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No
- 4.2 Patent Claim Number(s) (as listed in the patent) 1, 3, 5-6, 8, 11 Does (Do) the patent claim(s) referenced in 4.2 claim a Pending method of use for which approval is being sought in the pending NDA, amendment or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with specific reference to the proposed labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the proposed labeling.)
 Indication and Usage: ASMANEX HFA is a corticosteroid indicated for: Maintenance treatment of asthma as prophylactic therapy in patients 12 years of age or older.

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.

Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Matthew A. Leff

Date Signed
6/20/2013

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

☐ NDA Applicant/Holder	☒ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☒ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Matthew A. Leff, Director – Patents	
Address Merck, P.O. Box 2000, RY 86-2011A	City/State Rahway, NJ
ZIP Code 07065-0907	Telephone Number 732-594-1404
FAX Number (if available) 732-594-4720	E-Mail Address (if available) matthew_leff@merck.com

The public reporting burden for this collection of information has been estimated to average 20 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Department of Health and Human Services
Food and Drug Administration

**PATENT INFORMATION SUBMITTED WITH THE FILING
OF AN NDA, AMENDMENT OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and Composition)
and/or Method of Use*

NDA NUMBER

205-641

NAME OF APPLICANT / NDA HOLDER

Merck Sharp & Dohme Corp.

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

ASMANEX® HFA 100 mcg Inhalation Aerosol; ASMANEX® HFA 200 mcg Inhalation Aerosol

ACTIVE INGREDIENT(S)

Mometasone Furoate

STRENGTH(S)

mometasone furoate 100 mcg

mometasone furoate 200 mcg

DOSAGE FORM

Inhalation Aerosol

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the *only* information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

6,365,581

b. Issue Date of Patent

April 2, 2002

c. Expiration Date of Patent

January 27, 2014

d. Name of Patent Owner

Merck Sharp & Dohme Corp.

Address (of Patent Owner)

Office of General Counsel
One Merck Drive - WS3B-70A, P.O. Box 100

City/State

Whitehouse Station, NJ

ZIP Code

08889

FAX Number (if available)

(908) 735-1249

Telephone Number

(908) 423-3761

E-Mail Address (if available)

paul_matukaitis@merck.com

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

* Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

* If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment or supplement? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Patent Claim Number(s) (as listed in the patent) 1-3, 10-12, 14-16, 18-21, 23-24	Does (Do) the patent claim(s) referenced in 4.2 claim a Pending method of use for which approval is being sought in the pending NDA, amendment or supplement? ☒ Yes ☐ No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with specific reference to the proposed labeling for the drug product.	Use: (Submit indication or method of use information as identified specifically in the proposed labeling.) Indication and Usage: ASMANEX HFA is a corticosteroid indicated for: Maintenance treatment of asthma as prophylactic therapy in patients 12 years of age or older.

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.

Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed

Matthew A. Leff

6/20/2013

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Matthew A. Leff, Director – Patents

Address

Merck, P.O. Box 2000, RY 86-2011A

City/State

Rahway, NJ

ZIP Code

07065-0907

Telephone Number

732-594-1404

FAX Number (if available)

732-594-4720

E-Mail Address (if available)

matthew_leff@merck.com

The public reporting burden for this collection of information has been estimated to average 20 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

EXCLUSIVITY SUMMARY

NDA # 205641

SUPPL #

HFD #

Trade Name: Asmanex HFA Inhalation Aerosol

Generic Name: mometasone furoate

Applicant Name: Merck Sharp and Dohme Corp.

Approval Date, If Known: April 25, 2014

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#	021067 22518	Asmanex Twisthaler Dulera MDI
NDA#	019543 019625 019796	Elocon Ointment Elocon Cream Elocon Lotion
NDA#	020762	Nasonex Nasal Spray

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)

IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical

investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently

demonstrate the safety and effectiveness of this drug product?

YES NO X

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

P04334

P04431

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

- a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

Two pivotal studies P04334 and P04431 were submitted for NDA 22518 Dulera Inhalation Aerosol. Dulera consists of two active moieties, mometasone furoate and formoterol fumarate. The data for the individual components were not reviewed for efficacy in the review of the combination product. The two efficacy studies listed here P04334 and P0443 were reviewed again to support the efficacy of the single active moiety, mometasone furoate for the prophylaxis treatment of asthma.

- b) For each investigation identified as "essential to the approval", does the investigation

duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !
IND # YES ! NO !
! Explain:

Investigation #2 !
IND # YES ! NO !
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1
!
!
YES ! NO
Explain: ! Explain:

Investigation #2
!
!
YES ! NO
Explain: ! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES NO X

If yes, explain:

=====

Name of person completing form: Jessica Lee, Pharm.D.
Title: Regulatory Health Project Manager
Date: April 25, 2014

Name of Office/Division Director signing form: Lydia Gilbert-McClain, M.D.
Title: Deputy Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

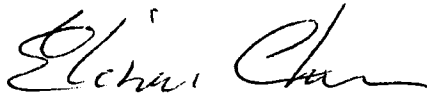
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JESSICA K LEE
04/25/2014

LYDIA I GILBERT MCCLAIN
04/25/2014

The applicant cited on the Form FDA 356h included with this submission hereby certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.



Elinor Chen, Ph.D.
Director
Worldwide Regulatory Affairs

June 18, 2013

Date

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 205641 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: Asmanex HFA Established/Proper Name: mometasone furoate Dosage Form: metered dose inhaler		Applicant: Merck Sharp & Dohme Corp. Agent for Applicant (if applicable):
RPM:		Division:
NDA Application Type: ☒ 505(b)(1) ☐ 505(b)(2) Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2) BLA Application Type: ☐ 351(k) ☐ 351(a) Efficacy Supplement: ☐ 351(k) ☐ 351(a)		For ALL 505(b)(2) applications, two months prior to EVERY action: Review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) ☐ No changes ☐ New patent/exclusivity <i>(notify CDER OND IO)</i> Date of check: <i>Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</i>
❖ Actions		
- Proposed action - User Fee Goal Date is <u>4/27/14</u>		☒ AP ☐ TA ☐ CR
Previous actions <i>(specify type and date for each action taken)</i>		☒ None
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____		☐ Received
❖ Application Characteristics ³		

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.

² For resubmissions, (b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

Review priority: Standard Priority
 Chemical classification (new NDAs only):
 (*confirm chemical classification at time of approval*)

☐ Fast Track	☐ Rx-to-OTC full switch
☐ Rolling Review	☐ Rx-to-OTC partial switch
☐ Orphan drug designation	☐ Direct-to-OTC
☐ Breakthrough Therapy designation	

NDAs: Subpart H

- Accelerated approval (21 CFR 314.510)
 Restricted distribution (21 CFR 314.520)

Subpart I

- Approval based on animal studies

- Submitted in response to a PMR
 Submitted in response to a PMC
 Submitted in response to a Pediatric Written Request

BLAs: Subpart E

- Accelerated approval (21 CFR 601.41)
 Restricted distribution (21 CFR 601.42)

Subpart H

- Approval based on animal studies

- REMS: MedGuide
 Communication Plan
 ETASU
 MedGuide w/o REMS
 REMS not required

Comments:

❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)	☐ Yes, dates
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)	☐ Yes ☐ No
❖ Public communications (<i>approvals only</i>)	
• Office of Executive Programs (OEP) liaison has been notified of action	☐ Yes ☒ No
• Indicate what types (if any) of information were issued	☒ None ☐ FDA Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)? • If so, specify the type	☒ No ☐ Yes
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
CONTENTS OF ACTION PACKAGE	
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included

Action Letters	
❖ Copies of all action letters <i>(including approval letter with final labeling)</i>	Action(s) and date(s) AP 4/25/14
Labeling	
❖ Package Insert <i>(write submission/communication date at upper right of first page of PI)</i>	
Most recent draft labeling <i>(if it is division-proposed labeling, it should be in track-changes format)</i>	☒ Included
Original applicant-proposed labeling	☒ Included
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling <i>(write submission/communication date at upper right of first page of each piece)</i>	☐ Medication Guide ☒ Patient Package Insert ☒ Instructions for Use ☐ Device Labeling ☐ None
Most-recent draft labeling <i>(if it is division-proposed labeling, it should be in track-changes format)</i>	☒ Included
Original applicant-proposed labeling	☒ Included
❖ Labels (full color carton and immediate-container labels) <i>(write submission/communication date on upper right of first page of each submission)</i>	
Most-recent draft labeling	☒ Included
❖ Proprietary Name	
- Acceptability/non-acceptability letter(s) <i>(indicate date(s))</i> - Review(s) <i>(indicate date(s))</i>	12/6/13 12/1/13
❖ Labeling reviews <i>(indicate dates of reviews)</i>	RPM: ☐ None 9/3/13 DMEPA: ☐ None 2/25/14 DMPP/PLT (DRISK): ☐ None 2/19/14; 3/24/14 OPDP: ☐ None 3/21/14 SEALD: ☐ None 4/14/14 CSS: ☒ None Other: ☒ None
Administrative / Regulatory Documents	
❖ Administrative Reviews <i>(e.g., RPM Filing Review⁴/Memo of Filing Meeting)</i> <i>(indicate date of each review)</i>	9/3/13
❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Committee	☒ Not a (b)(2)
❖ NDAs only: Exclusivity Summary <i>(signed by Division Director)</i>	☒ Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
Applicant is on the AIP	☐ Yes ☒ No

⁴ Filing reviews for scientific disciplines should be filed with the respective discipline.

• This application is on the AIP ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics (<i>approvals only</i>) • Date reviewed by PeRC <u>1/15/14</u> If PeRC review not necessary, explain: _____	
❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters) (<i>do not include previous action letters, as these are located elsewhere in package</i>)	7/9/13; 9/6/13; 3/27/14; 4/10/14; 4/11/14; 4/16/14; 4/18/14
❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes)	
❖ Minutes of Meetings • If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>) • Pre-NDA/BLA meeting (<i>indicate date of mtg</i>) • EOP2 meeting (<i>indicate date of mtg</i>) • Mid-cycle Communication (<i>indicate date of mtg</i>) • Late-cycle Meeting (<i>indicate date of mtg</i>) • Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)	☐ N/A or no mtg ☐ No mtg 9/9/11; 9/14/11 ☐ No mtg ☐ N/A ☐ N/A
❖ Advisory Committee Meeting(s) • Date(s) of Meeting(s)	☒ No AC meeting
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	☒ None
Division Director Summary Review (<i>indicate date for each review</i>)	☐ None 4/25/14
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	☐ None 4/4/14
PMR/PMC Development Templates (<i>indicate total number</i>)	☐ None 4/22/14 (3)
Clinical	
❖ Clinical Reviews • Clinical Team Leader Review(s) (<i>indicate date for each review</i>) • Clinical review(s) (<i>indicate date for each review</i>) • Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	☐ No separate review see CDTL Review 8/22/13; 3/21/14 ☒ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☐ and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	3/21/14 Clinical Primary Review & 4/22/14
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	☒ N/A

❖ Risk Management - REMS Documents and REMS Supporting Document (<i>indicate date(s) of submission(s)</i>) - REMS Memo(s) and letter(s) (<i>indicate date(s)</i>) - Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)	☒ None
❖ OSI Clinical Inspection Review Summary(ies) (<i>include copies of OSI letters to investigators</i>)	☒ None requested
Clinical Microbiology ☒ None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	☐ No separate review
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	☐ None
Biostatistics ☐ None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	☒ No separate review
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	☒ No separate review
Statistical Review(s) (<i>indicate date for each review</i>)	☐ None 8/28/13; 3/20/14
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	☒ No separate review
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	☒ No separate review
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	☐ None 8/20/13; 3/14/14
❖ OSI Clinical Pharmacology Inspection Review Summary (<i>include copies of OSI letters</i>)	☒ None requested
Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (<i>indicate date for each review</i>)	☒ No separate review
• Supervisory Review(s) (<i>indicate date for each review</i>)	☒ No separate review
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	☐ None 8/9/13; 3/7/14
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	☒ None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	☒ No carc
❖ ECAC/CAC report/memo of meeting	☒ None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary (<i>include copies of OSI letters</i>)	☒ None requested

Product Quality		☐ None
❖ Product Quality Discipline Reviews		
• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>		☒ No separate review
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>		☐ No separate review 3/18/14
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>		☐ None 7/24/13; 3/18/14; 4/23/14
❖ Microbiology Reviews		☐ Not needed 7/22/13
☒ NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i>		
☐ BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>		
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>		☒ None
❖ Environmental Assessment (check one) (original and supplemental applications)		
☒ Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>		3/18/14
☐ Review & FONSI <i>(indicate date of review)</i>		
☐ Review & Environmental Impact Statement <i>(indicate date of each review)</i>		
❖ Facilities Review/Inspection		
☐ NDAs: Facilities inspections (include EER printout or EER Summary Report only; do NOT include EER Detailed Report; date completed must be within 2 years of action date) <i>(only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁵)</i>		Date completed: 8/6/2013 ☒ Acceptable ☐ Withhold recommendation ☐ Not applicable
☐ BLAs: TB-EER (date of most recent TB-EER must be within 30 days of action date) <i>(original and supplemental BLAs)</i>		Date completed: ☐ Acceptable ☐ Withhold recommendation
❖ NDAs: Methods Validation <i>(check box only, do not include documents)</i>		☐ Completed ☐ Requested ☐ Not yet requested ☒ Not needed (per review)

⁵ i.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Day of Approval Activities	
❖ For all 505(b)(2) applications: • Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)	☐ No changes ☐ New patent/exclusivity (<i>Notify CDER OND IO</i>)
• Finalize 505(b)(2) assessment	☐ Done
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	☐ Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	☐ Done
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	☐ Done
❖ Ensure Pediatric Record is accurate	☐ Done
❖ Send approval email within one business day to CDER-APPROVALS	☐ Done

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/s/

JESSICA K LEE
04/25/2014

Your submission dated June 27, 2013, to NDA 205641, is currently under review. We request that you send your agreement to the following comments:

1. Update your post-approval long term ongoing stability study protocol to specify the storage orientation (valve up, down, or horizontal).
2. As required under 21 CFR 314.81(b)(1)(ii), commit to immediately discuss with the Agency any aberrations of the drug product from its approved specifications and to withdraw the affected lots from the market as warranted.

We request for your agreements and the projected date of submission for the requested information by close of business, Monday, April 21, 2014. The information can be sent by electronic mail to Jessica.Lee@fda.hhs.gov, followed by an official submission to the NDA. If you have any questions, please contact Jessica Lee, Regulatory Project Manager, at 301-796-3769.

NDA 205641
Asmanex HFA

Drafted by: JLee/4.18.14

Initialed by: LJafari/4.18.14
PPeri/4.18.14

Finalized by: JLee/4.18.14

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/s/

JESSICA K LEE
04/18/2014

Dear Mr. Hambaugh:

Your NDA submission dated June 27, 2013, is currently under review. We ask that you address the following. We have also attached the revised patient information leaflet and instructions for use. Please note insertions are underlined and deletions are strike out. Be advised that these labeling changes are not necessarily the Agency's final recommendations and that additional labeling changes may be forthcoming as the label is continued to be reviewed.

- Highlights (HL) must be in a minimum of 8 point font and should be in two-column format, with ½ inch margins on all sides and between columns. The top margin is > 1/2 inch in Highlights.
- The 4-digit year is missing and should state: "**2014**" for the Initial U.S. Approval in Highlights.
- The Revision Date in Highlights is missing and should state: "**4/2014**".
- There is excess white space between Table of Contents (TOC) and the horizontal line above Full Prescribing Information (FPI). For improved readability, consider deleting this excess white space.
- For improved readability, use bullets when there is more than one item (e.g., piece of information) under each heading in HL. Add bullets under Dosage & Administration.
- In Section 17, we recommend that information is organized by subsection headings or bullets (not subsection numbers). We recommend removing the subsection numbers and subheadings; this will also affect TOC. Use of command language is also recommended; see the draft [Patient Counseling Information section](#) guidance and the [Labeling Review Tool](#).

Submit a clean copy and a tracked-change version of the label incorporating our recommended changes to the NDA by close of business Friday, April 18, 2014. In addition, please send a copy of the revised label via email to Jessica.Lee@fda.hhs.gov.

If you have any questions, please contact Jessica Lee, Regulatory Project Manager, at 301-796-3769.

NDA 205641
Asmanex HFA

Drafted by: NTon/April 15, 2014
Cleared by: LJafari/April 15, 2014
KWitzmann/April 16, 2014
Finalized by: JLee/April 16, 2014

9 Page(s) of Draft Labeling have been Withheld in Full
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/s/

JESSICA K LEE
04/16/2014

NDA 205641
Asmanex HFA

Your submission dated June 27, 2013, to NDA 205641, is currently under review. We also refer to your submission dated April 4, 2014. We have the following comments. We have also attached the revised package insert and patient information leaflet. Please note insertions are underlined and deletions are ~~strike out~~. Please note that these comments are not the Agency's final comments and that we may have additional labeling recommendations as we continue to review your application.

In general, we agree with your changes, as noted in the revised draft labeling documents submitted on April 4, 2014. (b) (4)

We request you address the deficiencies and submit a corrected label by close of business, Wednesday, April 16, 2014. The information can be sent by electronic mail to Jessica.Lee@fda.hhs.gov, followed by an official submission to the NDA. If you have any questions, please contact Jessica Lee, Regulatory Project Manager, at 301-796-3769.

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/s/

JESSICA K LEE
04/11/2014

We are reviewing your NDA submission dated June 27, 2013, and the Pediatric Plan dated September 4, 2013. You propose to conduct pediatric studies in patients 5 through 11 years of age. We request that you submit your commitment to conduct these pediatric studies and provide the dates for Final Protocol Submission, Study Completion, and Final Report Submission for each of the studies listed below:

A 12-week, randomized, placebo-controlled, dose-ranging efficacy and safety study of mometasone furoate metered dose inhaler (MDI) in the treatment of children ages 5-11 years with persistent asthma.

Protocol Submission:
Study Completion:
Final Report Submission:

A 12-week, double-blind, active-controlled, efficacy and safety study of two doses of mometasone furoate/formoterol fumarate combination MDI compared with the corresponding doses of mometasone furoate monotherapy MDI in the treatment of children ages 5-11 with persistent asthma.

Protocol Submission:
Study Completion:
Final Report Submission:

A 6-month safety study, with a 6-month extension of two doses of mometasone furoate/formoterol fumarate combination MDI compared to fluticasone/salmeterol combination DPI in children 5-11 years of age with persistent asthma.

Protocol Submission:
Study Completion:
Final Report Submission:

Provide your response by Close of Business, Wednesday, April 16, 2014. The information can be sent by electronic mail to Jessica.Lee@fda.hhs.gov, followed by an official submission to the NDA. If you have any questions, please contact Jessica Lee, Regulatory Project Manager, at 301-796-3769.

NDA 205641
Asmanex HFA

Drafted by: JLee/4.8.14

Initialed by: LJafari/4.8.14
ADurmowicz/4.9.14
SSeymour/4.9.14

Finalized by: JLee/4.10.14

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/s/

JESSICA K LEE
04/10/2014

Your submission dated June 27, 2013, to NDA 205641, is currently under review. We have the following comments. Please note that these comments are not the Agency's final comments and that we may have additional labeling recommendations as we continue to review your application.

Package Insert (PI)

Refer to the attached PI for recommended changes.

Patient Package Insert (PPI)

Refer to the attached PPI for comments and recommendations.

Patient Instructions For Use (IFU)

1. Under the heading 'Before you use Asmanex HFA for the first time, you must prime the inhaler,' revise step one to read: 'To prime the inhaler, hold it in the upright position away from your face, and press down firmly and fully on the top of the canister until it stops moving in the actuator. Do this 4 times to release a total of 4 actuations (puffs) into the air.'
2. Refer to the attached IFU for additional comments and recommendations.

All Carton Labeling and Container Labels

1. Remove the line above the trade name and under the NDC number to increase readability.
2. Decrease the font size of the statement 'Shake well before using' as it competes for prominence with the proprietary name.
3. Unbold the 'Rx only' statement.

We request you address the deficiencies and submit a corrected label by noon, Wednesday, April 2, 2014. If you have any questions, please contact Jessica Lee, Regulatory Project Manager, at 301-796-3769.

32 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

NDA 205641
Asmanex HFA

Drafted by: JLee/March 27, 2014

Initialed by: LJafari/March 27, 2014

Finalized by: JLee/March 27, 2014

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/s/

JESSICA K LEE
03/27/2014

**PeRC PREA Subcommittee Meeting Minutes
January 15, 2014**

PeRC Members Attending:

Lynne Yao
Rosemary Addy
Hari Cheryl Sachs
George Greeley
Robert “Skip” Nelson
Jane Inglese
Wiley Chambers
Tom Smith
Karen Davis-Bruno
Shrikant Pagay
Lily Mulugeta
Dianne Murphy
William J. Rodriguez
Kevin Krudys (b) (4)
Maura O’Leary
Daiva Shetty
Coleen LoCicero
Peter Starke (b) (4)

Agenda

PREA

10:55	NDA	(b) (4)	Asmanex HFA (Partial Waiver/Deferral/Plan)	Maintenance treatment of asthma as a prophylactic therapy in patients 12 years of age and older (b) (4)

Asmanex HFA Partial Waiver/Deferral/Plan/Appropriately Labeled

- NDA 205641 seeks marketing approval for Asmanex HFA for the maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older.
- The application has a PDUFA goal date of April 27, 2014.
- The application triggers PREA as directed to a new dosing regimen.
- *PeRC Recommendations:*
 - The PeRC agreed with the Division to grant a partial waiver in patients less than five years of age because the product fails to offer a meaningful therapeutic benefit and a deferral studies in patients 5 to 11 years because studies are underway. The product is appropriately labeled for use in patients 12 years of age and older.

○  (b) (4)

 (b) (4)



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/s/

GEORGE E GREELEY
02/03/2014



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 205641

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Merck Sharp & Dohme Corp.
126 E. Lincoln Avenue
P.O. Box 2000
RY33-212
Rahway, NJ 07065-0900

Attention: Elinor Chen, Ph.D.
Director, Worldwide Regulatory Affairs

Dear Dr. Chen:

Please refer to your New Drug Application (NDA) dated June 26, 2013, received June 27, 2013, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Mometasone Furoate Inhalation Aerosol, 100 mcg and 200 mcg.

We also refer to your September 12, 2013, correspondence, received September 12, 2013, requesting review of your proposed proprietary name, Asmanex HFA. We have completed our review of the proposed proprietary name, Asmanex HFA, and have concluded that it is acceptable.

If **any** of the proposed product characteristics as stated in your September 12, 2013 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Nichelle Rashid, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3904. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Jessica Lee, at (301) 796-3769.

Sincerely,

{See appended electronic signature page}

Kellie A. Taylor, Pharm.D., MPH
Deputy Director
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

KELLIE A TAYLOR
12/06/2013



NDA 205641

**FILING COMMUNICATION –
NO FILING REVIEW ISSUES IDENTIFIED**

Merck Sharp & Dohme Corp.
One Merck Drive
P.O. Box 1000
Whitehouse Station, NJ 08889

Attention: Elinor Chen, PhD
Director, Worldwide Regulatory Affairs

Dear Dr. Chen:

Please refer to your New Drug Application (NDA) dated June 26, 2013, received June 27, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Asmanex HFA (mometasone furoate) 100 mcg and 200 mcg Inhalation Aerosol.

We also refer to your amendment dated September 4, 2013.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by March 30, 2014.

We request that you submit the following information:

1. Provide the PK data sets acquired from study P04275 and P03658.
2. Submit a request for evaluation of your proprietary name, Asmanex HFA, for NDA 205641. Please refer to the guidance entitled: Guidance for Industry: Contents of a

Complete Submission for the Evaluation of Proprietary Name
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf>.

Upon preliminary review of your submitted labeling, we have the following comment:

During our review, we will be assessing the appropriateness of inclusion of data from a combination program in the labeling for a monotherapy product, as well as the applicability of data from older monotherapy studies.

Please respond only to the above requests for information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

We acknowledge your request for a waiver of the requirement that the **Highlights** of Prescribing Information be limited to no more than one-half page. We will consider your request during labeling discussions. In the meantime, we encourage you to submit revised labeling that meets the half page requirement.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI), and patient PI (as applicable). Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Do not submit launch materials until you have received our proposed revisions to the package insert (PI), and patient PI (as applicable), and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>. If you have any questions, call OPDP at 301-796-1200.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Pediatric studies conducted under the terms of section 505B of the Federal Food, Drug, and Cosmetic Act (the Act) may also qualify for pediatric exclusivity under the terms of section 505A of the Act. If you wish to qualify for pediatric exclusivity please consult Division of Pulmonary, Allergy, and Rheumatology Products. Please note that satisfaction of the requirements in section 505B of the Act alone may not qualify you for pediatric exclusivity under 505A of the Act.

We acknowledge receipt of your request for a partial waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the partial waiver request is denied.

We acknowledge receipt of your request for a partial deferral of pediatric studies for this application. Once we have reviewed your request, we will notify you if the partial deferral request is denied.

If you have any questions, call Jessica Lee, Regulatory Project Manager, at (301) 796-3769.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, MD, PhD
Director
Division of Pulmonary, Allergy, and Rheumatology
Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

BADRUL A CHOWDHURY
09/06/2013



**NDA 205,641
Asmanex HFA
(inhaled mometasone furoate)
Merck
Filing Meeting**

**Kim Witzmann, MD
Medical Officer
Clinical Review
August 07, 2013**

Executive Summary

- 505(b)(1) for non-NME
- Proposed Indication:
“Maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older”
- Proposed Dose: 2 inhalations of 100mcg or 200mcg MF BID
- Related Products:
 - Dulera MDI (Mometasone Furoate/ Formoterol) 200/10 and 400/10mcg
 - Asmanex Twisthaler (mometasone Furoate) DPI, 110 and 220mcg
- Recommendation: **Fileable**
- Key Review Issues to be discussed in Planning Discussion
 - Labeling of efficacy data with older MF formulation (Pre-IND 9/14/2011)
 - No OSI Audit required (already done)
 - No AC required

MF Regulatory History

- 03/30/2005 Asmanex Twisthaler DPI Approved ($\geq$ 12yo)
- 02/01/2008 Asmanex Twisthaler DPI Approved ($\geq$ 4yo)
- 06/22/2010 Dulera MDI (MF/F) Approved ($\geq$ 12yo)
- 01/27/2012 Dulera MDI (COPD indication)- CR
- 04/11/2010 Response to DPARP IR:
 - Sponsor provides agreement on plans to develop a MF MDI monotherapy product for treatment of asthma
- 09/09/2011 Pre-IND Preliminary Meeting Comments
 - Two Issues raised:
 - 1) support for 400mcg dose (no placebo arm)
 - 2) Labeling with regard to studies of older MDI formulation
- 09/14/2011 DPARP Provides Clarifications, Meeting Cancelled

3

Briefly, the regulatory history for Mometasone Furoate for this Sponsor includes:

Approval of the DPI formulation of mometasone (As Asmanex Twisthaler) in March 2005,

And subsequent extension of indication down to 4yo for the DPI in 2008

Dulera HFA in two dose levels was approved in June, 2010, but the NDA for a COPD indication was given a Complete Response last year.

In the Dulera approval letter, we requested that the Sponsor consider development of the HFA mometasone monotherapy- to which they agreed, and Pre-IND package was submitted in August 2011. Written pre-meeting comments were sent in September, which confirmed that the Sponsor would not need additional studies to submit MF MDI for NDA, but raised two labeling issues, regarding support for the 400mcg dose, since there was no placebo, and with regard to supportive data from the Sponsor's old MDI development program, which utilized a somewhat different MDI product than that created for the Dulera program.

The meeting was cancelled.

Comments for the Sponsor

- Possible overview comment regarding labeling language
- other

4

I wanted to utilize today's discussion to get more of a sense if we need to send any high-level comments to the Sponsor at this time.

Primarily, a comment regarding labeling language,-

Additionally, contact Sponsor regarding need for PSP for the 5-11yo population, which will include the Duleria PSP (which is already evaluating the mometasone MDI component of that combination)

Clinical Development Program

P04334
 P04431
 P04703
 C97-208
 C97-224
 C97-225
 C87-226*
 C97-227*
 I97-200
 C97-222*
 C97-223*
 P04705
 P04139
 P03705
 P03418
 P03658
 P05644

* = Not previously reviewed in the Dulera Program

For Asmanex HFA, the Sponsor includes 17 studies in the clinical development program .

The Studies beginning with the letter “P” utilized the to-be-marketed formulation of Mometasone Furoate HFA, and studies were performed in the mid-2000’s. All of these studies have been reviewed as part of the Dulera NDA, which utilized a full factorial design for the combination product. (The only exception is the Phase 4 bone mineral density study, P03418, which was completed during the Dulera review cycle, which used the DPI formulation.)

Studies beginning with the letters “C” or “I” were from the original MDI program, and utilized a somewhat different formulation; these studies were conducted in the mid-1990’s, and completed in 1998-99. All but 4 of these studies, marked with an asteric, were also submitted as part of the Dulera NDA..

Clinical Development-Efficacy

P04334	Pivotal	MF/F 200/10 v. MF 200 v. F10 v. Placebo BID
P04431	Pivotal	MF/F 200/10 v. MF/F 400/10 v. MF 400 BID
C97-208		Dose-ranging
C97-224		3mo Dose-finding (endpoint decreased OCS use)
C97-225	}	12wk Dose-finding/dose-frequency
C87-226*		
C97-227*		
I97-200		
P04703		
C97-222*		
C97-223*		
P04705		
P04139		
P03705		
P03418		
P03658		
P05644		

With regard to efficacy, the Sponsor identifies 8 studies in support for the efficacy of Mometasone HFA, shown here in green. Studies P04334 and P04431 are identified as pivotal, and were the same pivotal trials used for Dulera.

The remaining 6 studies identified by the Sponsor from the mometasone monotherapy program in the mid-'90s, which utilized the older formulation.

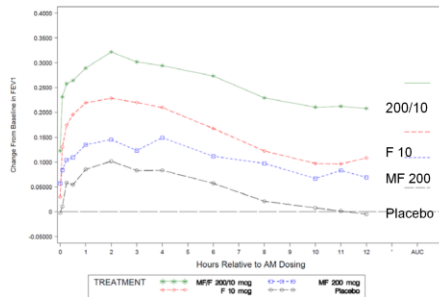
These 6 primarily dose-finding, utilizing a series of endpoints to measure efficacy, or dose-frequency studies, exploring one daily morning or evening dosing versus twice daily dosing.

They are, in general, supportive of the doses carried forward into the new formulation's Dulera and Asmanex HFA programs, but due to the differences in product, we cannot draw upon these directly for demonstration of efficacy.

Pivotal Efficacy

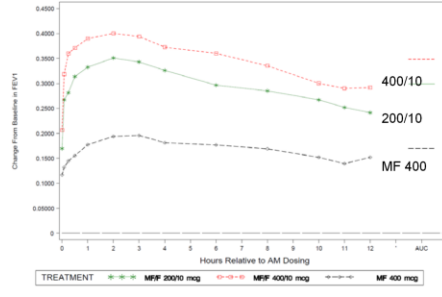
Study P04334

Figure 7 P04334: 12-hour serial evaluations of FEV1 at Week 12



Study P04431

Figure 10 P04431: 12-hour serial evaluations of FEV1 at Week 12



To briefly describe the PIVOTAL Study results, Study P04334 was a 26 week, R, DB, PC, full factorial study of MF/F, at 200/10mcg dose, compared to each of its individual components, as well as placebo. Previous review concluded that the 200mcg dose of MF demonstrated efficacy over placebo, as well as provided contribution to the efficacy of the combination, as shown in the graph on the left.

Time to first exacerbation favored treatment with MF over placebo, and Secondary endpoints were all generally supportive as well.

These results support the efficacy of MF 200 monotherapy.

Study P04431 was a 12 week, R, DB study of partial factorial design, because of safety concern for placebo, or a LABA alone. It compared the MF/F combination 200/10 to the 400/10 dose, as well as to the 400 MF monotherapy.

The co-primary efficacy endpoint of mean AUC0-12hr of change from baseline to week 12 was intended to assess the LABA contribution of the combination, comparing MF/F 400/10 to the 400mcg monotherapy, which demonstrated efficacy of the Formoterol component.

The key secondary endpoint of trough FEV1 at week 12 also demonstrated a numerical increase in mean change of the 400/10 dose compared to the 200/10 group, with a treatment difference of 0.05L (p= 0.145).

Together, these provide justification for the additional benefit of the 400mcg dose over the 200mcg dose in severe asthmatic patients, given that the effect of the formoterol 10mcg component would be expected to exert the same effect in both dose cohorts.

Secondary endpoints including onset of action, AQLQ, ACQ, nocturnal awakenings, peak flow, time-to-exacerbation, and rescue medication use also provided support for efficacy.

Clinical Development-Safety

P04334	Pivotal	26 wk PC
P04431	Pivotal	12wk
C97-208		
C97-224		3mo PC + 9mo LT
C97-225	}	12 wk PC
C87-226*		
C97-227*		
I97-200		12wk non-PC
P04703		OL Dose Counter
C97-222*		52wk non-PC
C97-223*		3mo PC + 9mo LT
P04705		12wk non-PC (closed early)
P04139		52wk non-PC
P03705		HPA Axis study
P03418		Bone Mineral Density (DPI)
P03658		Phase 1 DDI
P05644		Phase 1 PK/Dose proportionality

Module s 2.5, 2.7.3, 2.7.4, Modules 5.3.5.1, 5.3.5.4,

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In evaluation of safety,

The Sponsor identifies an additional 8 studies in support for the safety of MF HFA, shown here in purple.

Studies P04334 and P04431 are again identified as pivotal, same pivotal trials used for Dulera, data was pooled for the two studies.

The Sponsor groups the findings from the remaining studies in the Summary of Clinical Safety,

based on study design, so for example, studies C97-225, -226, and -227 are pooled, as 12wk placebo controlled trials.

Studies C97-223 and -224 were 3month PC studies with 9mo long-term safety data collected, so are grouped together, likewise, I97-200 and P04705 are grouped. The others are reported singly.

Also of safety note,

P03705 was the HPA axis study,

P03418 was the bone mineral density study

P04703 was the open-label dose counter study

P03658 and P05644 were Phase 1 PK studies that the Sponsor identified as important for safety, and were reviewed in Dulera.

Safety-Exposure

Across entire program(s),

- 4015 asthma patients (≥ 12 yo) received doses of MF
- 50mcg QD to 800mcg BID, or MF/F at doses from 100/10 BID to 400/10 BID for as long as 52 weeks
- 2,200 from Exposure in New MDI Program: P04334, P04431, P04139, P04703, P04705, P03705
- 1,800 exposed in older MDI program: C97-208, C97-222*, C97-223*, C97-224, C97-225, C97-226*, C97-227*, I97-200
- N = 1158 in older MDI program, not already reviewed for Dulera

SCS section 2.7.4.1.3, and Table 3, p.26.

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Because the submitted trials differ somewhat from the Dulera program, I looked briefly at patient exposure to mometasone for the HFA and older MDA formulation. Overall,

4015 patients 12 years and older were exposed to at least one dose of mometasone, With doses from 50mcg once daily to 800mcg BID for monotherapy, or the combination product 110/10 to 400/10 BID for as long as 52 weeks

A bit more than half of the patients received the approved formulation of MF/F HFA, or the equivalent HFA mometasone monotherapy Slightly less than half were from studies conducted in the mid-'90s with the older MDI formulation. Again, 4 of these studies, -222, -223, -226, and -227, were not reviewed in the Dulera NDA, which accounted for 1158 of the 1800 patients.

Major Safety Events

Deaths:

- Two subjects identified in Dulera review (pivotal studies)
- 26yo male in Study P03418 (bone mineral density)- homicide (unrelated)
- Two subjects died in C97-224 (steroid dependent patients)- one in 3-mo phase, another in 9-mo phase

Withdrawals due to Adverse Events:

- A total of 184 patients (any group) discontinued from safety studies due to AEs
- 129 treated with MF of 4015 (3%) withdrew
- 26 WD due to AE in pivotal study P04334
- 9 WD due to AE in pivotal study P04431
- 136 WD due to AE from supportive studies (any MDI treatment group)

AE and SAE:

- Majority of events already reviewed in Dulera NDA
- No significant outliers identified in older MDI program

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With regard to major safety events, Here I have briefly highlighted events seen in the pivotal trials or previously reviewed Dulera program, as compared to events that occurred in the older MDI studies not previously submitted.

As you can see, there were 5 total deaths; 2 from pivotal studies already reviewed, one in the bone mineral density study, and 2 others from C97-224

Withdrawals due to AEs , as well as AE and SAE s are noted here.

There do not appear to be any significant safety differences between the older and newer formulations of mometasone, but one aspect of my review will be to make sure there are no unusual events ,or higher frequencies of events, in those studies not previously reviewed.

Even if there are differences in the older program safety, it's unlikely this would significantly change anything, because these are all from the older formulation.

I think we can rely on the old program safety as supportive since exposure was the same or slightly higher with the old formulation (Reference to Craig's graphs and Sponsor's submission 5/26/2010, comparing old and new).

Filing Meeting: FILEABLE

- Clinical Filing Checklist completed, no omissions noted
- 505(b)(1)
- Pediatric Development Plan:
PMR for Dulera, waivers
- OSI Audits- completed under the Dulera review

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Pediatric Partial Waiver

Partial waiver requested for 5-11yo; due to pediatric studies for Dulera required by PREA, ongoing and planned

P04223- 12wk, R, PC, dose range/efficacy/safety (b) (4) MF 50mcg BID, 100 BID, 200BID, (b) (4) placebo

P04224- 12wk, DB, AC efficacy and safety (b) (4) MF/F (b) (4)
(b) (4), MF (b) (4)

P05415- 6month, LT safety w/ 6 mo extension of MF/F (b) (4) vs. fluticasone /salmeterol

--Do they need to provide PSP, not waiver, for this data?

Partial waiver was granted for Dulera for children 4 years and younger, based on LABA safety concerns, and available therapeutic alternatives
THEREFORE that waiver precludes the need to provide step-down from Dulera, so 21CFR 314.55 (c)(3)(1), "Product does not represent meaningful therapeutic benefit over existing therapies and is unlikely to be used in a substantial number of pediatric pts."

--Appears reasonable

Planning for Asmanex HFA

Review Issues:

- Demonstrated Efficacy and Safety already
- Consults- Standard
- Advisory Committee-not required
- Label Administrative Issues- how to translate data from a combination program into a label for the monotherapy

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Review issues are described here:

One point which make this application different from most others is that the efficacy and safety have already been demonstrated as part of the factorial design within the DULERA program

Standard consults are needed, and have been sent; OSE not required, as inspections were already completed under the DULERA program

AC not required, since this is a Non-NME, and no New Indication is being requested

Majority of issues will be regarding labeling, and how to translate the data from a combination program into a label for monotherapy. The Sponsor's approach in the submitted label was to use the DULERA label, and remove LABA-specific statements. In addition, they used the ASMANEX TWISTHALER for the INDICATION.

I will describe a bit more on the next slide

1 Page of Draft Labeling has been Withheld in Full as b4 (CCI/TS) immediately following this page

Comments for the Sponsor

- Possible overview comment regarding labeling language
- other

I wanted to utilize today's discussion to get more of a sense if we need to send any high-level comments to the Sponsor at this time.

Primarily, a comment regarding labeling language,-

Additionally, contact Sponsor regarding need for PSP for the 5-11yo population, which will include the Duleria PSP (which is already evaluating the mometasone MDI component of that combination)

Back up Slides

Pre-IND Comments-Q2

The Sponsor believes that the studies that were completed in the MF/F asthma program and in the original MF MDI program adequately characterize the efficacy and safety on MF monotherapy via MDI and that no additional clinical efficacy or safety studies will be required. Does the Agency agree?

- *Yes, we agree. However, we anticipate difficulty in describing efficacy information for the 400 mcg dose level in the label, since none of the placebo-controlled trials for the MF 400mcg dose level were performed with the to-be-marketed formulation. In addition, these placebo-controlled trials did not assess FEV1 at a pre-specified time point in the dosing interval, such as the trough.*

Referring to your response to Question 2, we understand the comment to be highlighting a potential labeling difficulty rather than one of approvability of the 400mcg strength. Please confirm that this interpretation is correct. One possible approach to labeling would be to describe the change from baseline data with the to-be-marketed product and then discuss efficacy data at that dose obtained with a similar MDI, with transparency regarding the conditions under which that data was collected.

- *The response to Question 2 is in reference to labeling, not to approvability. It is premature to discuss specific labeling at this time. In general, we note that inclusion of efficacy data using the older mometasone furoate formulation will be problematic.*

2.7.4.12.1.2 Summary of Severe Adverse Events During the Treatment Period – Pooled Pivotal Studies (P04431 and P04334)

	MF/F	MF/F	MF/MCI	MF/MCI	MF/MCI	F/MCI 10	Fluocin	Total
	MCI	MCI	200	400	800	10	0000	
	200/10	400/10	MCI	MCI	MCI	MCI		
	MG BID	MG BID	BID	BID	BID	BID		
	n=24	n=25	n=102	n=240	n=202	n=196	n=1059	
SUBJECTS REPORTING ANY ADVERSE EVENT	8 (1.5)	4 (1.5)	8 (2.2)	1 (0.4)	8 (4.0)	4 (2.0)	32 (2.2)	
GASTROINTESTINAL DISORDERS	1 (0.2)	1 (0.4)	3 (1.6)	0	0	2 (1.0)	7 (0.5)	
ABDOMINAL PAIN	1 (0.2)	0	0	0	0	0	1 (0.1)	
ABDOMINAL PAIN UPPER	0	1 (0.4)	0	0	0	0	1 (0.1)	
DIARRHOEA	0	0	1 (0.5)	0	0	1 (0.5)	2 (0.1)	
GASTROESOPHAGEAL REFLUX DISEASE	0	1 (0.4)	1 (0.5)	0	0	0	2 (0.1)	
TOOTHACHE	0	1 (0.4)	1 (0.5)	0	0	0	2 (0.1)	
VOMITING	0	0	1 (0.5)	0	0	1 (0.5)	2 (0.1)	
INFECTIONS AND INFESTATIONS	3 (0.7)	0	4 (2.1)	0	3 (1.5)	0	10 (0.7)	
ACUTE SINUSITIS	0	0	1 (0.5)	0	1 (0.5)	0	2 (0.1)	
BRONCHITIS	1 (0.2)	0	0	0	1 (0.5)	0	2 (0.1)	
CELLULITIS STAPHYLOCOCCAL	1 (0.2)	0	0	0	0	0	1 (0.1)	
GASTROENTERITIS	0	0	1 (0.5)	0	1 (0.5)	0	2 (0.1)	
INFLUENZA	0	0	1 (0.5)	0	0	0	1 (0.1)	
PNEUMONIA	0	0	1 (0.5)	0	0	0	1 (0.1)	
SUBCUTANEOUS ABSCESS	1 (0.2)	0	0	0	0	0	1 (0.1)	
UPPER RESPIRATORY TRACT INFECTION	0	0	0	0	1 (0.5)	0	1 (0.1)	
VIRAL INFECTION	1 (0.2)	0	0	0	0	0	1 (0.1)	
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.2)	0	0	0	0	0	1 (0.1)	
MUSCLE STRAIN	1 (0.2)	0	0	0	0	0	1 (0.1)	
METABOLISM AND NUTRITION DISORDERS	0	0	1 (0.5)	0	0	0	1 (0.1)	
HYPOGLYCAEMIA	0	0	1 (0.5)	0	0	0	1 (0.1)	
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	0	0	0	0	3 (1.5)	0	3 (0.2)	
ARTHRALGIA	0	0	0	0	1 (0.5)	0	1 (0.1)	
MUSCLE SPASMS	0	0	0	0	1 (0.5)	0	1 (0.1)	
PAIN IN JAW	0	0	0	0	1 (0.5)	0	1 (0.1)	
NERVOUS SYSTEM DISORDERS	2 (0.5)	0	1 (0.5)	0	1 (0.5)	0	4 (0.3)	
CONVULSION	1 (0.2)	0	0	0	0	0	1 (0.1)	
HEADACHE	1 (0.2)	0	1 (0.5)	0	1 (0.5)	0	3 (0.2)	
SINUS HEADACHE	0	0	1 (0.5)	0	0	0	1 (0.1)	
PSYCHIATRIC DISORDERS	1 (0.2)	0	0	0	0	0	1 (0.1)	
DEPRESSION	1 (0.2)	0	0	0	0	0	1 (0.1)	
RENAL AND URINARY DISORDERS	0	1 (0.4)	0	0	0	0	1 (0.1)	
RENAL ARTERY STENOSIS	0	1 (0.4)	0	0	0	0	1 (0.1)	
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	0	2 (0.8)	0	1 (0.4)	1 (0.5)	1 (0.5)	5 (0.3)	
ASTHMA	0	2 (0.8)	0	0	1 (0.5)	1 (0.5)	4 (0.3)	
HAEMOPTYSIS	0	0	0	1 (0.4)	0	0	1 (0.1)	
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	0	0	0	0	0	1 (0.5)	1 (0.1)	
DERMATITIS ATOPIC	0	0	0	0	0	1 (0.5)	1 (0.1)	
SURGICAL AND MEDICAL PROCEDURES	0	0	1 (0.5)	0	0	1 (0.5)	2 (0.1)	
SPINAL DECOMPRESSION	0	0	0	0	0	1 (0.5)	1 (0.1)	
TOOTH EXTRACTION	0	0	1 (0.5)	0	0	0	1 (0.1)	

SAEs in Pivotal

Severe Asthma-related AE

Table 12 List of Subjects Who Had Severe Asthma-Related Events
Protocol Nos. I97-200, C97-222, C97-224, C97-208, P04431, P04705, P04334 and P04139

Study/Center/Subject	Sex/Age/ ^a Race ^a	Asthma Adverse Event(s)	Relationship	Severity and Outcome
MF MDI 100 mcg BID				
I97-200-10/004	M/75/C	Asthma aggravated	Possible ^b	Severe, Hospitalized, D/C
9-Month Phase: MF MDI Variable Dose^c				
C97-224-05/069	F/27/C	Asthma aggravated	Unlikely	Severe, Hospitalized
C97-224-07/142	F/58/C	Asthma aggravated	Unlikely	Severe, Hospitalized
C97-224-12/161 ^d	F/29/C	Asthma aggravated	Unlikely	Hospitalized
C97-224-18/107	F/49/B	Asthma aggravated	Unlikely	Hospitalized
C97-224-11/031	F/42/C	Asthma aggravated	Unrelated	Life-threatening
MF MDI 200 mcg BID				
C97-222-20/342	F/71/C	Asthma aggravated	Unlikely	Severe, Hospitalized
C97-222-17/421	F/50/B	Asthma aggravated	Unrelated	Severe
3-Month Phase: MF MDI 400 mcg BID^e				
C97-224-05/070	F/42/C	Asthma aggravated	Unrelated	Severe
MF MDI 600 mcg BID				
C97-222-24/304	M/32/304	Asthma aggravated	Unlikely	Severe, Hospitalized
MF/F 400/10 mcg BID				
P04431/114/2194	M/55/W	Asthma Worsening	Unlikely	Severe, Hospitalized
P04431/27/0136	M/53/W	Asthma	Unlikely	Severe, D/C
F/SC MDI 250/50 mcg BID				
P04139/20/0043	F/34/W	Asthma Exacerbation	Unlikely	Severe, Hospitalized
F/SC DPI 250/50 mcg BID				
P04705/17/0180	F/52/W	Asthma	Unlikely	Severe, D/C
F 10 mcg BID				
P04334/86/4195	F/51/W	Asthma	Possibly	Severe, Hospitalized, D/C
BDP MDI 168 mcg BID				
C97-222-01/606	F/44/H	Asthma aggravated	Possible ^b	Life-threatening, Hospitalized
Placebo				
C97-208-22/189	M/13/C	Asthma aggravated	Unlikely	Hospitalized
P04334/5/3187	M/48/W	Asthma	Possibly	Severe, D/C

^a Sex: M = male; F = female. Age is in years. Race: B = Black; C = Caucasian, W = White. D/C = discontinued.

Treatment-Related AE

Table 8 Treatment-Emergent Adverse Events Occurring at an Incidence of ≥ 3 in Pivotal Studies in MF MDI Groups

Protocol Nos. P04334 and P04431

	MF MDI 200 MCG BID		MF MDI 400 MCG BID		Placebo	Total ^a
	n=192	n=240	n=240	n=196		
SUBJECTS REPORTING ANY ADVERSE EVENT	88 (45.8)	66 (27.5)	82 (41.8)	560 (37.1)		
INFECTIONS AND INFESTATIONS						
INFLUENZA	7 (3.6)	1 (0.4)	5 (2.6)	28 (1.9)		
NASOPHARYNGITIS	15 (7.8)	13 (5.4)	7 (3.6)	80 (5.3)		
PHARYNGITIS	6 (3.1)	3 (1.3)	6 (3.1)	29 (1.9)		
SINUSITIS	6 (3.1)	4 (1.7)	2 (1.0)	38 (2.5)		
UPPER RESPIRATORY TRACT INFECTION	16 (8.3)	4 (1.7)	17 (8.7)	72 (4.8)		
NERVOUS SYSTEM DISORDERS						
HEADACHE	10 (5.2)	8 (3.3)	7 (3.6)	55 (3.6)		
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS						
OROPHARYNGEAL PAIN	4 (2.1)	0	7 (3.6)	20 (1.3)		

Data Source: [Sec. 2.7.4.12.1.1]

Abbreviations: BID = twice daily; MDI = metered-dose inhaler; MF = mometasone furoate.

a: Total column also includes data from the MF/F and F treatment groups (data for these groups is presented in [Sec. 2.7.4.12.1.1])

Treatment-related Adverse Events, pooled for the pivotal trials, for the mometasone-only treatment arms, are shown here. There are no unexpected terms, in line with other ICS programs.

The other studies identified by the Sponsor as providing supportive safety have similar reported treatment related AEs.

I will look more closely at those studies not reviewed in the Dulera program, to make sure there are no other outliers or concerns.



NDA 205641

NDA ACKNOWLEDGMENT

Merck Sharp & Dohme Corp.
One Merck Drive
P.O. Box 100
Whitehouse Station, NJ 08889

Attention: Elinor Chen, PhD
Director, Worldwide Regulatory Affairs

Dear Dr. Chen:

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

Name of Drug Product: Asmanex HFA

Date of Application: June 26, 2013

Date of Receipt: June 27, 2013

Our Reference Number: NDA 205641

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 August 26, 2013, in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

The NDA number provided above should be cited 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, please see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications. If you have any questions, call me at (301) 796-3769.

Sincerely,

{See appended electronic signature page}

Jessica K. Lee, PharmD
Regulatory Project Manager
Division of Pulmonary, Allergy, and Rheumatology
Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

JESSICA K LEE
07/09/2013

We refer to the Preliminary Meeting Comments sent to you on September 9, 2011. In an email correspondence you requested clarification of comments. Below are FDA's responses (in normal font) to your questions (*italics*).

1. *Referring to your response to Question 1a, it is our understanding that this is requesting an analysis similar to that provided for in-vitro dose proportionality for MF MDI in Section 3.2.P.2.4.7., In-Vitro Dose Proportionality, in the Dulera NDA 22-518. Please clarify whether we are interpreting this comment correctly.*

Yes, we request that you submit an analysis for in-vitro dose proportionality similar to that provided in NDA 22-518 for Dulera.

2. *Referring to your response to Question 2, we understand the comment to be highlighting a potential labeling difficulty rather than one of approvability of the 400 mcg strength. Please confirm that this interpretation is correct. One possible approach to labeling would be to describe the change from baseline data with the to-be-marketed product and then discuss efficacy data at that dose obtained with a similar MDI, with transparency regarding the conditions under which that data was collected. While we appreciate that detailed labeling discussions may be premature at this time, your comments on the acceptability of this general approach would be helpful to us going forward.*

The response to Question 2 is in reference to labeling, not to approvability. It is premature to discuss specific labeling at this time. In general, we note that inclusion of efficacy data using the older mometasone furoate formulation will be problematic.

PIND 112669
Mometasone MDI

Drafted by: C Chung/ September 13, 2011

Initialed by: Sandy Barnes/ September 14, 2011
P Peri for A Schroeder/ September 14, 2011
P Peri/ September 14, 2011
S Chaudhry/ September 14, 2011
Susan Limb/ September 14, 2011
Badrul A. Chowdhury/ September 14, 2011

Finalized by: cchung/ September 14, 2011

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

/s/

CHRISTINE H CHUNG
09/14/2011



PIND 112669

MEETING PRELIMINARY COMMENTS

Merck & Co., Inc.
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attention: Elinor Chen, Ph.D.
Director, Worldwide Regulatory Affairs

Dear Dr. Chen:

Please refer to your Pre-Investigational New Drug Application (PIND) file for Mometasone Furoate Metered Dose Inhaler (MDI).

We also refer to your July 12, 2011, correspondence, received July 12, 2011, requesting a meeting to discuss the planned NDA for mometasone furoate MDI for maintenance treatment of asthma in patients 12 years of age and older.

This material consists of our preliminary responses to your questions and any additional comments in preparation for the discussion at the meeting scheduled for September 13, 2011, at 4:00 P.M., between Merck & Co, Inc. and the Division of Pulmonary, Allergy, and Rheumatology Products. We are sharing this material to promote a collaborative and successful discussion at the meeting. The meeting minutes will reflect agreements, important issues, and any action items discussed during the meeting and may not be identical to these preliminary comments following substantive discussion at the meeting. However, if these answers and comments are clear to you and you determine that further discussion is not required, you have the option of cancelling the meeting (contact the regulatory project manager (RPM)). If you choose to cancel the meeting, this document will represent the official record of the meeting. If you determine that discussion is needed for only some of the original questions, you have the option of reducing the agenda and/or changing the format of the meeting (e.g., from face to face to teleconference). It is important to remember that some meetings, particularly milestone meetings, can be valuable even if the premeeting communications are considered sufficient to answer the questions. Note that if there are any major changes to your development plan, the purpose of the meeting, or the questions based on our preliminary responses, we may not be prepared to discuss or reach agreement on such changes at the meeting although we will try to do so if possible. If any modifications to the development plan or additional questions for which you would like CDER feedback arise before the meeting, contact the RPM to discuss the possibility of including these items for discussion at the meeting. Attached are the FDA responses (normal font) to your questions (*italics*)

QUESTIONS AND RESPONSES

Chemistry, Manufacturing and Controls

Question 1a: *Does the Agency agree that the characterization studies conducted for MF/F are applicable to the MF MDI and do not need to be repeated?*

Yes, we agree, with the exception that dose proportionality testing should be repeated on the proposed mometasone furoate (MF) MDI.

Question 1b: *Does the Agency agree with the proposed stability strategy to support the NDA?*

You have proposed one new batch of MF MDI product per strength to be placed on stability with 12 months of data in the NDA, and one batch per strength of the older clinical/stability batches with 24 months of data in the NDA.

Yes, we concur.

Additional Comment:

Include the following in your future NDA: complete CMC information and data (including stability data) for the older mometasone furoate MDI (i.e., "Asmanex MDI") used in your clinical studies. In addition, provide comparative summary data for the performance of this Asmanex MDI product with the proposed to-be-marketed mometasone furoate MDI (e.g., graphical and tabular data).

Clinical

Question 2: *The Sponsor believes that the studies that were completed in the MF/F asthma program and in the original MF MDI program adequately characterize the efficacy and safety of MF monotherapy via an MDI device and that no additional clinical efficacy or safety studies will be required. Does the Agency agree?*

Yes, we agree. However, we anticipate difficulty in describing efficacy information for the 400 mcg dose level in the label since none of the placebo-controlled trials for the MF 400 mcg dose level were performed with the to-be-marketed formulation. In addition, these placebo-controlled trials did not assess FEV1 at a prespecified timepoint in the dosing interval such as the trough.

Clinical Pharmacology

Question 3: *The Sponsor believes that the proposed studies contained in the Clinical Pharmacology program submitted for the MF/F asthma program adequately characterize the pharmacokinetics of MF from the proposed new MF MDI and that no additional clinical pharmacology studies will be required. Does the Agency agree?*

Yes, we agree.

DATA STANDARDS FOR STUDIES

CDER strongly encourages IND sponsors to consider the implementation and use of data standards for the submission of applications for product registration. Such implementation should occur as early as possible in the product development lifecycle, so that data standards are accounted for in the design, conduct, and analysis of studies. CDER has produced a web page that provides specifications for sponsors regarding implementation and submission of study data in a standardized format. This web page will be updated regularly to reflect CDER's growing experience in order to meet the needs of its reviewers. The web page may be found at the following link:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm248635.htm>

PRESCRIBING INFORMATION

Proposed prescribing information (PI) submitted with your application must conform to the content and format regulations found at 21 CFR 201.56 and 201.57.

Summary of the Final Rule on the Requirements for Prescribing Information for Drug and Biological Products, labeling guidances, sample tool illustrating Highlights and Table of Contents, an educational module concerning prescription drug labeling, and fictitious prototypes of prescribing information are available at:

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm>. We encourage you to review the information at this website and use it as you draft prescribing information for your application.

MANUFACTURING FACILITIES

To facilitate our inspectional process, the Division of Manufacturing and Product Quality in CDER's Office of Compliance requests that you clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided in the attachment titled, "Product name, NDA/BLA 012345, Establishment Information for Form 356h."

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
1.				
2.				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
1.				
2.				

You should provide, to the Regulatory Project Manager, a hardcopy or electronic version of any materials (i.e., slides or handouts) to be presented and/or discussed at the meeting.

If you have any questions, call me Christine Chung, Regulatory Project Manager, at (301) 796-3420.

Sincerely,

{See appended electronic signature page}

Christine Chung, RPh
 CDR, U.S. Public Health Service
 Sr. Regulatory Management Officer
 Division of Pulmonary, Allergy, and Rheumatology Products
 Office of Drug Evaluation II
 Center for Drug Evaluation and Research

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

/s/

CHRISTINE H CHUNG
09/09/2011