CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20983

CORRESPONDENCE

January 2, 2001

Robert J. Meyer, M.D., Director
Division of Pulmonary and Allergy Drug Products
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Food and Drug Administration
HFD-570, Room 10B-3
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-983; VENTOLIN® HFA (albuterol sulfate, USP inhalation aerosol)
Response to FDA Request/Comment: Other

Dear Dr. Meyer:

Reference is made to the New Drug Application identified above for VENTOLIN® HFA Inhalation Aerosol. On December 4, 2000, we received a request from the Division to either request a waiver or a deferral of the new Pediatric Rule requiring that new products be studied in pediatric populations.

The new HFA-formulation of VENTOLIN Inhalation Aerosol has not been studied in pediatric patients less than four years of age, consistent with the proposed labeling statement (under the heading "Pediatric Use" in the "Precautions" section of the prescribing information) that "safety and effectiveness in children below 4 years of age have not been established." Glaxo Wellcome has no plans to conduct studies in this pediatric subpopulation, and does not believe submission of a deferral or waiver request under 21 C.F.R. § 314.55 is necessary. Our position is that a pediatric "assessment" under 21 C.F.R. § 314.55 is not required in this "unclaimed" pediatric subpopulation because the pending application does *not* propose a "new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration." See 21 C.F.R. § 314.55(a) (specifying applications that are subject to "required assessments"). Rather, this application simply proposes for marketing the reformulation of a product that remains identical to its predecessor in its active moiety (albuterol), its indication ("the prevention and relief of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease and for the prevention of exercise-induced bronchospasm in patients 4 years of age and older"), its dosage form ("aerosol, metered," as stated in the *Orange Book*), and its route of administration ("inhalation," again as stated in the *Orange Book*).

From a policy standpoint, it would be inequitable and inappropriate for the new HFA-formulation of VENTOLIN® Inhalation Aerosol to be subject to the requirement of mandatory pediatric testing. In crafting the pediatric rule, FDA looked principally toward a future in which pediatric study of all *new* therapeutic options would be presumptively required, and would be waived only according to defined criteria. Already marketed products, in contrast, would become subject to mandatory pediatric testing only if FDA affirmatively acted – on narrow grounds not applicable here – to impose the requirements. (So far as we know, FDA has not yet invoked this authority.) The HFA-formulation of VENTOLIN® Inhalation Aerosol is simply a new formulation of an old product. Although the product may have changed from an environmental standpoint, it has not changed from a clinical standpoint, and it therefore must enjoy the same (essentially "grandfathered") status as other products that are not "new" for purposes of the pediatric rule. To penalize the product with a different status, simply because of the highly unusual need to conduct comparability trials in the absence of accepted standards for demonstrating bioequivalence, would be grossly unfair.

We would appreciate your concurrence with this assessment. If you have any questions or require additional information regarding this submission, please contact me at (919) 483-5140.

Sincerely,

Sara A Nelson

Sara A. Nelson
Associate Director
Regulatory Affairs

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-983

Glaxo Wellcome Inc.
Five Moore Drive
P.O.Box 13358
Research Triangle Park, North Carolina 27709

Attention: Michael Golden:
Product Director, Regulatory Affairs

Dear Mr. Golden:

We acknowledge receipt on January 5, 2001, of your January 4, 2001, resubmission to your new drug application (NDA) for Ventolin-HFA (albuterol sulfate) Inhalation Aerosol.

This resubmission contains additional information submitted in response to our January 3, 2001, action letter.

We consider this a complete class 1 response to our action letter. Therefore, the primary user fee goal date is March 5, 2001, and the secondary user fee goal date is May 5, 2001.

If you have any questions, call me at (301) 827-1064.

Sincerely yours,

Parinda Jani
Project Manager
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

/s/

Parinda Jani
1/16/01 01:52:24 PM

PARINOA

NDA 20-983

AUG 17 2000

Glaxo Wellcome Inc.
Five Moore Drive
P.O.Box 13358
Research Triangle Park, North Carolina 27709

Attention: Michael Golden
Product Director, Regulatory Affairs

Dear Mr. Golden:

Please refer to your new drug application (NDA) dated June 30, 1998, received July 1, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ventolin HFA (albuterol sulfate) Inhalation Aerosol.

We also refer to your submissions dated June 29 and July 19, 2000.

Our review of the Chemistry, Manufacturing and Controls (CMC) section of your submission is complete, and we have identified the following deficiencies. Comment numbers in parentheses refer to the July 1, 1999, "approvable" letter.

1. Submit the master batch record for the drug substance preparation that indicates that only an micronizer is used for the milling of the drug substance. Flag the appropriate portion(s) of the record. (comment 3.a)

2. In order to ensure reproducibility of both the micronization and testing of the particle size distribution for the drug substance, tighten the acceptance criteria ranges for the median particle size (MPS) and the % < 1 μm. (comment 3.b)

3. Provide clarification of the points below regarding the interim procedure

4. We remind you of your agreement, as outlined in the response to comment 8 of the July 1, 1999, approvable letter, to implement by the 4th quarter of 2001, an test with an appropriate subsequent equilibration period for % of each batch of product. The final testing should be implemented by a prior-approval supplement. (comment 8)

5. We remind you of your agreement to provide the results of the supporting study for the 21-day equilibration period for the drug product by September 2000. (comment 8)

6. Replace the word "nozzle" with "valve" in the label and labeling statement "store canister with the nozzle end down."" (comment 9)

7. The following revisions and clarifications pertain to the mean and individual dose content uniformity specification.

8. Moisture content method should be revised to include detail on the equipment used and associated operating parameters in order for Agency laboratories to make the appropriate assessment of the methodology. (comment 13)

9. In terms of the periodic verification of the supplier results for valve delivery testing performed on incoming valve lots, the interval for the performance of this testing by Glaxo-Wellcome should be indicated in the application, and because individual (as opposed to mean) valve delivery is not being controlled at release of the drug product, the frequency of your periodic evaluation should be higher than what may be typical. (comment 21)

10. Provide the data referred to on p. 102 (v.1) of the Jun 29, 2000, amendment for the levels of extractives found from the analysis of the "large number of can batches" which support the claim that previously levels of the 2-(2-butoxyethoxy)ethyl acetate extractive were atypically high. (comment 22)

11. We acknowledge your withdrawal of the proposal for testing of extractables from incoming canisters. Any future similar proposals with supporting data should be submitted via a prior-approval supplement. (comment 23)

12. Although the performance of duplicate analyses for from the valves by the contract laboratories does provide a measure of intermediate precision, it does not provide the necessary validation of their results (reproducibility). Provide such data and revise the methods to indicate the frequency of the periodic verification of the results of extractables testing of incoming valve components. (comment 25)

13. Provide clarification of how the (as per method provided on p. 133, v.1 of the June 29, 2000, amendment) of the placebo MDI (presumably containing only HFA-134a propellant with a boiling point of –26°C) can be visualized by the analyst on both the glass and paper substrates. Revise the method accordingly. (comment 30.a)

14. Propose an acceptance criterion for the size of the for incoming actuators from (comment 30.a)

15. Submit the updated specification sheet for the actuator that reflects the proposed acceptance criteria for the diameter and length of the as well as the size and diameter ratio for the (comment 30.a and 30.b)

16. Indicate if any actuators supplied by (DMF were used to prepare drug product batches in support of this application. If this is the case then data should still be provided to demonstrate the comparability of actuators obtained from the two suppliers in terms of critical dimensions, extractables, and performance characteristics. If applicable, future additions of an alternate actuator supplier should be supported via a prior-approval supplement. (comment 30.c)

17. DMF for overwrap laminate was reviewed on February 2, 2000, and was found to be inadequate to support your application. A deficiency letter dated February 3, 2000, was forwarded to the holder and no response has been received as of August 14, 2000. (comment 31)

18. The "in-use" data provided in response to comment 35.d of the July 1, 1999, letter do appear less variable and more consistent than those provided for the primary stability batches with the original submission. Normally, 3.5 months of "in-use" data is not of sufficient duration for justification of a 3 month "in-use" period after removal of the protective packaging. Provide updated "in-use" data, for our continued evaluation, on the aged 7ZX027 sub-batches and series batches beyond the 3.5 month test point. (comment 35.d)

19. Indicate or provide reference to pertinent sections of previous submissions that indicate the frequency of the in-process checks on crimp height and diameter performed during drug product manufacturing. Provide a master batch record that is flagged to indicate these checks.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Ms. Parinda Jani, Project Manager, at (301) 827-1064.

Sincerely yours,

Guirag Poochikian, Ph.D.
Chemistry Team Leader
Division of Pulmonary and Allergy Drug Products,
HFD-570
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:
Archival NDA 20-983
HFD-570/Div. Files
HFD-570/J.Parinda
HFD-570/Bertha/8-17-00 8/17/00
HFD-570/Poochikian/8-17-00
HFD-820/DNDC Division Director 8/17/00
DISTRICT OFFICE

Drafted by: /August 16, 2000
Initialed by: barnes/8-16-00
Final:jani/8-17-00
Filename: c:\data\my documents\n20983.ir2

DISCIPLINE REVIEW LETTER (DR)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 20-983

OCT 26 1998

Glaxo Wellcome Inc.
Five Moore Drive
P.O.Box 13358
Research Triangle Park, North Carolina 27709

Attention: C. Elaine Jones, Ph.D.
Product Director, Regulatory Affairs

Dear Dr. Jones:

Please refer to your pending June 30, 1998, new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ventolin-HFA (albuterol sulfate) Inhalation Aerosol.

We also refer to your submissions dated July 10, 23 and 27, 1998.

We have completed our review of the Chemistry, Manufacturing, and Controls (CMC) section of your submission and have the following comments and information requests.

1. The following comments pertain to the intermediate forms of albuterol used in preparing the drug substance, i.e., the conditioned (and micronized) albuterol sulfate.

   a. Reinstate the specification for boron levels in the albuterol base with an acceptance criterion that is reflective of typical data. Provide boron data on recent batches of albuterol for justification of the proposed limit.

   b. A specific test and an appropriate acceptance criterion should be put in place for levels of Pd^0 catalyst in the albuterol base.

   c. Provide data on the ethanol and methanol levels found in historical batches of albuterol sulfate produced at the _facility so that the current proposed specification limits of NGT _% ethanol w/w and NGT _% methanol w/w can be evaluated.

   d. Submit amended specifications reflecting the above modifications.

2. The following comments pertain to the drug substance particle size specifications and micronization.

   a. The particle size specifications for the conditioned albuterol sulfate (method should have acceptance criterion for particles with sizes between µm to help define the profile of the fine particles, e.g., an additional cut-off at µm. Provide data to support an acceptance criterion for such a cut-off.

   b. It is recommended that the mean mass diameter (MMD) for the conditioned albuterol sulfate be controlled with an acceptance criterion, e.g. MMD µm.

   c. The acceptance criterion for the particle size cut-off at 1 µm for the conditioned albuterol sulfate should include an upper as well as a lower limit, e.g., %.

   d. In terms of the data provided for the conditioned albuterol sulfate stored for 18 months at 30°C/60%RH with sealed foil overwrap, the specification limits for the w/w % of particles µm should be tightened to more closely reflect the data, e.g., % w/w µm NLT %.

   e. Since the use of the or the to prepare the drug substance suspension for the particle size determination test produced slightly different results for particles with sizes less than µm in diameter, it is recommended that the method be revised to specify the use of only one of these sonicators.

   f. The methods used for determination of the particle size of the micronized and conditioned albuterol sulfate and for the determination of the Moisture Sorption Profile of the conditioned material lack sufficient detail in order to allow Agency laboratories to verify these methods as suitable for regulatory purposes. Revise the methods to specify the instruments and software used, all pertinent analysis conditions and parameters, etc. The methods validation package for the application should be modified to include test results, lists of samples, and validation data for these method.

   g. From data collected on conditioned albuterol sulfate from the sites (batches R10419/002, R10419/003, WC159799AN, WC15800AN stored with foil protection at 40°C/75%RH for 6 months) it appears that particle size, in general, is smaller for the batches. Please address this observation and provide detailed descriptions of the micronization equipment, operating parameters (feed rate, air pressure, etc.), typical batch sizes, environmental controls, in-process controls, and any differences between the two micronization sites in terms of these details.

Include specific micronization operating parameters in the procedures from each site. Provide updated particle size data for multiple batches of conditioned material prepared at both to give assurance that materials from these sites will be comparable for this parameter.

3. The following comments pertain to remaining specifications for the drug substance.

4. Include testing at the 9- and 18-month time-point for the future stability test protocol for annual batches of conditioned albuterol sulfate.

5. As confirmed by Dr. Golden of your company on August 10, 1998, the re-test period proposed for non-micronized, micronized, and conditioned albuterol sulfate is 24 months (all relative to release of the non-micronized albuterol sulfate) with a maximum extension of 12 months. Justify the proposed re-test period of 24 months by submission of updated stability data for multiple batches of the conditioned albuterol sulfate from both sites in support of the proposal.

6. The following comments pertain to the propellant GR106642X.

   a. Please be aware that DMF [ ] was found to be inadequate to support your application and the holder has been notified of the deficiencies.

   b. Update the acceptance specifications for the propellant 1,1,1,2-tetrafluoroethane. You are encouraged to contact your supplier in this regard.

   c. The test methodology should be in place for the periodic validation of the supplier's results on the certificate of analysis for all attributes of the incoming propellant GR106642X (1,1,1,2-tetrafluoroethane).

7. The following comments pertain to the manufacturing and in-process controls of the drug product.

Redacted 3

pages of trade secret and/or confidential commercial information

8. Provide a summary of orientation(s) of the drug product (upright, inverted, horizontal) during shipping and storage, as well as any recommendations that will be made to pharmacies or patients in this regard.

9. The following comments pertain to the specifications and tests for the drug product.

10. The following comments pertain to the container closure system of the drug product.

a. Please indicate or provide reference to the information via drug master file [ ] the exact dimensional measurements and tolerances for the canisters used in the primary stability and clinical batches (6ZX012, 6ZX013, 6ZX015) and those for the canisters intended for market (used for batch 7ZX027).

b. DMF[ ]was reviewed and was found to be inadequate to support your application. The holder has been notified by letter of the deficiencies.

c. DMF[ ]was reviewed and was found to be inadequate to support your application. The holder has been notified by letter of the deficiencies.

d. The testing for acceptance of metering valve batches should include a criterion for individual valve delivery weights, e.g., no individuals outside of % of the target of mg. Additionally, provide weight per actuation data (means and individuals) obtained upon acceptance of recent consecutive lots of valves.

e. The following comments pertain to extractives from container closure components.

(1) Upon the acceptance of coated canisters from the supplier, extractables testing should be performed on representative samples and associated acceptance criteria should be proposed for the extracted compound(s) (e.g.,[ ]based on data from multiple incoming batches. Extraction solvents should be chosen to result in levels of extractables preferably greater than the levels of the compounds leached into the drug product formulation during shelf life. Once the reliability of the supplier is demonstrated,

testing may be proposed.

(2) Verify the presence or absence of valve lubricants that may leach into the product formulation and any necessary tests and controls for these.

(3) Test results for extractives from the components determined by the valve manufacturer before assembly of the valves, should be validated by you on a periodic basis if these materials are accepted based on a certificate of analysis supplied by the manufacturer. In addition, amend the application to include the methods used for determination of the levels of the following Acceptance criteria should be in place for the levels of extractives from these valve components.

(4) Tighten the acceptance criteria for the extractives found in the rubber (v1.3, p. 67 to reflect the data presented for the multiple batches (v1.3, p. 64-66). See related comment 10.e.(5) below.

(5) Since the levels of extractives obtained by extraction of incoming are similar to the levels of these compounds found in drug product after storage at room temperature for 12 months (v1.5, p. 28), the choice of solvent may not be optimal and should be re-examined particularly in terms of the safety qualification of the extracts and the proposed extractable acceptance criteria for incoming valve components. This would be particularly important if control of extractives in the drug product formulation is done indirectly by controlling the extractives from incoming container closure components.

(6) Since the majority of the plastic components of the metering valve that are in continued contact with the formulation are prepared from resin, with the exception of the gathering ring, provide the results of investigations into the levels of found in the drug product formulation after contact with these components for extended periods of time.

(7) For the setting of the upper acceptance criteria limits for the quantity of the in the incoming components (or raw resin) and the upper limits for the material, the proposal to use the % tolerance limit based on the mean level of these extractable in batches from a one year period may not be sufficiently stringent and the variability in the data and trends may need to be considered. Further comments on

the acceptance criteria for testing may be forwarded once proposed limits and associated data are provided in the amendment.

f. The tabular heading (v1.3, p. 72) for raw material grades and suppliers uses the description of "typical." Please be aware that for the critical components of the drug product container-closure system (device components that contact either the patient or the formulation, components that impact the mechanics of the overall performance of the device, or any necessary secondary packaging), any changes in resin or supplier, manufacturer or manufacturing, etc. should be reported in a prior approval supplement and be accompanied with the appropriate supporting data.

g. DMF and DMF were reviewed and were found to be inadequate to support your application. The holder has been notified by letter of the deficiencies.

h. Please be aware that comments pertaining to the lack of specifications controlling container closure extractives appearing in the drug product formulation during shelf-life (stability) may be forthcoming once complete data and proposed controls are made available for extractives from the container closure components in contact with the formulation (canister and valve). See related comment 10.e.(5) above and 12.a.(1) below.

i. Clarify the meaning of the word "typically" in the context of the description of the supplier of the resins used for manufacture of the actuator and strap-cap (v1.3, p. 86).

j. The location of the confidential information regarding the manufacturer's acceptance tests for raw materials, complete composition (resins, colorants, additives, etc.), and manufacturer's release tests and specifications for the actuators and strap-caps in the drug master files and is not specified and could not be determined. This information is required and it is recommended that letters of authorization be supplied that provide specific reference with identity, item number(s), page number(s), and submission date(s). These DMFs are currently considered inadequate for support of your application.

k. Provide the acceptance criteria for the various actuator acceptance tests listed (v1.3, p. 88).

l. In terms of your method for monitoring the extractives profile of actuators by as an indirect control on the composition, provide a commitment to internally investigate any occurrences of unusual spectral changes that are not of sufficient magnitude to fail the proposed specification that are provided on

p..91 (v1.3).

m. An acceptance test for identity of the desiccant should be performed on each batch of incoming desiccant units from either [redacted] or [redacted] in addition to the determination of weight and moisture content.

n. DMF [redacted] was reviewed and was found to be inadequate to support your application. The holder has been notified by letter of the deficiencies.

11. Provide data from studies which demonstrate the effect of HFA-134a on the viability of bacteria and fungi which may be present. Provide information concerning bioburden present in HFA-134a and, if necessary, propose specifications for microbial limits for the propellant. Conduct a one-time study to evaluate the fate of drug product which is intentionally inoculated in the [redacted] 100 to 1000 CFU/g range with test organisms.

12. The following comments pertain to the stability of the drug product.

a. The following comments pertain to your stability protocol for the first three production and annual batches (v1.4, pp. 109-110).

(1) The protocol for both the first three production and annual batches should be revised as follows: 1) add testing parameters for water content, dose content uniformity (individuals) both at beginning and end-of-use, and valve delivery; and 2) with the exception of the microscopic evaluation and microbial testing, the frequency of testing should be quarterly the first year, semi-annually the second and annually thereafter. Once sufficient experience and data are obtained for the product, deletion of test parameters and changes in testing frequency may be considered post-approval and should be made via a prior-approval supplement. The absence of tests and controls for extractives (leachables) will be considered further once full controls and supporting data are provided for extractives from incoming container closure components.

(2) The protocol should also include a commitment to withdraw from the market any lots of drug product found to fall outside the approved specifications (see section on stability commitment in the "Guideline for Submitting Documentation for the Stability of Human Drugs and Biologics," February, 1987).

(3) Since the drug product includes protective overwrap, stability storage conditions for the first three production and subsequent annual batches of drug product should include, in addition to storage at

25°C/60%RH, storage at 25°C/75%RH for 1/3 of the proposed expiry period of 18 months, i.e., 6 months.

b. Indicate the actual number of canisters filled for each of the primary stability batches and if significantly less than the theoretical amount _ units), provide data to support comparability of product filled with the beginning, middle, and end of a production scale suspension.

c. It is requested that, if possible, the updated stability data for all parameters be submitted in Excel format and, for ease of sorting, in columnar format with the following types of headings: batch, storage condition, month, protected or unprotected, inverted or upright storage, beginning/end, determination (data), etc.

d. Comments on the proposed expiration dating period of 18 months will be withheld pending the revision of the drug product specifications. The calculations outlined in the original application (v1.4, pp. 58-67) should be performed on the 18 month stability data using the specifications. Please refer to comment 9.h above in terms of the mean albuterol content per minimum dose.

e. Please be aware that comments related to the evaluation of the stability data for the batch 7ZX027 (a, b, and c canister batches) in comparison to analogous data for the primary stability batches may be forthcoming subsequent to the submission of the former data.

f. The in-use period of 6 months proposed for the product after the removal of the overwrap is not justified and should be reassessed with consideration given to the magnitudes of the shifts in the particle size distribution for non-overwrapped product.

g. Provide an explanation of the distinct difference in the dosing behavior of the primary stability batch 6ZX013 stored protected and inverted at 25°C/60%RH for 12 months in terms of the 3 and 6 month time-points.

h. In order to fully assess product and formulation quality of the to-be-marketed product in terms of the dosing and particle size distribution of the emitted dose, stability data for these parameters should be generated for product stored in protective packaging at 25°C/75%RH for at least 1/3rd of the proposed expiration dating period. See related comments 7.b, 9.h, and 9.m.

13. Provide data for determination of the amount of drug substance delivered from the valve per actuation or per minimum dose.

14. The investigation to support the cleaning instructions should be repeated and the particle size distribution by should also be determined after

Please also indicate the number of units tested to generate the data presented on p. 98 (v1.5).

15. Provide data that support the cleaning frequency proposed, i.e., every 7 days.

16. Provide data characterizing the plume geometry of the drug product.

17. A study should be conducted to determine the profile of the aerodynamic particle size distribution versus individual actuation number from the point at which the labeled number of actuations have been dispensed until canister exhaustion.

18. The labels and labeling have been reviewed and we have the following preliminary comments. Additional comments may be forthcoming.

g. The following comments pertain to the Patient Instruction's for Use.

(1) A statement instructing the patient to confirm that the canister is fully seated in the mouthpiece should be included in the instructions involving cleaning of the mouthpiece.

(2) Revise step 1 to include a patient inspection for the presence of foreign objects if the cap remains connected to the unit but is not used.

(3) Priming and re-priming instructions of step 7 should be placed at the beginning of the instructions.

We would appreciate your prompt written response so we can continue our evaluation of your NDA.

These comments are being provided to you prior to completion of our review of the application to give you preliminary notice of issues that have been identified. Per the user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and are subject to change as the review of your application is finalized. In addition, we may identify other information that must be provided prior to approval of this application. If you choose to respond to the issues raised in this letter during this review cycle, depending on the timing of your response, as per the user fee reauthorization agreements, we may or may not be able to consider your response prior to taking an action on your application during this review cycle.

If you have any questions, contact Parinda Jani, Project Manager, at (301) 827-1064.

Sincerely yours,

/S/

Guirag Poochikian, Ph.D.
Chemistry Team Leader for
Division of Pulmonary Drug Products,
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

NDA 20-983

JUL 14 1998

Glaxo Wellcome Inc.
Five Moore Drive
Research Triangle Park, North Carolina 27709

Attention: C. Elaine Jones, Ph.D.
Product Director
Regulatory Affairs

Dear Dr. Jones:

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

Name of Drug Product: Ventolin HFA (albuterol sulfate inhalation aerosol)

Review Priority Classification: Standard

Date of Application: June 30, 1998

Date of Receipt: July 1, 1998

Our Reference Number: 20-983

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on August 29, 1998, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be July 1, 1999.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

If you have any questions concerning this NDA, please contact Ms. Parinda Jani, Project Manager, at (301) 827-1064.

Sincerely yours,

Cathie Schumaker
Chief, Project Management Staff
Division of Pulmonary Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research