CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-121/S009

ADMINISTRATIVE DOCUMENTS

I. ITEM 13 PATENT INFORMATION FOR FLONASE® NASAL SPRAY IN PERENNIAL NONALLERGIC RHINITIS NDA 20-121

Active Ingredient:	fluticasone propionate
Dosage Form:	Nasal Spray
Strength of Drug Product:	50 micrograms of fluticasone propionate per actuation
Route of Administration:	intranasal
Applicant Firm Name:	Glaxo Wellcome Inc.
Patent Number:	**4,335,121**
Coverage:	Fluticasone Propionate per se, compositions, processes for preparation and various methods of use
Issue Date:	June 15, 1982
Expiration Date:	November 14, 2003

The Undersigned certifies to the best of his knowledge and belief the above listed patent is valid, claiming fluticasone propionate, the subject of a New Drug Application.

04/23/97
Date

Charles E. Dadswell
Registered Patent Attorney
United States Registration No. 35,851

EXCLUSIVITY SUMMARY FOR NDA # 20-121 SUPPL # 009

Trade Name Flonase Generic Name fluticasone propionate

Applicant Name GlaxoWellcome HFD # 570

Approval Date If Known _____

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

a) Is it an original NDA?

YES /__/ NO /X/

b) Is it an effectiveness supplement?

YES /X/ NO /__/

If yes, what type? (SE1, SE2, etc.) SE1

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 /X/ 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:

_____

_____

Form OGD-011347 Revised 10/13/98

cc: Original NDA Division File HFD-93 Mary Ann Holovac

d) Did the applicant request exclusivity?

YES /X/ 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?

No

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use? (Rx to OTC switches should be answered NO-please indicate as such)

YES /__/ NO /X/

If yes, NDA #_____. Drug Name _____.

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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

YES /__/ NO /X/

IF THE ANSWER TO QUESTION 3 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 /X/ NO /__/

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

NDA# 20-121 Flonase Nasal Spray

NDA# 19-957 Cutivate [redacted] Ointment

NDA# 19-958 Cutivate Cream

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. IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S 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 /X/ 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 /X/ 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 /X/ 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 /X/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /__/ NO /X/

If yes, explain: _____

_____

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

FLT 3010

FLT 351

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

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

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

Investigation #1 YES /___/ NO /X/

Investigation #2 YES /___/ NO /X/

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?

Investigation #1 YES /___/ NO /X/

Investigation #2 YES /___/ NO /X/

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"):

FLT 3010 FLT 351

FLT 350 _____

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

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

Investigation #1

IND # [redacted] YES /X/ ! NO /___/ Explain: _____

! _____

Investigation #2 !

IND # [redacted] YES /X/ ! NO /___/ Explain: _____

_____

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

Investigation #1

YES /___/ Explain _____ ! NO /___/ Explain _____

_____ ! _____

_____ ! _____

Investigation #2

YES /___/ Explain _____ ! NO /___/ Explain _____

_____ ! _____

_____ ! _____

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

YES /___/ NO /X/

If yes, explain: _____

_____

/S/ 12-4-98
Signature Date
Title: Project Manager

/S/ 12/10/98
Signature of Office/ Date
Division Director

cc: Original NDA Division File HFD-93 Mary Ann Holovac

APPEARS THIS WAY
ON ORIGINAL

III. MARKETING EXCLUSIVITY

NDA 20-121

Flonase® (fluticasone propionate) Nasal Spray 0.05% w/w

Request for Marketing Exclusivity

Pursuant to Section 505(c)(3)(D)(iv) and 505(j)(4)(D)(iv) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.108(b)(5), Glaxo Wellcome Inc. requests three years of exclusivity from the date of approval of this sNDA for Flonase (fluticasone propionate) Nasal Spray, for the management of perennial nonallergic rhinitis.

We hereby certify as to the following:

Section 8, Item V.F. of this application contains a list of published studies or publicly available reports of clinical investigations known to Glaxo Wellcome through a literature search that are relevant to the use of Flonase Nasal Spray in the management of perennial nonallergic rhinitis. The results of literature searches have not revealed publications which would, in our opinion, provide sufficient sole basis for approval of the indication to which this application refers.

Thus, Glaxo Wellcome Inc. is entitled to exclusivity as this application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and sponsored by Glaxo Wellcome Inc. The following investigations are 'essential to the approval of the application' in that there are no other data available that could support approval:

- RM1996/00243/00: A double-blind, randomized, placebo-controlled study of the efficacy and safety of fluticasone propionate aqueous nasal spray versus placebo followed by a six-month open-label safety extension in subjects with perennial nonallergic rhinitis (Protocol FLTA3010)

- RM1996/00242/00: A double-blind, randomized, placebo-controlled study of the efficacy and safety of fluticasone propionate aqueous nasal spray given twice daily versus placebo for four weeks in patients with perennial nonallergic rhinitis (Protocol FLN-351)

- RM1996/00244/00: A double-blind, randomized, placebo-controlled study of the efficacy and safety of two doses of fluticasone propionate aqueous nasal spray given twice daily versus placebo for four weeks in patients with perennial nonallergic rhinitis (Protocol FLN-350)

These clinical investigations are defined as 'new' because they have not been relied on by the FDA to demonstrate substantial evidence of effectiveness of a previously approved drug product for any indication, or of safety for a new patient population, and do not duplicate the results of another investigation that was relied on by FDA to demonstrate the effectiveness or safety in a new patient population of a previously approved drug application. In this regard, it is noted that summary data from protocols FLN-351 and FLN-350 were previously filed to NDA 20-121 but to the best of our knowledge, were not relied upon by FDA for approval of that NDA.

Each of these investigations was 'conducted or sponsored by Glaxo Wellcome' in that Glaxo Wellcome Inc. was the sponsor of the investigational new drug applications (IND [redacted] under which clinical studies FLTA3010, FLN-351, and FLN-350 were conducted.

Alison Bowers
Project Director, Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA/BLA Number: 20121 **Trade Name:** FLONASE NASAL SPRAY
Supplement Number: 9 **Generic Name:** FLUTICASONE PROPIONATE
Supplement Type: SE1 **Dosage Form:** Spray; Nasal
Regulatory Action: AP **Proposed Indication:** Perennial nonallergic rhinitis (PNAR)

IS THERE PEDIATRIC CONTENT IN THIS SUBMISSION? YES

What are the INTENDED Pediatric Age Groups for this submission?

____NeoNates (0-30 Days) ____Children (25 Months-12 years)
____Infants (1-24 Months) _X_Adolescents (13-16 Years)
_X_Other Age Groups (listed): 4-12 years

Label Status ADEQUATE Labeling for ALL PEDIATRIC ages
Formulation Status NO NEW FORMULATION is needed
Studies Needed No further STUDIES are needed
Study Status

Are there any Pediatric Phase 4 Commitments in the Action Letter for the Original Submission? NO

COMMENTS & RECOMMENDATIONS:

This Page was completed based on information from a Project Manager/Consumer Safety Officer, DAVID HILFIKER.

/S/ 12-4-98

Signature Date

APPEARS THIS WAY
ON ORIGINAL

NDA 20-121

Supplemental New Drug Application

Flonase® (fluticasone propionate) Nasal Spray 0.05% w/w

DEBARMENT CERTIFICATION

Glaxo Wellcome hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with this application.

Shelly A Schiff for Charles E. Mueller — 4 DEC 98

Charles E. Mueller
Head, International Compliance Services
World Wide Compliance

Date

APPEARS THIS WAY
ON ORIGINAL