CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205625Orig1s000

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

Form Approved: OMB No. 0910-0513
Expiration Date: 10/31/2013
See OMB Statement on Page 3.

NDA NUMBER
205625

NAME OF APPLICANT/NDA HOLDER
Glaxo Group Limited d/b/a GlaxoSmithKline

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)
(b) (4)™ ELLIPTA™

ACTIVE INGREDIENT(S)	STRENGTH(S)
fluticasone furoate	100 mcg and 200 mcg

DOSAGE FORM
Dry Powder for Oral Inhalation

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 (only) 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 submit 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	b. Issue Date of Patent	c. Expiration Date of Patent
7,629,335	12/08/2009	08/03/2021

d. Name of Patent Owner
GlaxoSmithKline Intellectual Property Management Limited

Address *(of Patent Owner)*
980 Great West Road

City/State
Brentford, Middlesex, TW8 9GS England

ZIP Code

FAX Number *(if available)*

Telephone Number

E-Mail Address *(if available)*

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)

Charles M. Kinzig, Esq.
Vice President, Global Patents

Address *(of agent or representative named in 1.e.)*
GlaxoSmithKline-UW2220, 709 Swedeland Road, P.O. Box 1539

City/State
King of Prussia, PA

ZIP Code
19406-0939

FAX Number *(if available)*
(610) 270-5090

Telephone Number
(610) 270-5021

E-Mail Address *(if available)*
charles.m.kinzig@gsk.com

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)*	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 reference to the proposed labeling for the drug product.	Use: *(Submit indication or method of use information as identified specifically in the proposed labeling.)*	

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
	28 May 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 James P. Riek	
Address Five Moore Drive, PO Box 13398	City/State Research Triangle Park, NC
ZIP Code 27709-3398	Telephone Number (919) 483-8022
FAX Number *(if available)* (919) 483-7988	E-Mail Address *(if available)* jim.p.riek@gsk.com

INFORMATION AND INSTRUCTIONS FOR FORM 3542a

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

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.
- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: *http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html.*

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.

1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

2.4) Name the polymorphic form of the drug identified by the patent.

2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.

2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement (pending method of use).

4.2) For each pending method of use claimed by the patent, identify by number the claim(s) in the patent that claim the pending use of the drug. An applicant may list together multiple patent claim numbers and information for each pending method of use, if applicable. However, each pending method of use must be separately listed within this section of the form.

4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

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

Form Approved: OMB No. 0910-0513
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NDA NUMBER
205625

NAME OF APPLICANT/NDA HOLDER
Glaxo Group Limited d/b/a GlaxoSmithKline

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)
(b) (4)™ ELLIPTA™

ACTIVE INGREDIENT(S)	STRENGTH(S)
Fluticasone furoate	100 mcg and 200 mcg per actuation

DOSAGE FORM
Dry Powder for Oral Inhalation

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 (only) 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 submit 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	b. Issue Date of Patent	c. Expiration Date of Patent
7,101,866	5 September 2006	3 August 2021

d. Name of Patent Owner
GlaxoSmithKline Intellectual Property Management Limited

Address (of Patent Owner)
980 Great West Road

City/State
Brentford, Middlesex, TW8 9GS ENGLAND

ZIP Code | FAX Number *(if available)*

Telephone Number | E-Mail Address *(if available)*

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)

Charles M. Kinzig, Esq.
Vice President, Global Patents

Address (of agent or representative named in 1.e.)
GlaxoSmithKline-UW2220, 709 Swedeland Road, P.O. Box 1539

City/State
King of Prussia, PA

ZIP Code
19406-0939

FAX Number *(if available)*
(610) 270-5090

Telephone Number
(610) 270-5021

E-Mail Address *(if available)*
charles.m.kinzig@gsk.com

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)*: 21, 48-51, 53-54, 58-62, 90-94, 96-97, 101-105 — 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 reference to the proposed labeling for the drug product.

Use: *(Submit indication or method of use information as identified specifically in the proposed labeling.)*

Fluticasone furoate is an inhaled corticosteroid indicated for the long-term once-daily treatment of asthma as prophylactic therapy in patients 12 years 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
	28 May 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 James P. Rick	
Address Five Moore Drive, PO Box 13398	City/State Research Triangle Park, NC
ZIP Code 27709-3398	Telephone Number (919) 483-8022
FAX Number *(if available)* (919) 483-7988	E-Mail Address *(if available)* jim.p.riek@gsk.com

INFORMATION AND INSTRUCTIONS FOR FORM 3542a

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

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
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- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
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- Additional copies of these forms may be downloaded from the Internet at: *http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html*.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.

1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

2.4) Name the polymorphic form of the drug identified by the patent.

2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.

2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement (pending method of use).

4.2) For each pending method of use claimed by the patent, identify by number the claim(s) in the patent that claim the pending use of the drug. An applicant may list together multiple patent claim numbers and information for each pending method of use, if applicable. However, each pending method of use must be separately listed within this section of the form.

4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

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

Form Approved: OMB No. 0910-0513
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NDA NUMBER
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NAME OF APPLICANT/NDA HOLDER
Glaxo Group Limited d/b/a GlaxoSmithKline

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)
(b) (4) TM ELLIPTA TM

ACTIVE INGREDIENT(S)	STRENGTH(S)
fluticasone furoate	100 mcg and 200 mcg

DOSAGE FORM
Dry Powder for Oral inhalation

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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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	b. Issue Date of Patent	c. Expiration Date of Patent
5,873,360	02/23/1999	02/23/2016

d. Name of Patent Owner	Address *(of Patent Owner)*	
Glaxo Group Limited	980 Great West Road	
	City/State: Brentford, Middlesex, TW8 9GS England	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

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.)*	
Charles M. Kinzig, Esq. Vice President, Global Patents	GlaxoSmithKline-UW2220, 709 Swedeland Road, P.O. Box 1539	
	City/State: King of Prussia, PA	
	ZIP Code: 19406-0939	FAX Number *(if available)*: (610) 270-5090
	Telephone Number: (610) 270-5021	E-Mail Address *(if available)*: charles.m.kinzig@gsk.com

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)*	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 reference to the proposed labeling for the drug product.	Use: *(Submit indication or method of use information as identified specifically in the proposed labeling.)*		

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
Robert J. Smith	5-28-13

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 Robert J. Smith	
Address Five Moore Drive, PO Box 13398	City/State Research Triangle Park, NC
ZIP Code 27709-3398	Telephone Number (919) 483-9616
FAX Number *(if available)* 919-483-7988	E-Mail Address *(if available)* robert.j.smith@gsk.com

INFORMATION AND INSTRUCTIONS FOR FORM 3542a

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

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.
- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: *http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html.*

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.

1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

2.4) Name the polymorphic form of the drug identified by the patent.

2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.

2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement (pending method of use).

4.2) For each pending method of use claimed by the patent, identify by number the claim(s) in the patent that claim the pending use of the drug. An applicant may list together multiple patent claim numbers and information for each pending method of use, if applicable. However, each pending method of use must be separately listed within this section of the form.

4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

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

Form Approved: OMB No. 0910-0513
Expiration Date: 10/31/2013
See OMB Statement on Page 3.

NDA NUMBER
205625

NAME OF APPLICANT/NDA HOLDER
Glaxo Group Limited d/b/a GlaxoSmithKline

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)
(b) (4) ELLIPTA™

ACTIVE INGREDIENT(S)	STRENGTH(S)
fluticasone furoate	100 mcg and 200 mcg

DOSAGE FORM
Dry Powder for Oral Inhalation

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 (only) 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 submit 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	b. Issue Date of Patent	c. Expiration Date of Patent
8,113,199	02/14/2012	10/23/2027

d. Name of Patent Owner	Address *(of Patent Owner)*	
Glaxo Group Limited	980 Great West Road	
	City/State: Brentford, Middlesex, TW8 9GS England	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

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.)*	
Charles M. Kinzig, Esq. Vice President, Global Patents	GlaxoSmithKline-UW2220, 709 Swedeland Road, P.O. Box 1539	
	City/State: King of Prussia, PA	
	ZIP Code: 19406-0939	FAX Number *(if available)*: (610) 270-5090
	Telephone Number: (610) 270-5021	E-Mail Address *(if available)*: charles.m.kinzig@gsk.com

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)*	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 reference to the proposed labeling for the drug product.	Use: *(Submit indication or method of use information as identified specifically in the proposed labeling.)*	

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
	28 May 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 James P. Rick	
Address Five Moore Drive, PO Box 13398	City/State Research Triangle Park, NC
ZIP Code 27709-3398	Telephone Number (919) 483-8022
FAX Number *(if available)* (919) 483-7988	E-Mail Address *(if available)* jim.p.rick@gsk.com

INFORMATION AND INSTRUCTIONS FOR FORM 3542a

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

General Information

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- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.
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First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

1c) Include patent expiration date, including any Hatch-Waxman patent extension already **granted**. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.

1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

2.4) Name the polymorphic form of the drug identified by the patent.

2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.

2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement (pending method of use).

4.2) For each pending method of use claimed by the patent, identify by number the claim(s) in the patent that claim the pending use of the drug. An applicant may list together multiple patent claim numbers and information for each pending method of use, if applicable. However, each pending method of use must be separately listed within this section of the form.

4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

EXCLUSIVITY SUMMARY

NDA # 205625 SUPPL # HFD #

Trade Name Arnuity Ellipta

Generic Name Fluticasone Furoate

Applicant Name GlaxoSmithKline

Approval Date, If Known 8/20/2014

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?

3 years

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# 022051 Veramyst (fluticasone furoate) Nasal Spray

NDA# 204275 Breo Ellipta (fluticasone furoate and vilanterol tridenatate inhalation powder)

NDA#

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 ☒

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:

FFA 112059
HZA 106827
FFA 114496
HZA 106829

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.")

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:

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?

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"):

FFA 112059
HZA 106827
FFA 114496
HZA 106829

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?

All investigations were carried out under IND 070297

(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?

(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 ☒

If yes, explain:

==========

Name of person completing form: Nina Ton, Pharm.D.
Title: Regulatory Project Manager
Date: August 20, 2014

Name of Office/Division Director signing form: Badrul A. Chowdhury, M.D., Ph.D.
Title: Division 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/

PHUONG N TON
08/20/2014

BADRUL A CHOWDHURY
08/20/2014

DEBARMENT CERTIFICATION

GlaxoSmithKline 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 (NDA 205625 Original NDA for (b) (4) ELLIPTA (fluticasone furoate) 100/200 Inhalation Powder).

Craig Wozniak

May 2013

Head, Americas Clinical Operations

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]

NDA # 205625 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type:
Proprietary Name: Arnuity Ellipta Established/Proper Name: fluticasone furoate Dosage Form: Inhalation Powder		Applicant: GlaxoSmithKline Agent for Applicant (if applicable):
RPM: Nina Ton		Division: DPARP

NDAs and NDA Efficacy Supplements:

NDA Application Type: ☒ 505(b)(1) ☐ 505(b)(2)
Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2)

(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)

505(b)(2) Original NDAs and 505(b)(2) NDA supplements:

Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):

Provide a brief explanation of how this product is different from the listed drug.

☐ This application does not reply upon a listed drug.
☐ This application relies on literature.
☐ This application relies on a final OTC monograph.
☐ This application relies on (explain)

For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft[2] to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.

On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.

☐ No changes ☐ Updated Date of check:

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.

❖ Actions	
• Proposed action • User Fee Goal Date is August 22, 2014	☒ AP ☐ TA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☒ None

[1] The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 5) 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., nrew listed drug, patent certification revised).

❖ 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]	

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only): 6

☐ Fast Track
☐ Rolling Review
☐ Orphan drug designation

☐ Rx-to-OTC full switch
☐ Rx-to-OTC partial switch
☐ Direct-to-OTC

NDAs: Subpart H
☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ 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

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

Comments:

❖ BLAs only: Ensure *RMS-BLA Product Information Sheet for TBP* and *RMS-BLA Facility Information Sheet for TBP* 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 *(approvals only)*	☐ Yes ☐ No
❖ Public communications *(approvals only)*	
• Office of Executive Programs (OEP) liaison has been notified of action	☐ Yes ☒ No
• Press Office notified of action (by OEP)	☐ Yes ☒ No
• Indicate what types (if any) of information dissemination are anticipated	☒ None ☐ HHS Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other

[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.

❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity?	☒ No ☐ Yes
• NDAs and BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.*	☒ No ☐ Yes If, yes, NDA/BLA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application)? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☐ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☐ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☐ No ☐ Yes If yes, NDA # and date exclusivity expires:
• NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? *(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
• Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	21 CFR 314.50(i)(1)(*i*)(A) ☐ Verified 21 CFR 314.50(i)(1) ☐ (ii) ☐ (iii)
• [505(b)(2) applications] If the application includes a **paragraph III** certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	☐ No paragraph III certification Date patent will expire
• [505(b)(2) applications] For **each paragraph IV** certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (*Summary Reviews*)).*	☐ N/A (no paragraph IV certification) ☐ Verified

Version: 07/17/2013

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

  Answer the following questions for **each** paragraph IV certification:

  (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification? ☐ Yes ☐ No

  (Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e))).

  *If "**Yes**," skip to question (4) below. If "**No**," continue with question (2).*

  (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)? ☐ Yes ☐ No

  *If "**Yes,**" there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.*

  *If "**No**," continue with question (3).*

  (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant? ☐ Yes ☐ No

  (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2))).

  *If "**No**," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.*

  (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)? ☐ Yes ☐ No

  *If "**Yes,**" there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).*

  *If "**No**," continue with question (5).*

(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification? (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period). *If "**No**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).* *If "**Yes**," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.*	☐ Yes ☐ No

CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist[4]	8/20/2014
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list *(approvals only)*	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included
Action Letters	
❖ Copies of all action letters *(including approval letter with final labeling)*	Action(s) and date(s) Approval on 8/20/2014
Labeling	
❖ Package Insert *(write submission/communication date at upper right of first page of PI)*	
• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	8/13/2014
• Original applicant-proposed labeling	10/22/2013
• Example of class labeling, if applicable	N/A

[4] Fill in blanks with dates of reviews, letters, etc.

❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling *(write submission/communication date at upper right of first page of each piece)*	☐ Medication Guide ☒ Patient Package Insert ☒ Instructions for Use ☐ Device Labeling ☐ None
• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	8/13/2014
• Original applicant-proposed labeling	10/22/2013
• Example of class labeling, if applicable	
❖ Labels (**full color** carton and immediate-container labels) *(write submission/communication date on upper right of first page of each submission)*	
• Most-recent draft labeling	8/1/2014
❖ Proprietary Name • Acceptability/non-acceptability letter(s) *(indicate date(s))* • Review(s) *(indicate date(s)* • *Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name.*	Acceptable letter: 3/4/2014 Review: 2/27/2014
❖ Labeling reviews *(indicate dates of reviews and meetings)*	☒ RPM 11/26/2013 ☒ DMEPA 7/7/2014 ☒ DMPP/PLT 7/23/2014 ☒ ODPD (DDMAC) 7/18/2014 ☐ SEALD ☐ CSS ☐ Other reviews
Administrative / Regulatory Documents	
❖ Administrative Reviews *(e.g., RPM Filing Review[5]/Memo of Filing Meeting) (indicate date of each review)* ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment *(indicate date)*	RPM Filing Review: 12/16/2013 ☐ Not a (b)(2) ☐ Not a (b)(2)
❖ NDAs only: Exclusivity Summary *(signed by Division Director)*	☒ 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
• This application is on the AIP o If yes, Center Director's Exception for Review memo *(indicate date)* o If yes, OC clearance for approval *(indicate date of clearance communication)*	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics *(approvals only)* • Date reviewed by PeRC 6/11/2014 If PeRC review not necessary, explain: _____ • Pediatric Page/Record *(approvals only, must be reviewed by PERC before finalized)*	☒ Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent *(include certification)*	☒ Verified, statement is acceptable

[5] Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ Outgoing communications *(letters, including response to FDRR (do not include previous action letters in this tab), emails, faxes, telecons)*	10/25/2013, 12/27/2013, 1/8/2014, 3/4/2014, 4/3/2014, 4/10/2014, 5/6/2014, 7/29/2014, 8/6/2014, 8/8/2014, 8/12/2014, 8/18/2014
❖ Internal memoranda, telecons, etc.	8/4/2014
❖ Minutes of Meetings	
• Regulatory Briefing *(indicate date of mtg)*	☒ No mtg
• If not the first review cycle, any end-of-review meeting *(indicate date of mtg)*	☐ N/A or no mtg
• Pre-NDA/BLA meeting *(indicate date of mtg)*	☐ No mtg 2/11/2013
• EOP2 meeting *(indicate date of mtg)*	☐ No mtg 3/16/2011
• Other milestone meetings (e.g., EOP2a, CMC pilots) *(indicate dates of mtgs)*	
❖ Advisory Committee Meeting(s)	☒ No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available *(do not include transcript)*	
Decisional and Summary Memos	
❖ Office Director Decisional Memo *(indicate date for each review)*	☒ None
Division Director Summary Review *(indicate date for each review)*	☐ None 8/20/2014
Cross-Discipline Team Leader Review *(indicate date for each review)*	☐ None 7/23/2014
PMR/PMC Development Templates *(indicate total number)*	☐ None 4
Clinical Information[6]	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) *(indicate date for each review)*	
• Clinical review(s) *(indicate date for each review)*	7/18/2014, 12/20/2013
• Social scientist review(s) (if OTC drug) *(indicate date for each review)*	☐ 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 *(indicate date of review/memo)*	See Page 12 of Medical Officer Review dated 7/18/2014
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers *(indicate date of each review)*	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation *(indicate date of each review)*	☒ Not applicable
❖ Risk Management • REMS Documents and REMS Supporting Document *(indicate date(s) of submission(s))* • REMS Memo(s) and letter(s) *(indicate date(s))* • Risk management review(s) and recommendations (including those by OSE and CSS) *(indicate date of each review and indicate location/date if incorporated into another review)*	☒ None
❖ OSI Clinical Inspection Review Summary(ies) *(include copies of OSI letters to investigators)*	☒ None requested

[6] Filing reviews should be filed with the discipline reviews.

Clinical Microbiology ☒ None	
❖ Clinical Microbiology Team Leader Review(s) *(indicate date for each review)*	☒ None
Clinical Microbiology Review(s) *(indicate date for each review)*	☐ None
Biostatistics ☐ None	
❖ Statistical Division Director Review(s) *(indicate date for each review)*	☒ None
Statistical Team Leader Review(s) *(indicate date for each review)*	☐ None
Statistical Review(s) *(indicate date for each review)*	☐ None 7/18/2014, 12/18/2013
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) *(indicate date for each review)*	☒ None
Clinical Pharmacology Team Leader Review(s) *(indicate date for each review)*	☐ None
Clinical Pharmacology review(s) *(indicate date for each review)*	☐ None 7/18/2014, 12/26/2013
❖ DSI Clinical Pharmacology Inspection Review Summary *(include copies of OSI letters)*	☐ None
Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) *(indicate date for each review)*	☒ None
• Supervisory Review(s) *(indicate date for each review)*	☐ None 7/25/2014
• Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	☐ None 7/17/2014, 12/13/2013
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	☒ None
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	☐ No carc
❖ ECAC/CAC report/memo of meeting	☐ None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary *(include copies of OSI letters)*	☐ None requested
Product Quality ☐ None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) *(indicate date for each review)*	☒ None
• Branch Chief/Team Leader Review(s) *(indicate date for each review)*	☒ None
• Product quality review(s) including ONDQA biopharmaceutics reviews *(indicate date for each review)*	☐ None 7/18/2014, 11/26/2013
❖ Microbiology Reviews ☒ NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) *(indicate date of each review)* ☐ BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) *(indicate date of each review)*	☐ Not needed 6/20/2014, 10/30/2013
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer *(indicate date of each review)*	☒ None

❖ Environmental Assessment (check one) (original and supplemental applications)	
☒ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	7/18/2014
☐ Review & FONSI *(indicate date of review)*	
☐ Review & Environmental Impact Statement *(indicate date of each review)*	
❖ 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) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites[7])*	Date completed: 12/23/2013 ☒ Acceptable ☐ Withhold recommendation ☐ Not applicable
☐ BLAs: TB-EER *(date of most recent TB-EER must be within **30 days** of action date) (original and supplemental BLAs)*	Date completed: ☐ Acceptable ☐ Withhold recommendation
❖ NDAs: Methods Validation *(check box only, do not include documents)*	☐ Completed ☐ Requested ☐ Not yet requested ☒ Not needed (per review)

[7] 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.

Appendix to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

(1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
(2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
(3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations(see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

(1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
(2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
(3) **And** all other “criteria” are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

(1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
(2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
(3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE’s ADRA.

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

/s/

PHUONG N TON
08/20/2014

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

Date: August 18, 2014

To: Christopher J. Stotka, Pharm.D. Director, Global Regulatory Affairs	From: Nina Ton, Pharm.D. Regulatory Project Manager
Company: GlaxoSmithKline Five Moore Drive P.O. Box 13398 Research Triangle Park, NC 27709	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (919) 315-0033	Fax number: 301-796-9728
Phone number: (919) 483-5711	Phone number: 301-796-1648

Subject: NDA 205625 Arnuity Ellipta PMR Timelines

Total no. of pages including cover and signature page: 3

Comments: Please acknowledge receipt

Document to be emailed to: christopher.j.stotka@gsk.com

Dear Dr. Stotka:

We acknowledge your August 14, 2014, submission with revised timelines and justification for the proposed milestones for your pediatric studies. Since PREA studies must be submitted as a supplement and your supplement should include the knemometry and HPA axis studies, we have maintained the June 2017 final report submission date. We included a sentence (underlined) in the description of PMR#1 to provide clarification for the delay in final report submission. The following are the PMR studies for NDA 205625.

2765-1: Conduct a 12-week, randomized, double-blind, double-dummy, parallel group, placebo-controlled, dose-ranging, efficacy, and safety study in children 5-11 years of age with asthma. <u>The final study report will be submitted as a supplement with the results of the knemometry and HPA axis studies.</u>

Final Protocol Submission:	February 2012
Study Completion:	September 2014
Final Report Submission:	June 2017

2765-2: Conduct a 2-week randomized, double-blind, placebo-controlled, 2-way crossover, knemometry growth rate study in children 5-11 years of age with asthma.

Final Protocol Submission:	September 2015
Study Completion:	March 2016
Final Report Submission:	June 2017

2765-3: Conduct a 52-week, randomized, double-blind, parallel group, active controlled, growth study in females 5-<8 years of age and males 5-<9 years of age with asthma.

Final Protocol Submission:	October 2016
Study Completion:	October 2021
Final Report Submission:	June 2022

2765-4: Conduct a 6-week, randomized, double-blind, parallel group, placebo-controlled, HPA-axis study in children 5-11 years of age with asthma.

Final Protocol Submission:	September 2015
Study Completion:	November 2016
Final Report Submission:	June 2017

Drafted by: NTon/August 18, 2014
Cleared by: SSeymour/August 18, 2014
LJafari/August 18, 2014
Finalized by: NTon/August 18, 2014

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

/s/

PHUONG N TON
08/18/2014

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

Date: August 12, 2014

To: Christopher J. Stotka, Pharm.D. Director, Global Regulatory Affairs	From: Nina Ton, Pharm.D. Regulatory Project Manager
Company: GlaxoSmithKline Five Moore Drive P.O. Box 13398 Research Triangle Park, NC 27709	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (919) 315-0033	Fax number: 301-796-9728
Phone number: (919) 483-5711	Phone number: 301-796-1648

Subject: NDA 205625 Information Request

Total no. of pages including cover and signature page: 3

Comments: Please acknowledge receipt and respond as soon as possible but no later than Thursday, August 14, 2014

Document to be emailed to: christopher.j.stotka@gsk.com

Dear Dr. Stotka:

We are reviewing your submission dated October 22, 2013, and the timelines provided for your pediatric studies on August 8, 2014. We have the following comments and requests for information:

1. We have concerns regarding the milestones for your pediatric studies. We note that the final report submission date for your dose ranging/efficacy/safety trial is in June 2017. As this study is to be completed in September 2014, the long delay between study completion and report submission is excessive. Additionally, final protocol submissions for the knemometry, HPA axis, and growth studies also appear to be excessively long given the standard design/conduct of these studies. [redacted] (b) (4) provide justification to support the proposed milestones. Address the following in your response.

   - Submit an earlier timeline for the submission of the final report of the dose ranging/efficacy/ safety study.
   - Submit earlier timelines for the final protocol submissions of the HPA axis, knemometry, and growth studies.

2. It is possible that the growth, knemometry, and HPA axis studies will be FDAAA PMR studies, as these studies are primarily safety studies. This is being discussed internally; we will provide further feedback as we have additional information.

3. We will be adding "efficacy and safety" to the description of PMR #1:
   Conduct a 12-week, randomized, double-blind, double-dummy, parallel group, placebo-controlled, dose-ranging, efficacy, and safety study in children 5-11 years of age with asthma.

In order to facilitate the review of your submission, provide the requested information as soon as possible but no later than the close of business Thursday, August 14, 2014. You may submit your response by fax to 301-796-9728, or by email to phuong.ton@fda.hhs.gov, followed by an official submission to your NDA.

If you have any questions, please contact Nina Ton, Regulatory Project Manager, at 301-796-1648.

Drafted by: NTon/August 12, 2014
Cleared by: SSeymour/August 12, 2014
BKarimi-Shah/August 12, 2014
TKruzick/August 12, 2014
LJafari/August 12, 2014
Finalized by: NTon/August 12, 2014

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

/s/

PHUONG N TON
08/12/2014

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

Date: August 8, 2014

To: Christopher J. Stotka, Pharm.D. Director, Global Regulatory Affairs	From: Nina Ton, Pharm.D. Regulatory Project Manager
Company: GlaxoSmithKline Five Moore Drive P.O. Box 13398 Research Triangle Park, NC 27709	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (919) 315-0033	Fax number: 301-796-9728
Phone number: (919) 483-5711	Phone number: 301-796-1648

Subject: NDA 205625 Arnuity Ellipta Labeling Comments #2

Total no. of pages including cover and signature page: 37

Comments: Please acknowledge receipt and respond by COB, Wednesday August 13, 2014

Document to be emailed to: christopher.j.stotka@gsk.com

NDA 205625
GlaxoSmithKline

Dear Dr. Stotka:

Your submission dated October 22, 2013, is currently under review. Attached are our revisions to your proposed package insert (PI). The FDA-proposed insertions are underlined, deletions are in strike-out, and comments are included adjacent to the labeling text. 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.

Submit a clean copy and a tracked-change version of the label incorporating our recommended changes to the NDA by August 13, 2014. In addition, please send me a copy of the revised label via email.

If you have any questions, please contact Nina Ton, Regulatory Project Manager, at 301-796-1648.

Drafted by: NTon/August 8, 2014
Cleared by: BKarimi-Shah/August 8, 2014
TKruzick/August 8, 2014
Finalized by: NTon/August 8, 2014

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

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/s/

PHUONG N TON
08/08/2014

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

Date: August 6, 2014

To: Christopher J. Stotka, Pharm.D. Director, Global Regulatory Affairs	From: Nina Ton, Pharm.D. Regulatory Project Manager
Company: GlaxoSmithKline Five Moore Drive P.O. Box 13398 Research Triangle Park, NC 27709	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (919) 315-0033	Fax number: 301-796-9728
Phone number: (919) 483-5711	Phone number: 301-796-1648

Subject: NDA 205625 Information Request

Total no. of pages including cover and signature page: 3

Comments: Please acknowledge receipt and respond by Friday, August 8, 2014

Document to be emailed to: christopher.j.stotka@gsk.com

Dear Dr. Stotka:

We are reviewing your submission dated October 22, 2013, and have the following request for information.

Provide your commitment to conduct the following pediatric trials and provide the final protocol submission date, trial completion date and the final report submission date for each of the studies listed below.

PMR-1: Conduct a 12 week randomized, double-blind, double-dummy, parallel group, placebo-controlled dose ranging study in children 5-11 years of age.

Final Protocol Submission:	**Insert Date**
Study Completion:	**Insert Date**
Final Report Submission:	**Insert Date**

PMR-2: Conduct a 2 week randomized, double-blind, placebo-controlled, 2-way crossover knemometry growth rate study in children 5-11 years of age.

Final Protocol Submission:	**Insert Date**
Study Completion:	**Insert Date**
Final Report Submission:	**Insert Date**

PMR-3: Conduct a 52 week randomized, double-blind, parallel group, active controlled growth study in females 5-<8 years of age and males 5-<9 years of age.

Final Protocol Submission:	**Insert Date**
Study Completion:	**Insert Date**
Final Report Submission:	**Insert Date**

PMR-4: Conduct a 6 week randomized, double-blind, parallel group, placebo-controlled HPA-axis study in children 5-11 years of age.

Final Protocol Submission:	**Insert Date**
Study Completion:	**Insert Date**
Final Report Submission:	**Insert Date**

In order to facilitate the review of your submission, provide the requested information no later than close of business Friday, August 8, 2014. You may submit your response by fax to 301-796-9728, or by email to phuong.ton@fda.hhs.gov, followed by an official submission to your NDA.

If you have any questions, please contact Nina Ton, Regulatory Project Manager, at 301-796-1648.

Drafted by: NTon/August 5, 2014
Cleared by: LJafari/August 5, 2014
SSeymour/August 5, 2014
BKarimi-Shah/August 5, 2014
Finalized by: NTon/August 6, 2014

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/s/

PHUONG N TON
08/06/2014

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

Date: July 29, 2014

To: Christopher J. Stotka, Pharm.D. Director, Global Regulatory Affairs	From: Nina Ton, Pharm.D. Regulatory Project Manager
Company: GlaxoSmithKline Five Moore Drive P.O. Box 13398 Research Triangle Park, NC 27709	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (919) 315-0033	Fax number: 301-796-9728
Phone number: (919) 483-5711	Phone number: 301-796-1648

Subject: NDA 205625 Arnuity Ellipta Labeling Comments #1

Total no. of pages including cover and signature page: 46

Comments: Please acknowledge receipt and respond by COB, Friday August 1, 2014

Document to be emailed to: christopher.j.stotka@gsk.com

NDA 205625
GlaxoSmithKline

Dear Dr. Stotka:

Your submission dated October 22, 2013, is currently under review. Attached are our revisions to your proposed package insert (PI), patient information, and instructions for use (IFU). The following comments provide additional clarification as to some of the changes made in the attached label. The FDA-proposed insertions are underlined, deletions are in strike-out, and comments are included adjacent to the labeling text. 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.

General Comments

1. For all container labels and labeling, replace the name '(b) (4)' with the approved 'Arnuity Ellipta'.

2. Revise the labels so that (b) (4), i.e. Arnuity Ellipta (Fluticasone Furoate Inhalation Powder) (b) (4).

3. Throughout the package insert, we have denoted missing values (patient number, percentage of patients) with an X. Provide the appropriate values.

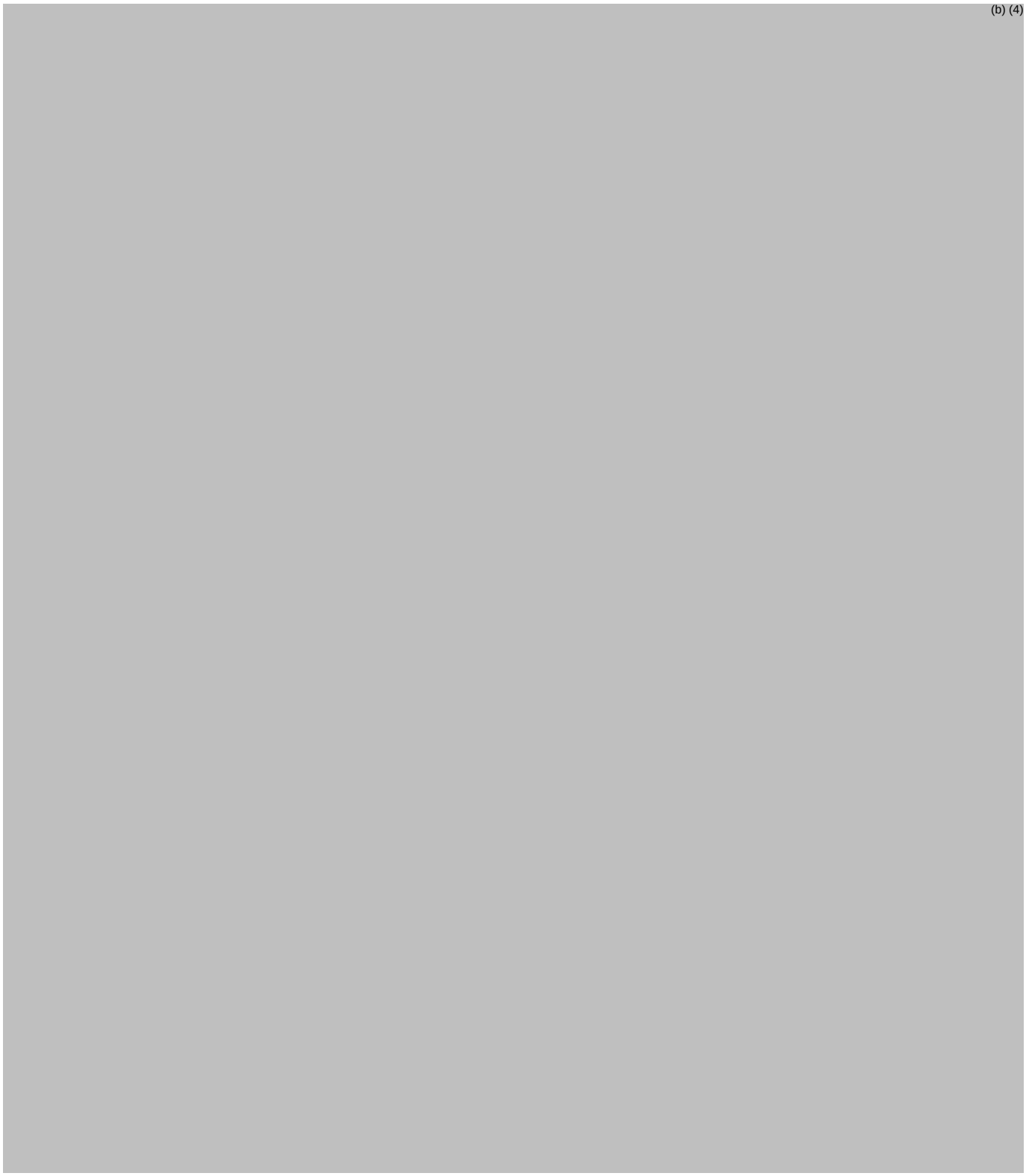
4. We have added language throughout the entire label to make it more consistent with the labeling for the most recently approved inhaled corticosteroid (ICS).

5. Insert white space before each major heading in Highlights.

Comments Pertaining to Specific Sections of the Package Insert

(b) (4)

(b) (4)



Submit a clean copy and a tracked-change version of the label incorporating our recommended changes to the NDA by August 1, 2014. In addition, please send me a copy of the revised label via email.

If you have any questions, please contact Nina Ton, Regulatory Project Manager, at 301-796-1648.

Drafted by: NTon/July 28, 2014
Cleared by: TKruzick/July 28, 2014
LJafari/July 29, 2014
Finalized by: NTon/July 29, 2014

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/s/

PHUONG N TON
07/29/2014

PeRC PREA Subcommittee Meeting Minutes
June 11, 2014

PeRC Members Attending:
Lynne Yao
Rosemary Addy
Jane Inglese
George Greeley
Hari Cheryl Sachs
Wiley Chambers
Tom Smith
Peter Starke
Gregory Reaman
Kristiana Brugger
Freda Cooner
Kevin Krudys
Maura O'Leary (only reviewed Arnuity Ellipta)
Rachel Witten
Robert Nelson
Dianne Murphy (did not review (b)(4) and/or non-responsive)

Agenda

NDA	205625	Arnuity Ellipta (fluticasone furoate) Partial Waiver_Deferral_Plan	Once daily maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older

(b)(4) and/or non-responsive

[redacted]

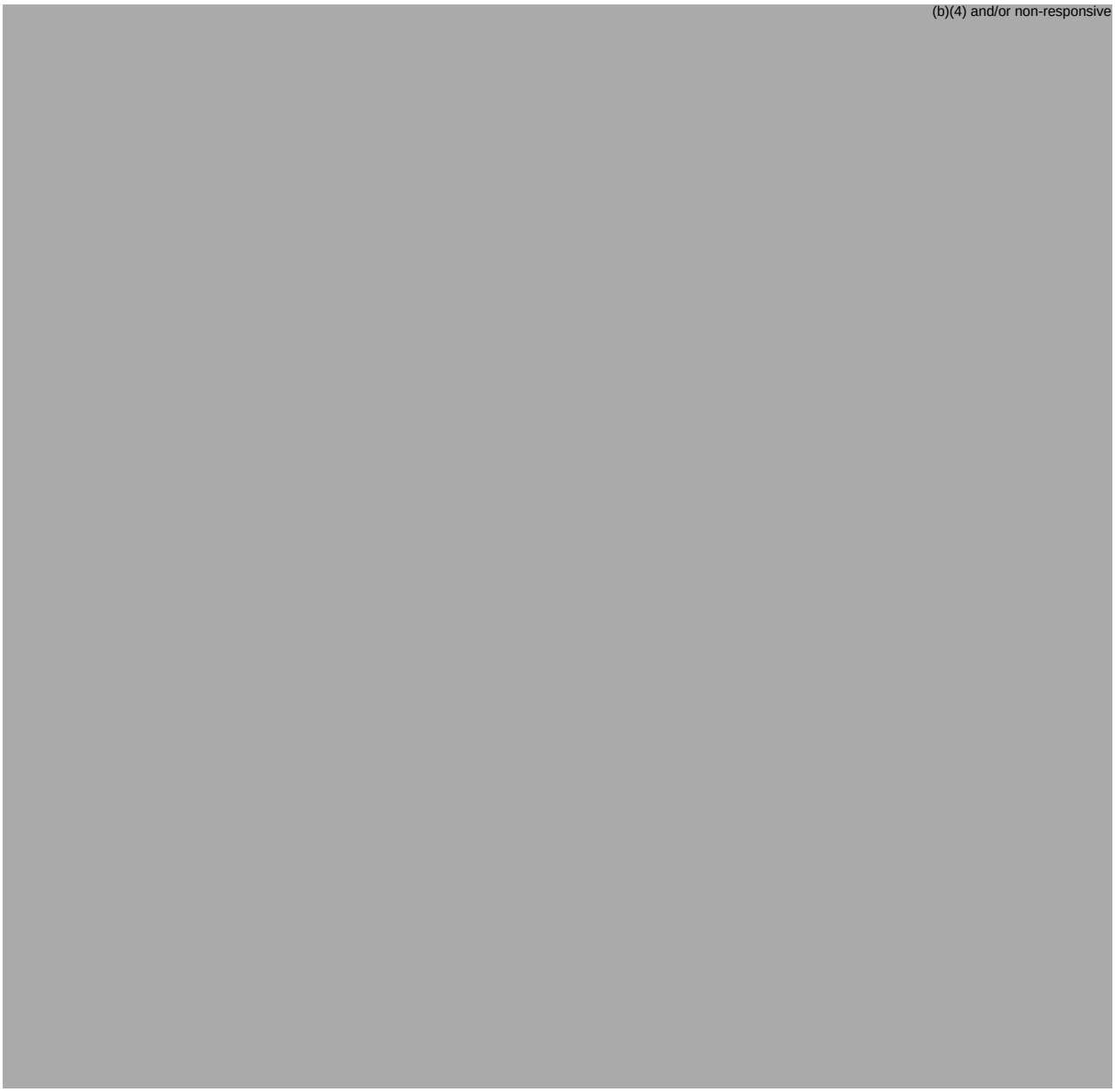
Arnuity Ellipta (fluticasone furoate) Partial Waiver_Deferral_Plan

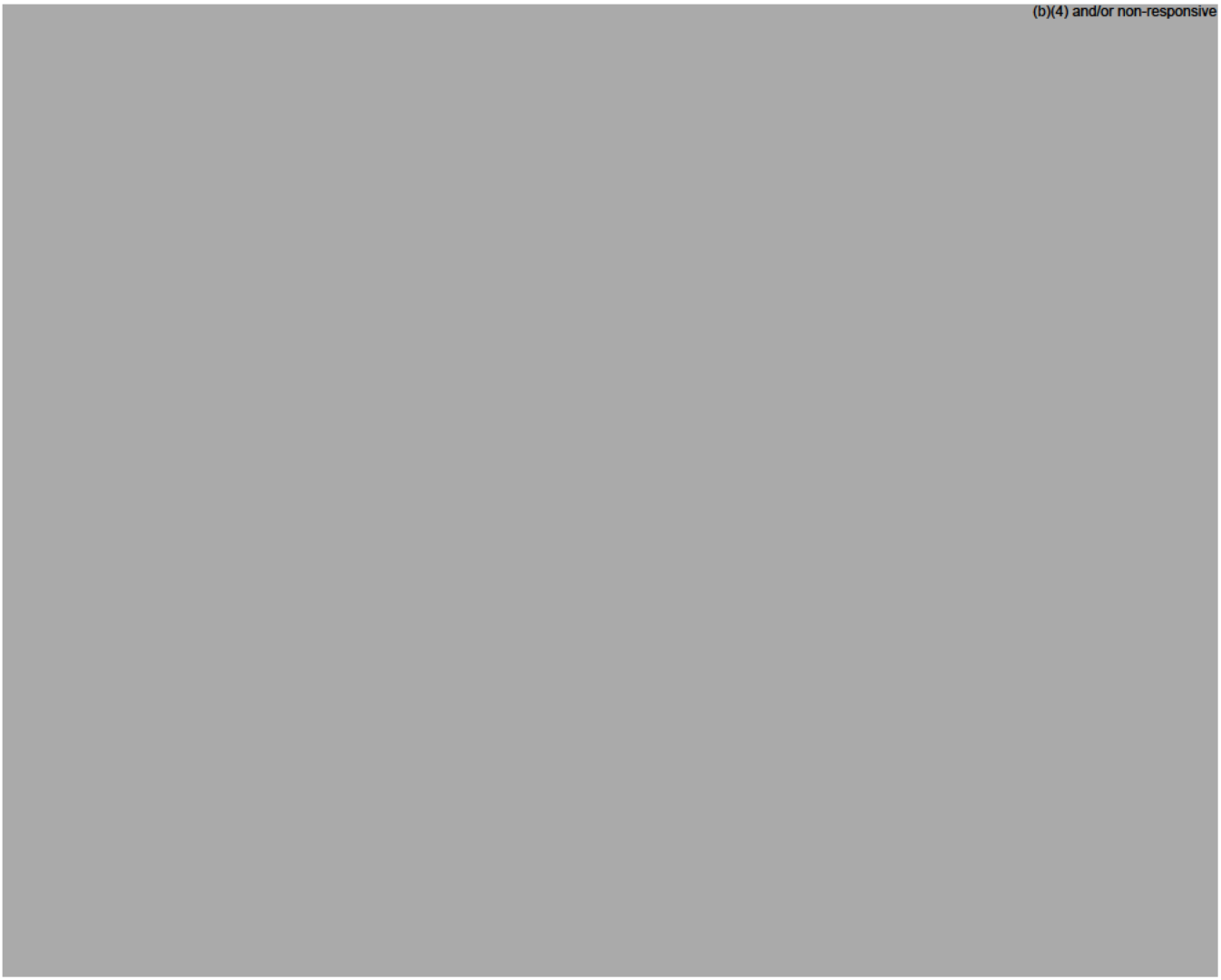
- NDA 205625 seeks marketing approval for Arnuity Ellipta (fluticasone furoate) for once daily maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older.
- The application triggers PREA as directed to a new active ingredient.
- The application has a PDUFA a goal date of August 22, 2014.
- *PeRC Recommendations:*
  - The PeRC agreed with a partial waiver for pediatric patients aged birth to less than 5 years (or PREA is not applicable to this age group) because (b) (4), (b) (5) [redacted]
  - The PeRC agreed with a deferral for pediatric patients aged 5 to less than (b) (4) years because adult studies have been completed and the product is ready for approval.
  - Pediatric patients aged 12 to 17 years of age were included in the adult clinical studies. No new pediatric safety issues were identified in these studies.
  - The PeRC had further discussions about (b) (5) [redacted] (b) (5)

(b)(4) and/or non-responsive

[redacted]


(b)(4) and/or non-responsive


(b)(4) and/or non-responsive


(b)(4) and/or non-responsive


(b)(4) and/or non-responsive

(b) (4)

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/s/

JANE E INGLESE
06/23/2014

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

Date: May 6, 2014

To: Christopher J. Stotka, Pharm.D. Director, Global Regulatory Affairs	From: Nina Ton, Pharm.D. Regulatory Project Manager
Company: GlaxoSmithKline Five Moore Drive P.O. Box 13398 Research Triangle Park, NC 27709	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (919) 315-0033	Fax number: 301-796-9728
Phone number: (919) 483-5711	Phone number: 301-796-1648

Subject: NDA 205625 Information Request

Total no. of pages including cover and signature page: 3

Comments: Please acknowledge receipt and respond by May 16, 2014

Document to be emailed to: christopher.j.stotka@gsk.com

Dear Dr. Stotka:

We are reviewing your submission dated October 22, 2013, and have the following request for information:

The reported results for the co-primary endpoint weighted mean FEV_1 in Study HZA106827 (Table 18 in the study report) indicate that Week 12 change from baseline measurements were available on 95 and 106 patients in the placebo and FF 100 treatment groups, respectively. Clarify how many total patients from each treatment arm were enrolled in the subset of sites that performed serial FEV1 measurements, and provide a disposition table (similar to Table 7 in the study report) for that subset of sites.

In order to facilitate the review of your submission, provide the requested information no later than close of business Friday, **May 16, 2014**. You may submit your response by fax to 301-796-9728, or by email to phuong.ton@fda.hhs.gov, followed by an official submission to your NDA.

If you have any questions, please contact Nina Ton, Regulatory Project Manager, at 301-796-1648.

Drafted by: NTon/May 6, 2014
Cleared by: GLevin/May 6, 2014
LJafari/May 6, 2014
Finalized by: NTon/May 6, 2014

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/s/

PHUONG N TON
05/06/2014

Liu, Youbang

From: Liu, Youbang
Sent: Thursday, April 10, 2014 6:18 PM
To: 'Susan.M.Holmes@gsk.com'
Subject: Information Request for NDA 205625

NDA 205625

Glaxo Group Limited d/b/a GlaxoSmithKline.
Attention: Susan Holmes
Director, CMC Regulatory Affairs
Five Moore Drive, P.O. Box 13398
Research Triangle Park, NC 27709

Dear Ms. Holmes:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for fluticasone furoate inhalation powder.

We are reviewing the CMC section of your submission and have the following comments and information requests. We request a prompt written response (preferably by April 25, 2014) in order to continue our evaluation of your NDA.

1. (b) (4)
2.

Please acknowledge the receipt of this email.

Sincerely,

Youbang Liu, Ph.D.
Regulatory Project Manager
Division III, ONDQA/OPS/CDER/FDA
10903 New Hampshire Avenue

Building 21, Room 2525
Silver Spring, MD 20993
Phone: (301) 796-1926

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/s/

YOUBANG LIU
04/10/2014

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

Date: April 3, 2014

To: Christopher J. Stotka, Pharm.D. Director, Global Regulatory Affairs	From: Nina Ton, Pharm.D. Regulatory Project Manager
Company: GlaxoSmithKline Five Moore Drive P.O. Box 13398 Research Triangle Park, NC 27709	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (919) 315-0033	Fax number: 301-796-9728
Phone number: (919) 483-5711	Phone number: 301-796-1648

Subject: NDA 205625 Information Request

Total no. of pages including cover and signature page: 3

Comments: Please acknowledge receipt and respond by April 17, 2014

Document to be emailed to: christopher.j.stotka@gsk.com

Dear Dr. Stotka:

We are reviewing your submission dated October 22, 2013, and have the following requests for information:

Submit an updated summary population PK report including PK dataset from study FFA115440. The PK data acquired from the FFA115440 study should be incorporated into the population PK analysis. The report should include prediction of FF PK exposures (Cmax and AUC0-24) by dose and configuration (as presented in Table 9 in report 2013N162904) based on your updated population PK analysis.

Data, model codes or control streams, and scripts used to generate the corresponding analyses should be provided for the final population PK models. Data files should be submitted as SAS transport files with *.xpt extension (eg. Data1.xpt) and other files be submitted as ASCII text files with *.txt extension (e.g.:myfile_ctl.txt, myfile_out.txt).

In order to facilitate the review of your submission, provide the requested information no later than close of business Thursday**, April 17, 2014**. You may submit your response by fax to 301-796-9728, or by email to phuong.ton@fda.hhs.gov, followed by an official submission to your NDA.

If you have any questions, please contact Nina Ton, Regulatory Project Manager, at 301-796-1648.

Drafted by: NTon/April 3, 2014
Cleared by: LJafari/LJafari/April 3, 2014
JChen/April 3, 2014
LZhao/April 2, 2014
SBrar/April 2, 2014
Finalized by: NTon/April 3, 2014

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/s/

PHUONG N TON
04/03/2014

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

Date: January 8, 2014

To: Christopher J. Stotka, Pharm.D. Director, Global Regulatory Affairs	From: Nina Ton, Pharm.D. Regulatory Project Manager
Company: GlaxoSmithKline Five Moore Drive P.O. Box 13398 Research Triangle Park, NC 27709	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (919) 315-0033	Fax number: 301-796-9728
Phone number: (919) 483-5711	Phone number: 301-796-1648

Subject: NDA 205625 Information Request

Total no. of pages including cover and signature page: 3

Comments: Please acknowledge receipt and respond by January 15, 2014

Document to be emailed to: christopher.j.stotka@gsk.com

Dear Dr. Stotka:

We are reviewing your submission dated October 22, 2013, and have the following requests for information:

- Submit all the NONMEM control files, the associated .lst files, and the datasets referenced in technical reports 2013N162904, 2011N30718, 2011N30480 and 2011N30478.

- Provide data, model codes or control streams, and scripts used to generate the corresponding analyses for the final population PK or PK-PD models.

- Submit data files as SAS transport files with *.xpt extension (eg. Data1.xpt) and submit other files as ASCII text files with *.txt extension (e.g.:myfile_ctl.txt, myfile_out.txt).

In order to facilitate the review of your submission, provide the requested information no later than close of business Wednesday, January 15, 2014. You may submit your response by fax to 301-796-9728, or by email to phuong.ton@fda.hhs.gov, followed by an official submission to your NDA.

If you have any questions, please contact Nina Ton, Regulatory Project Manager, at 301-796-1648.

Drafted by: NTon/January 8, 2014
Cleared by: LJafari/January 8, 2014
JChen/January 8, 2014
Finalized by: NTon/January 8, 2014

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/s/

PHUONG N TON
01/08/2014

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 205625

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Glaxo Group Limited d/b/a GlaxoSmithKline
c/o Christopher J. Stotka
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

ATTENTION: Christopher J. Stotka, PharmD
Director, Global Regulatory Affairs

Dear Dr. Stotka:

Please refer to your New Drug Application (NDA) dated October 22, 2013, received October 22, 2013, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Fluticasone Furoate Inhalation Powder, 100 mcg and 200 mcg.

We also refer to your December 19, 2013, correspondence, received December 19, 2013, requesting review of your proposed proprietary name, Arnuity Ellipta. We have completed our review of the proposed proprietary name, Arnuity Ellipta, and have concluded that it is acceptable.

If **any** of the proposed product characteristics as stated in your December 19, 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 Nina Ton, Regulatory Project Manager, in the Office of New Drugs at (301) 796-1648.

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/

TODD D BRIDGES on behalf of KELLIE A TAYLOR
03/04/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205625

FILING COMMUNICATION -
FILING REVIEW ISSUES IDENTIFIED

GlaxoSmithKline
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

Attention: Christopher J. Stotka, Pharm.D.
Director, Global Regulatory Affairs

Dear Dr. Stotka:

Please refer to your New Drug Application (NDA) dated October 22, 2013, received October 22, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Fluticasone Furoate Inhalation Powder, 100 mcg and 200 mcg.

We also refer to your amendments dated November 25 and December 19, 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**. Therefore, the user fee goal date is August 22, 2014.

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 July 25, 2014. We are not currently planning to hold an advisory committee meeting to discuss this application.

During our filing review of your application, we identified the following potential review issues:

CLINICAL

1. The relative exposure to fluticasone furoate (FF) delivered via the single strip device compared with the double strip device will require further review. Due to potential differences in systemic exposure to FF between the two devices (i.e. less exposure via the double strip device), the ability of study HZA106839 to support the long-term safety of FF 200 mcg will be a review issue.

We are providing the above comment to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application.

We request that you submit the following information:

1. With respect to the potential impact of missing data, we do not find the supportive analyses you provided to be sufficient. Both the primary analysis based on last-observation-carried-forward (LOCF) imputation, and the supportive analysis based on a mixed effects model for repeated measures (MMRM), more or less assume that any treatment effect observed prior to dropout would have persisted in patients after treatment discontinuation. This may not be appropriate, since any positive effects of fluticasone furoate (FF) on FEV1 prior to dropout likely declined or went completely away once the patient stopped taking the therapy. We request that you provide results based on additional supportive model(s) that do not preserve any pre-dropout treatment effect after patients stop taking the therapy. For example, the "copy reference" and "jump to reference" multiple imputation approaches that the applicant implemented under NDAs 203-975 and 205-382 are additional models of interest. These supportive results are of particular interest for the comparisons of FF 100 against placebo with respect to the primary and secondary endpoints in Studies HZA106827 and FFA112059.

Please respond only to the above request 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.

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. 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, 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 requests for a partial waiver and partial deferral of pediatric studies for this application. Once we have reviewed your requests, we will notify you if the partial waiver and partial deferral requests are denied.

We note that you have submitted pediatric studies with this application for pediatric patients 12 to 17. Once the review of this application is complete we will notify you whether you have fulfilled the pediatric study requirement for this age group.

If you have any questions, call Nina Ton, Regulatory Project Manager, at (301) 796-1648.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
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
12/27/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205625

NDA ACKNOWLEDGMENT

GlaxoSmithKline
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

Attention: Christopher J. Stotka, Pharm.D.
Director, Global Regulatory Affairs

Dear Dr. Stotka:

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: Fluticasone furoate inhalation powder

Date of Application: October 22, 2013

Date of Receipt: October 22, 2013

Our Reference Number: NDA 205625

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 December 21, 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) 796-1648.

Sincerely,

{See appended electronic signature page}

Nina Ton, Pharm.D.
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/

PHUONG N TON
10/25/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 70297

MEETING MINUTES

GlaxoSmithKline
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709-

Attention: Christopher Stotka, Pharm.D.
Director, Respiratory Group, Global Regulatory Affairs

Dear Dr. Stotka:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for fluticasone furoate.

We also refer to the teleconference between representatives of your firm and the FDA on February 11, 2013. The purpose of the meeting was to plans for submission of the NDA for the use of fluticasone furoate in the treatment of asthma.

A copy of the official minutes of the teleconference is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call me at (301) 796-2284.

Sincerely,

{See appended electronic signature page}

Angela Ramsey R.N., M.S.N
Senior Program Management Officer
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure:
Meeting Minutes

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Type:	Type B
Meeting Category:	Pre-NDA
Meeting Date and Time:	February 11, 2013
Meeting Location:	Teleconference
Application Number:	IND 70297
Product Name:	fluticasone furoate
Indication:	Asthma
Sponsor/Applicant Name:	GlaxoSmithKline (GSK)
Meeting Chair:	Badrul A. Chowdhury, M.D., Ph.D.
Meeting Recorder:	Angela Ramsey R.N., M.S.N

FDA ATTENDEES

Badrul A. Chowdhury, M.D., Ph.D., Director
Angela Ramsey, RN, MSN, Senior Regulatory Project Manager
Susan Limb, M.D., Clinical Team Leader
Tracy Kruzick, M.D. Ph.D., M.P.H., Clinical Reviewer
Timothy Robison, Ph.D., Pharmacology/Toxicology Team Leader
Craig M. Bertha, Ph.D., Chemistry Reviewer
Suresh Doddapaneni, Clinical Pharmacology Team Leader
Arun Agrawal, Clinical Pharmacology Reviewer
Joan Buenconsejo, Ph. D., Statistician Team Leader
Yongman Kim, Ph.D., Statistician

SPONSOR ATTENDEES

Pietro Ventresca, MD, Vice President, Respiratory Clinical Development
Loretta Jacques, PhD, Director, Asthma Clinical Development
Leslie Andersen, Director, Asthma Clinical Development
Mauri Fitzgerald, Vice President, Global Regulatory Affairs
Christopher Stotka, Pharm.D., Director, Global Regulatory Affairs
Caroline Goldfrad, Associate Director, Statistics
Ann Allen, Principle Clinical Pharmacokineticist, Pharmacokinetics

BACKGROUND

GlaxoSmithKline (GSK) submitted a Type B meeting request dated, November 27, 2012, to discuss plans for submission of the NDA for the use of fluticasone furoate in the treatment of asthma. GSK submitted the briefing package on December 19, 2012. Upon review of the material, the Division responded via secure email on February 8, 2013. GSK requested to convert the face-to-face meeting to a teleconference to discuss responses to questions 3, 18, and 19 and to clarify the anticipated review clock for the application.

The content of the email is below. Any discussions that occurred during the meeting are captured directly under the relevant response. The sponsor's questions are in ***bold italic;*** the Division's response is in *italics;* and the discussion is in normal font.

DISCUSSION

Question 1:
In light of the results of the FF 50 studies, which evaluated a short-acting beta$_2$-agonist population where the results did not replicate, does the Division agree that FF 50 should not be filed in this NDA as the strength of FF appropriate for a short-acting beta$_2$-agonist patient population?

FDA Response:
Based on the results you have provided, your plan appears acceptable.

Discussion:
No discussion occurred.

Question 2:
Does the Division agree that the FF data provide substantial evidence to include both FF 100 and 200 doses in the original NDA for FF monotherapy?

FDA Response:
Your plan to include both FF 100 and 200 in the original NDA for FF monotherapy is acceptable. However, based on the preliminary efficacy data you have provided, whether there exists support for the added benefit of FF 200 over FF 100, is unclear, and will be a review issue.

Discussion:
No discussion occurred.

Question 3:
What is the Division's advice for providing FF monotherapy treatment in a short-acting beta2-agonist patient population which has only been evaluated in Phase III studies with FF 50, aside from the 8-week dose ranging study (FFA109687) that evaluated FF doses of 25 to 200 mcg?

FDA Response:
Based on the results you have provided in your briefing package, FF 50 mcg failed to show replicate evidence of efficacy. As such, proceeding with submission of the 100 mcg and 200 mcg dose strengths, although not studied in a SABA-only population, is reasonable.

Discussion:
GSK asked the Division whether data from a Phase IIb dose-ranging trial, FFA109687, in SABA-only patients could be used potentially to support labeling of FF 100 mcg for this patient population. The Division responded that labeling usually includes a description of the patient population studied and noted that other labels have featured Phase II dose-ranging data, so there is precedent for this approach. The Division stated that the acceptability of this data for inclusion in the label would be a review issue.

Question 4:
Does the Division agree that the size of the safety database for FF Inhalation Powder, as described in Section 4, will provide an adequate safety database to support the NDA for the 100 and 200 mcg doses of FF Inhalation Powder?

FDA Response:
The adequacy of your safety database will depend on the ability of the double-strip data to support the single-strip data, and will be a review issue. If the double-strip configuration is found to support the proposed to-be-marketed single-strip configuration, the size of the safety database appears adequate pending review of your NDA. However, if a safety signal is noted, further safety data may be required.

Discussion:
No discussion occurred.

Question 5:
(b) (4)
(b) (4) ***, but incorporate the data by cross-reference to IND*** (b) (4) ***Does the Division agree with this approach?***

FDA Response:
We agree.

Discussion:
No discussion occurred.

Question 6:

[redacted] ***, but rather incorporate the data by cross-reference to IND*** [redacted] ***. Does the Division agree with this approach?***

FDA Response:
We agree.
Discussion:
No discussion occurred.

Question 7:
As the model estimated $AUC_{(0-24)}$ values for FFA114496 with FF single strip DPI were similar to or lower than those estimated for studies HZA106839 and HZA106851 following administration as FF/VI, does the Division agree this supports the use of data from long-term safety and HPA-axis following FF/VI 200/25 to support the registration of FF 200?

FDA Response:
If the systemic exposure is lower or similar, the HPA axis data obtained with FF/VI 200/25 may be relied upon for FF 200. This will be a review issue.

Discussion:
No discussion occurred.

Question 8:
To support the registration of FF Nasal Spray (NDA 022051), the results of the thorough QT study for FF (FFR101888) were submitted as part of the 120-Day Safety Update on 18 October 2006. This study shows that inhaled FF 4000 does not have any effect on QT interval. GSK plans to include this study report in the FF asthma NDA submission. Will the submission of this study report fulfill the QT requirements for this NDA submission, as it did for the FF Nasal Spray NDA?

FDA Response:
Please note that there is no separate QT requirement for this product. Report of study FFR101888 was previously reviewed and the results are described in the Veramyst package insert. You can provide an assessment of relative systemic exposures from FF 200 to those seen in study FFR101888 to show the applicability of those results to this product.

Discussion:
No discussion occurred.

Question 9:
Does the Division have any further comments regarding the Clinical Pharmacology package?

FDA Response:
We do not have any further comments at this time.

Discussion:
No discussion occurred.

Question 10:
Section 7 outlines GSK's plans for the integrating/pooling of the efficacy data, including study groupings, subgroups, country groupings and analysis plans. Does the Division agree with the proposals?

FDA Response:
The efficacy portion of the NDA review will focus primarily on the un-pooled data from the individual trials. The decision to integrate and pool efficacy data is at your discretion.

Discussion:
No discussion occurred.

Question 11:
Section 8 outlines how GSK plans for the integrating/pooling of the safety data, including study groupings, subgroups, country groupings and analysis plans. Does the Division agree with the proposals?

FDA Response:
We agree. In addition, as stated in our written responses dated October 11, 2012, we also request that for trials longer than 24 weeks in duration, the data be presented for both the first 24 weeks of exposure as well as for the total duration of exposure in order to facilitate comparison of the data from the 24-week single strip trials.

Discussion:
No discussion occurred.

Question 12:
Does the Division agree with the proposed list of AEs of Special Interest as described in Section 8?

FDA Response:
We agree.

Discussion:
No discussion occurred.

Question 13:
Some studies containing an FF treatment arm will be ongoing at the time of submission of the NDA for FF Inhalation Powder. GSK proposes to include synopses of these studies as well as listings of blinded death, SAE and pregnancy data, but will not include any other data from these ongoing studies in the NDA. Does the Division agree with this approach?

FDA Response:
As the results will be blinded, these results will be of limited utility in our review. Therefore, the inclusion of this data is at your discretion.

Discussion:
No discussion occurred.

Question 14:
GSK intends to include AE reports from the literature as part of the ISS and SCS. Does the Division agree that this reporting should be limited to nonclinical data and to orally inhaled FF clinical data?

FDA Response:
The safety evaluation of FF will rely on the submitted data from your development program. Inclusion of literature reports is at your discretion, but will not be a focus of our review.

Discussion:
No discussion occurred.

Question 15:
For all fatal and non-fatal SAEs and for subjects withdrawn from treatment due to an AE for all completed studies, a table in the ISS will provide the locations of the case narratives in the individual clinical study reports. Case report forms will be provided for all fatal SAEs and for subjects withdrawn from treatment due to an AE for all completed studies. No narratives or case report forms will be provided for studies ongoing at the time of submission; however, listings will be provided for deaths, SAEs and pregnancy reports. Does the Division agree with this proposal?

FDA Response:
Your proposal is acceptable.

Discussion:
No discussion occurred.

Question 16:
Does the Division have any comments on the statistical analysis methods proposed in the SDAPs for the ISE and ISS?

FDA Response:
We do not have further comments. The proposed statistical methods appear reasonable.

Discussion:
No discussion occurred.

Question 17:
Does the Division agree with the proposal to provide datasets in IDSL format with SAS transport, data definition and eCRF files?

FDA Response:
We agree with your proposal to provide datasets in IDSL format, as long as the variables are clearly defined and derivations are well-documented with appropriate links to the eCRF files and to the raw datasets.

Discussion:
No discussion occurred.

Question 18:
Would the Division find any value in reviewing a test data package of the datasets in the IDSL format?

FDA Response:
Your proposal to submit a test data package for review is acceptable.

Discussion:
GSK questioned whether submitting a mock data set would be useful to the Division. The Division is willing to accept mock data set for review, but questioned the rationale for using the IDSL format instead of following the CDISC guideline. GSK stated that the initial studies were not done in CDISC SDTM and ADaM formats, but intends on using these formats for future developments. GSK will provide the Division with a break down of what information will be in CDISC SDTM/ADaM and IDSL format.

Question 19:
Does the Division foresee a need for including analysis programs (executable or non-executable), as part of GSK's submission?

FDA Response:
We recommend that you include the programs used for creating the main efficacy analysis datasets from submitted raw datasets and the programs used for the efficacy and main safety analyses. In addition, provide a document that explains what each program is used for.

Discussion:
The Division stated that the submission of analysis programs in non-executable codes is reasonable. The submission should include all programs used to generate the key efficacy results contained in the proposed label and study reports.

Question 20:
Since GSK submitted our pediatric development plans in the 9 April 2012 Briefing Document, does this fulfill the FDASIA requirement, listed under Milestone #1 in Section 10.2, to submit an initial Pediatric Study Plan to the Division?

FDA Response:
As your EOP2 meeting occurred prior to November 16, 2012, and your application is expected to be submitted prior to January 5, 2014, you should include your pediatric plan with your NDA submission using the enclosed template.

Discussion:
No discussion occurred.

Question 21:
Since GSK met with the Division on 11 May 2012 to discuss and reach agreements on the proposed pediatric development plan, does this fulfill the FDASIA requirement, listed under Milestone #2 in Section 10.2, for the FDA and the sponsor to meet to discuss the pediatric study plan?

FDA Response:
See response to question #20.

Discussion:
No discussion occurred.

Question 22:
Based on FDA's meeting minutes for the pediatric advice meeting, if GSK submits a written agreement to these minutes marked "Agreed Initial Pediatric Study Plan," would that fulfill the FDASIA requirement, listed under Milestone #3 in Section 10.2, for the sponsor to submit their written agreement with FDA's comments on the pediatric study plan?

FDA Response:
See response to question #20.

Discussion:
No discussion occurred.

Question 23:
If FDA confirms this agreement in writing with GSK, will this fulfill the FDASIA requirement, listed under Milestone #4 in Section 10.2, for FDA to provide written confirmation of the agreed initial pediatric study plan?

FDA Response:
See response to question #20.

Discussion:
No discussion occurred.

Question 24:
If GSK has not fulfilled the FDASIA PSP requirements via the above process, will the Division provide guidance on the steps that should be taken to comply with these new requirements?

FDA Response:
See response to question #20.

Discussion:
No discussion occurred.

Question 25:
GSK understands that PREA requirements will inform requirements for a Proposed Pediatric Study Request to initiate the Written Request / pediatric exclusivity process. Is there a mechanism whereby GSK can determine whether FF is eligible for pediatric exclusivity so we can factor this into our pediatric timelines?

FDA Response:
Discussion of pediatric exclusivity is premature at this time.

Discussion:
No discussion occurred.

Question 26:
If the Division agrees with the proposal for the adolescent and adult NDA to provide datasets in IDSL format with SAS transport, data definition and eCRF files, does the Division also agree with using this same format for the pediatric sNDA submission?

FDA Response:
We would like to have consistent format between the two programs. However, you are encouraged to follow the CDISC standards (SDTM and ADaM formats) in your future drug development.
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm248635.htm

Discussion:
No discussion occurred.

Question 27:
A comprehensive package of nonclinical studies on FF in accordance with the ICH M3 (R) Guidelines will be available at the time of file. Does the Division agree that no further nonclinical studies are required to support the registration of FF Inhalation Powder?

FDA Response:
We agree that no further nonclinical studies are required to support the filing of an NDA for FF Inhalation Powder. The registration is a review issue. See additional nonclinical comments.

Additional Nonclinical Comments:
For the NDA, qualify any impurities or degradants exceeding ICH Q3A(R) and Q3B(R) guidelines, respectively.

Discussion:
No discussion occurred.

Question 28:
Based on the design of the Phase III efficacy studies, does the Division agree with the proposed indication statement?

FDA Response:
In general, this proposed indication statement appears acceptable. However, this will ultimately be a review issue.

Discussion:
No discussion occurred.

Question 29:
Does the Division have any comments on the draft language for the Dosage and Administration section of labeling?

FDA Response:
The general language as proposed in the Dosage and Administration section of labeling is consistent with that of other inhaled corticosteroid products for asthma. However, discussion of the specific dose strengths is premature prior to our review of the efficacy and safety data in your application, and therefore we have no further comments on the draft language at this time.

Discussion:
No discussion occurred.

Question 30:
In the written advice received from the Division on 11 October 2012, the Division asked GSK to consider how the clinical program will be described in the product label and how best to represent data obtained with the two-strip product versus the to-be-marketed single-strip product. GSK proposes to address this as noted above. GSK would appreciate the Division's feedback on this proposal. Specifically:

- ***Does the Division agree in principle with the proposal to describe the*** (b) (4) ***in the PK section of labeling?***

FDA Response:
In principle, we agree. However, (b) (4) *this information may not need to be included in the label.*

Discussion:
No discussion occurred.

- ***Does this address the Division's advice on how to*** (b) (4) ***? Or does the Division have other considerations*** (b) (4) ***?***

FDA Response:
See response to question 30, bullet 1.

Discussion:
No discussion occurred.

Question 31:
Does the Division agree with the proposal for the Risk Management Plan?

FDA Response:
We agree.

Discussion:
No discussion occurred.

Question 32:
The specifications and file formats that GSK proposes to use are as noted in Section 14. These items are fully consistent with the Division's guidance documents as referenced within Section 14. Does the Division agree that these specifications and file formats are acceptable for the NDA?

FDA Response:
We agree.

Discussion:
No discussion occurred.

Question 33:
Since the submission will include datasets, as outlined in Section 14.2, GSK does not intend to submit CRF tabulations/Patient Profiles. Does the Division agree with this approach?

FDA Response:
We agree.

Discussion:
No discussion occurred.

Question 34:
Does the Division agree with the level of hyperlinking proposed for the NDA?

FDA Response:
We agree.
Discussion:
No discussion occurred.

Additional Discussion
GSK asked whether the FF application would be considered an NME or non-NME. The Division stated that FF 100 mcg for asthma would be considered a non-NME and would be reviewed on a 10-month clock.

DISCUSSION OF THE CONTENT OF A COMPLETE APPLICATION

As stated in our November 27, 2012, communication granting this meeting, if, at the time of submission, the application that is the subject of this meeting is for a new molecular entity or an original biologic, the application will be subject to "the Program" under PDUFA V. Therefore, at this meeting be prepared to discuss and reach agreement with FDA on the content of a complete application, including preliminary discussions on the need for risk evaluation and mitigation strategies (REMS) or other risk management actions. You and FDA may also reach agreement on submission of a limited number of minor application components to be submitted not later than 30 days after the submission of the original application. These submissions must be of a type that would not be expected to materially impact the ability of the review team to begin its review. All major components of the application are expected to be included in the original application and are not subject to agreement for late submission.

Discussions and agreements will be summarized at the conclusion of the meeting and reflected in FDA's meeting minutes. If you decide to cancel this meeting and do not have agreement with FDA on the content of a complete application or late submission of any minor application components, your application is expected to be complete at the time of original submission.

In addition, we remind you that the application is expected to include a comprehensive and readily located list of all clinical sites and manufacturing facilities.

Finally, in accordance with the PDUFA V agreement, FDA has contracted with an independent contractor, Eastern Research Group, Inc. (ERG), to conduct an assessment of the Program. ERG will be in attendance at this meeting as silent observers to evaluate the meeting and will not participate in the discussion. Please note that ERG has signed a non-disclosure agreement.

Information on PDUFA V and the Program is available at http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm.

PREA PEDIATRIC STUDY PLAN

The Food and Drug Administration Safety and Innovation Act of 2012 changes the timeline for submission of a PREA Pediatric Study Plan and includes a timeline for the implementation of these changes. You should review this law and assess if your application will be affected by these changes. If you have any questions, please email the Pediatric Team at Pedsdrugs@fda.hhs.gov.

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 Office 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.				

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

/s/

ANGELA H RAMSEY
02/12/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 70,297

MEETING MINUTES

GlaxoSmithKline
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709-

Attention: Patrick D. Wire, Pharm D 5.5604
Product Director, Respiratory Group

Dear Dr. Wire:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for fluticasone furoate Inhalation Powder.

We also refer to the meeting between representatives of your firm and the FDA on March 16, 2011. The purpose of the meeting was to discuss the Phase 3 development plans for fluticasone furoate in the treatment of asthma.

A copy of the official minutes of the meeting is attached for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call me at (301) 796-2284.

Sincerely,

{See appended electronic signature page}

Angela Ramsey, RN, MSN
Senior Regulatory Project Manager
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE:
Meeting Minutes

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Type:	Type B
Meeting Category:	EOP 2
Meeting Date and Time:	March 16, 2011 10:30am- 12:00pm EST
Meeting Location:	FDA White Oak, Bldg 22, Conference Room 1415
Application Number:	IND 70,297
Product Name:	Fluticasone Furoate Inhalation Powder
Indication:	Treatment of Asthma
Sponsor/Applicant Name:	GlaxoSmithKline
Meeting Chair:	Badrul A. Chowdhury, M.D., Ph.D., Director,
Meeting Recorder:	Angela Ramsey RN, MSN, Senior Regulatory Project Manager

FDA ATTENDEES

Badrul A. Chowdhury, M.D., Ph.D., Director
Angela Ramsey, RN, MSN, Senior Regulatory Project Manager
Susan Limb, M.D., Clinical Team Leader
Brian Porter, M.D. Ph.D., M.P.H., Clinical Reviewer
Craig M. Bertha, Ph.D., Chemistry Reviewer
Suresh Doddapaneni, Clinical Pharmacology Team Leader
Ying Fan, Clinical Pharmacology Reviewer
Joan Buenconsejo, Ph. D., Statistician Team Leader
David Hoberman, Ph.D., Statistician

SPONSOR ATTENDEES

Brett Haumann, M.D., Medicine Development Leader
Dennis Brindley, Biomedical Data Sciences
Loretta Jacques, M.D., Director Asthma Clinical Development
Susan Holmes, Director, CMC Global Regulatory Affairs
Patrick Wire, Pharm D., Director, Global Regulatory Affairs
Paul Johnson, Medicine & Process Delivery
Ann Allen, Clinical Pharmacology
Munir Abdullah, Global Regulatory Affairs

BACKGROUND

GlaxoSmithKline (GSK) submitted a Type B meeting request dated, January 7, 2011, to discuss the Phase 3 development plans for fluticasone furoate in the treatment of asthma. GSK submitted the briefing package on February 16, 2011. Upon review of the material, the Division responded via secure email on March 14, 2011. GSK requested to continue with the face-to-face meeting as scheduled to discuss responses to questions 1, 4, 6 and 8.

The content of the email is below. Any discussions that occurred during the meeting are captured directly under the relevant response. The sponsor's questions are in ***bold italic;*** the Division's response is in *italics;* and the discussion is in normal font.

Clinical Questions

Question 1

Does the Agency agree that the completed Phase IIb Studies with FF (which utilised the novel inhaler with two strips, one containing FF and the second containing (b) (4) ***have identified 3 strengths of FF: 50 mcg, 100 mcg and 200 mcg to progress to Phase III? In particular, please comment on the following:***

- ***The data from the dose ranging studies for FF (which contains twin strips) can be utilised to select doses to progress to Phase III studies for the single strip monotherapy product, which GSK plans to commercialise.***
- ***There are minimal differences within the respirable fraction of the overall particle size distribution, i.e. <*** (b) ***µm (represented by sum of stages 3 and below of the Next Generation Inhaler) between single strip and twin strip (estimated as*** (b) (4) ***%). Slight differences within the Throat and Pre-separator (particles of aerodynamic size >*** (b) (4) ***µm) are observed between the single and twin strip products; however the sum of these stages is similar for each product type. Slight differences within the Aerodynamic Particle Size Distribution (APSD) are typical of normal product variability and the associated analytical capability of the method. The small differences noted within the in vitro particle size distribution between the single strip and twin strip are not believed to be clinically significant.***

FDA Response:

We generally recommend that dose ranging trials and Phase 3 efficacy and safety trials be conducted with the same, to-be-marketed product. We note the greater respirable fraction of fine particles in the single-strip fluticasone furoate (FF) monotherapy DPI compared to the dual-strip product. The clinical impact of these differences, if any, is not known. Therefore, while the proposed doses of 50, 100, and 200 mcg FF appear reasonable based on the available information, the acceptability of the dose-ranging data will ultimately be a review issue and should be addressed in the NDA application.

Discussion:
The Division stated that using dual-strip FF data from the FF/vilanterol combination program to support the proposed single-strip FF product was acceptable in principle. The extent to which information could be borrowed will depend on the extent of the differences identified between the dual-strip and single-strip products, e.g. differences in fine particle mass. A lower fine particle mass from the dual-strip FF product compared to the single-strip FF product has different implications for safety versus efficacy. The relevance of data from the combination program will also depend on the sequence of application submission and approval status.

GSK reiterated that the differences in the fine particle mass (FPM) delivery by the aerodynamic particle size distribution testing, for the single versus the dual strip version of the Fluticasone Furoate (FF) monotherapy product was small, and ranged from (b) (4) %. The Division questioned this range based on the data supplied on pp. 143, 145, and 147 of the package. GSK attempted to clarify in general how they arrived at that range but indicated that there was not enough information included in the package to reproduce or explain that approach. GSK will provide more clarification either to the IND prior to the pre-NDA meeting or this issue may be part of the pre-NDA package and subsequent meeting discussion. GSK asked what magnitude of difference in the FPM would the Division consider to acceptable such that the dual strip FF monotherapy product data could substitute for the single strip FF monotherapy product for support of the NDA for the planned to-be-marketed FF single strip version. The Division referred to the 1998 draft *Guidance for Industry, MDI and DPI Drug Products, CMC Documentation*, where it refers to a change of greater than 10% in the relevant fine particles (e.g., < 5 mcm) as being considered significant. GSK claimed that their two FF monotherapy versions (single and dual strip) delivered FPM with difference (b) (4). Another point which was brought up with respect to the data on the above referenced pages of the package was that the Phase IIb FF dual strip product differed more greatly in FPM delivery when compared to the FF single strip product than when the latter was compared to the Phase III FF dual strip product. These differences were said to be mainly due to differences in total dose delivery, which had been matched more closely with the Phase III FF dual strip product.

Question #2
Does the Division agree with the design of the proposed FF Phase III efficacy studies (FFA115283 – FF50 vs placebo; 12 weeks and FFA115285 – FF50 vs placebo; 24 weeks) to support the proposed dosing recommendations for maintenance treatment for asthma in (b) (4) ***In particular please comment on the following aspects:***

- ***The study population (symptomatic on non-ICS therapy (short-acting beta-agonists [SABA] and leukotriene modifiers)***
- ***Study duration for FFA115283 of 12 weeks and FFA115285 of 24 weeks.***
- ***Primary efficacy trough (pre-bronchodilator and pre-dose) forced expiratory volume in one second (FEV_1)***
- ***Secondary endpoints (rescue-free 24-hour periods, trough PM peak expiratory flow (PEF), AM PEF, symptom-free 24 hour periods, total AQLQ score).***

- ***Safety measures (adverse events, severe asthma exacerbations, physical examinations, blood chemistry and hematology at baseline only, pre-dose vital signs, and oropharyngeal examinations. Note we do not propose to do 24-hour urinary cortisol as the results of the HPA axis study, HZA106851, did not show any effect on 24-hour serum cortisol levels for either FF/VI 200/25 mcg or FF/VI 100/25 mcg.***

FDA Response:

The design, duration, and designated endpoints of FFA115283 and FFA115285 are appropriate to evaluate the efficacy of low-dose FF in mild persistent asthmatics (b) (4)

However, we recommend omitting the fluticasone propionate (FP) 100 mcg arm in FFA15285. Inclusion of the active comparator arm necessitates use of a double-dummy design with administration of an extra placebo dose in the evening to reconcile the once daily and twice daily dosing regimens. Comparison to FP is not required in the clinical program and appears to (b) (4). *A similar comment applies to the proposed trial FFA112059 and the FF/VI combination trial HZA106829 in persistent asthmatics.*

The decision to omit 24-hour urinary cortisol from these trials is at your discretion. See our response to Question #5 regarding the evaluation of HPA axis effects.

Discussion:

The Sponsor clarified that the inclusion of a fluticasone propionate (FP) active comparator arm in the proposed 24-week trials was intended to (b) (4) The Sponsor understands that this comparison will be insufficient for a comparative labeling claim in the U.S. The Division acknowledged the requirement for (b) (4).

Question #3

Does the Division agree that ongoing study FFA112059 (FF100 vs placebo; 24 weeks) supported by data from HZA106827 (FF100 vs placebo, 12 weeks, also ongoing) provides adequate data to support the use of FF 100 mcg in the treatment of asthma? In particular, please comment on the following:

- ***The study population (uncontrolled on low-mid dose ICS in FFA112059 [FF100 vs placebo; 24 weeks] and uncontrolled on low-mid dose ICS or low dose ICS/LABA in HZA106827 [FF100 vs placebo, 12 weeks]).***
- ***Single strip inhaler is used in FFA112059 (FF100 vs placebo; 24 weeks) and twin strip in HZA106827 (FF100 vs placebo, 12 weeks).***

- ***Primary efficacy trough (pre-bronchodilator and pre-dose) FEV_1***
- ***Secondary endpoints (rescue-free 24-hour periods, trough PM PEF, AM PEF, symptom-free 24 hour periods, total AQLQ score).***
- ***Safety measures (adverse events, severe asthma exacerbations, physical examinations, blood chemistry and hematology at baseline only, blood liver assessment at baseline and after 12 and 24 weeks treatment, pre-dose vital signs, oropharyngeal examinations, and 24-hour urinary cortisol at baseline and end of treatment).***

FDA Response:

The design, duration, and designated endpoints of FFA112059 are appropriate to evaluate the efficacy of mid-dose FF in mild to moderate persistent asthmatic subjects, but we recommend omission of the FP 250 mcg arm as stated in the response to Clinical Question #2. In general, the acceptability of data from HZA106827 to support the efficacy of the single-strip FF product will be a review issue. See the response to Clinical Question #1.

Discussion:

No Discussion occurred.

Question #4

Does the Division agree that a single study FFA114496 (FF100, FF200; 12 weeks), supported by the non inferiority comparison of FF 200 mcg and FP 500 mcg BID in HZA106829 (FF200, 24 weeks), will support the proposed dosing recommendation of FF 200 mcg as the highest recommended dose for the maintenance treatment of asthma? In particular, please comment on the following aspects of FFA114496:

- ***The study population (uncontrolled on mid/high dose ICS).***
- ***Single strip inhaler used in FFA114496 and twin strip inhaler in HZA106829.***
- ***Efficacy endpoints to include trough (pre-bronchodilator and pre-dose) FEV_1, rescue-free 24-hour periods, trough PM PEF, AM PEF, symptom-free 24-hour periods.***
- ***Placebo or other control arm is not included and thus no formal statistical analysis to be conducted; only summary statistics will be provided with the aim of showing a numerical benefit on one or more efficacy endpoints (See Section*** *Error! Reference source not found.* ***for rationale on proposed study design). If no difference is seen in the total population, exploratory analyses may be conducted on subgroups in order to identify a group of patients who may require the higher 200 mcg dose.***

- ***Safety measures (adverse events, severe asthma exacerbations, physical examinations, blood chemistry including liver assessments at baseline and end of treatment, 24-hour urinary cortisol at baseline and end of treatment, pre-dose vital signs, and oropharyngeal examinations).***

- ***Pop PK included in FFA114496 to characterise FF pharmacokinetics for single strip inhaler in target patient population.***

FDA Response:

The design and designated endpoints of FFA114496 are acceptable to support the FF 200 mcg dose, provided that the trial demonstrates a clinically relevant difference between the mid- and high-dose levels. To justify the need for both dose levels, we expect a numerical dose response for the primary endpoint, as well as support from other efficacy or pharmacodynamic variables. In addition, the clinical program must include robust, replicate, placebo-controlled evidence of efficacy for the FF 100 mcg dose.

Comparison to fluticasone propionate 500 mcg in HZA106829 may provide supportive results but will be considered as secondary support. Also, (b) (4) *. See the response to Clinical Question #2.*

Proposed pop PK approach seems reasonable.

Discussion:

GSK stated that FFA114496 is not powered to demonstrate a statistical difference in efficacy between the 100 mcg and 200 mcg FF doses. The Division replied that a clinically relevant numerical separation in the primary outcome measure of FFA114496 was expected, with supportive data from other endpoints. Pharmacodynamic data from this trial or other trials in the clinical program could also be used. The Division cited examples of potential PD markers that could support the higher FF dose, including cyclic AMP, which had been used by the Sponsor in past development programs, and exhaled nitric oxide (eNO). Of note, the Division indicated that changes in oral corticosteroid use would be of limited value in terms of supporting the highest dose.

GSK questioned whether replicate placebo-controlled data from the lowest proposed dose, FF 50 mcg, would be sufficient. The Division replied that if the FF 50 mcg dose is not shown to be efficacious in replicate trials, replicate data for the FF 100 mcg dose will be required to support both the FF 100 mcg and FF 200 mcg dose levels. GSK asked if data for FF 100 mcg delivered via the dual-strip device would be acceptable as replicate evidence. The Division responded that this approach would be acceptable, presuming that the differences in fine particle mass were supported.

Question #5

Does the Division agree that an additional HPA axis study with FF monotherapy is not required, as the completed study with the FF/VI combination (the HPA-axis study HZA106851, FF100 and FF200 in combination with VI [114 subjects]) will provide adequate data since systemic exposure is similar regardless of whether FF is delivered as monotherapy or as part of FF/VI?

FDA Response:

Pending thorough review of the HPA axis study data, your proposal not to conduct additional HPA axis study with FF monotherapy appears reasonable, provided that the systemic exposure from FF monotherapy single strip product is similar to the FF monotherapy twin strip.

Discussion:

No Discussion occurred.

Question #6

Does the Division agree that the long-term safety data for FF may be obtained from the ongoing FF/VI programme? In particular, please comment on

- ***Use of HZA106839 (Long Term safety; FF100 & FF200 in combination with VI and no FF monotherapy arms) and HZA106837 (FF100; exacerbation study) which includes FF/VI 100/25 mcg and FF 100 mcg monotherapy arm to provide information on long term effects of FF on adverse events and on ocular effects.***
- The acceptability of using FF/VI to provide long term safety data as exposure to FF (in terms of both Cmax and AUC) is similar for FF delivered as part of FF/VI or as monotherapy using twin strip inhaler. The proposed relative bioavailability clinical pharmacology study will aim to show similarity of FF exposure regardless of whether FF is delivered via single or twin strip device (see Section **Error! Reference source not found.**)

FDA Response:

No, we do not agree. Long-term safety data with FF/VI will not be sufficient to support FF monotherapy. We note differences in the fine particle distribution of the single-strip versus dual-strip DPI products, and there may also be differences in device performance and durability over time. While safety data from FF/VI or FF delivered by the dual-strip DPI may be used as secondary support, you will need to provide long-term safety and device robustness data for the to-be-marketed product.

Discussion:

GSK stated that they have long-term safety data with FF monotherapy and will show comparability of the dual and single-strip DPI devices. GSK questioned whether 12 month safety data would be required with the to-be-marketed device. The Division indicated that the duration of long- term safety data using the to-be-marketed product was up for discussion, but in principle, 6-month safety data may be adequate depending upon the extent of data available from the dual-strip program and the bridge established between the dual-strip and the single-strip products. Long- term data from the highest proposed dose was expected.

GSK clarified that an application for the FF/vilanterol combination product in COPD would be submitted first. Additional information from the asthma combination program would be included at the time of the submission of the FF for asthma application. Therefore, GSK anticipated that a large safety database for the dual-strip FF product will be available to supplement the single-strip FF safety database. The Division stated that this approach appeared reasonable but with some caveats. Safety data from a COPD population would be of limited utility for the asthma application. Also, the utility of information from the combination program would depend to some extent on the approval status of the combination product.

The Division stated that the long-term trials should evaluate device durability and user-related issues over the life cycle of the device and over multiple cycles of use, i.e. patients may handle the device differently after several months of use compared to after initial introduction to the device. The Division referenced the albuterol CFC to HFA switch programs as an example of the type of long-term evaluations expected.

GSK asked specifically whether LOCS data from the combination program would be acceptable. The Division responded that this approach appeared reasonable.

Question #7

Does the Division agree that the proposed safety monitoring from both the monotherapy and combination programs provide an adequate safety database to support the indication and labelling of (b) (4), FF 100 mcg, and FF 200 mcg monotherapy dosages for the maintenance treatment of asthma?

- ***Exposure of over 3800 subjects with over 2800 total patient years of exposure to FF (FF monotherapy – estimated 1935 subjects with approximately 1300 patient years of exposure; FF/VI – estimated 1865 subjects with approximately 1500 patient years of exposure).***

FDA Response:

While the proposed assessments and size of the safety database appear reasonable, the adequacy of the overall program will depend on the safety profile of the FF monotherapy product and will be a review issue. Also, as stated in our response to Clinical Question #6, long-term safety data with the to-be-marketed FF product is required.

Discussion:
No Discussion occurred

Clinical Pharmacology Questions

Question #8

Does the Division agree with the proposed clinical pharmacology plan? In particular please comment on the following aspects:

- ***The acceptability of the clinical pharmacology FF monotherapy study designs (FFA115440 and FFA115441).***
- ***The acceptability of using clinical pharmacology study data generated with the FF/VI combination to support the FF monotherapy submission.***
- ***The acceptability of the planned population PK analyses.***

FDA Response:

Your planned population PK analyses seem reasonable.

In the dose proportionality study/absolute bioavailability FFA115440 study, you are proposing administration of (b) (4)

The rationale for assessing the relative bioavailability (b) (4) *single strip and twin strip FF monotherapy products in the HZA115440 study is unclear. Since the purpose of the study is to test the formulation differences and a single dose study is more sensitive in assessing formulation differences, we recommend that you administer single doses of the single strip and twin strip products in this study.*

Discussion:

(b) (4)

For the relative bioavailability study, the Division stated that it is more sensitive to assess bioequivalence with a single dose study than multiple dose study to assess the formulation differences. If it not able to detect the drug concentration levels in their proposed dose, the sponsor can increase the dose level providing data that the dose is safe to use.

CMC Questions

Question #9

GSK plans to use the development data generated for the combination Fluticasone Furoate/Vilanterol Inhalation Powder and Fluticasone Furoate Inhalation Powder (twin strips) to supplement the data for Fluticasone Furoate Inhalation Powder (single strip) in the NDA. Does the Agency agree that this proposal is appropriate?

FDA Response:

We acknowledge that you will be using a risk-based approach to decide where data for the twin strip products are appropriate to support the Fluticasone Furoate Inhalation Powder (single strip) product. We agree that such an approach can be used as part of your program in support of your NDA. Any tests associated with the delivery of formulation from the combination drug product would likely not be supportive of the monotherapy product as there are noted in vitro differences (see clinical comment 1).

Discussion:

No discussion occurred.

Question #10

Whilst GSK recognises that the acceptability of the control strategy for the commercial drug product is a review issue, GSK would like to ascertain whether the approach to define the stage of the manufacturing process where the (b) (4) ***tests are conducted is acceptable to the Agency?***

FDA Response:

The approach to determine whether the (b) (4) *testing can be performed before the addition of the protective packaging is acceptable. Data should be supplied in conjunction with whatever type(s) of protective packaging (overwrap or tray) will be used in association with the process(es) with* (b) (4)

Discussion:

No discussion occurred.

Question #11

GSK proposes to provide primary stability data for the overwrapped Fluticasone Furoate Inhalation Powder (single strip) product but does not propose to repeat these studies for the product in a tray as:

- ***The product performance of the foil laminate overwrapped Fluticasone Furoate Inhalation Powder (single strip) product and the combination Fluticasone Furoate/Vilanterol Inhalation Powder is comparable. Preliminary data are provided for ongoing stability studies to demonstrate the comparability at initial and on storage.***

- ***The foil (b) (4) tray is being developed to provide similar protection to the overwrap. Preliminary data to demonstrate comparability of Fluticasone Furoate/Vilanterol Inhalation Powder in an overwrap and tray are provided and will be supplemented with additional data in the NDA for Fluticasone Furoate Inhalation Powder (single strip).***

Therefore it is considered that the stability of the overwrapped Fluticasone Furoate Inhalation Powder (single strip) product is representative of the product in a tray. Does the Agency agree with this approach?

FDA Response:

We generally recommend that the primary stability batches of drug product have the configuration of the final to-be-marketed drug product. Your assumption that comparable

stability (6 months stability long term and accelerated data) demonstrated for the Fluticasone Furoate/Vilanterol combination product with the two types of protective packaging would suggest comparability of the analogous stability data for the Fluticasone Furoate Inhalation Powder (single strip), is reasonable. If such comparability for the combination product is demonstrated, the stability data for the monotherapy product (with the not-to-be-marketed overwrap) could still be considered to be primary and the main support for your expiration dating period.

Provide a commitment to update the application with release and stability data for the first three commercial scale batches of the monotherapy product having the to-be-marketed configuration.

Discussion:

No discussion occurred.

Additional Comment

We recommend that about 100 apparently normally functioning, partially-used devices be returned for in vitro testing from the phase 3trials (e.g., dose delivery, functionality), and at least a quarter of these be tested for aerodynamic particle size distribution. In addition to the return and in vitro testing of non-complaint devices that have been partially used in the clinical trials, it is expected that all complaint devices be returned for an examination and in vitro testing to determine the cause for the complaint.

Discussion:

No discussion occurred.

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/s/

ANGELA H RAMSEY
04/01/2011