CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-702

CORRESPONDENCE

Pharmaceuticals, Inc. | 8500 Hidden River Parkway, Tampa FL 33637 | 813 975 7700, Fax 813 975 7770

BAUSCH & LOMB

March 13, 2001

NEW CORRESP

NC

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

Re: ANDA 75-702
Cromolyn Sodium Nasal Solution, USP (40 mg/mL)
Withdrawal of June 19, 2000 Amendment (Addition of 13 mL Fill Size)

Dear Sir or Madam:

The purpose of this communication is to request withdrawal of our June 19, 2000 Amendment to the above referenced abbreviated new drug application. The amendment sought an additional fill size (13 mL) for the drug product. We ask that this amendment be withdrawn without prejudice to any future filing as allowed by 21 CFR 314.65.

We continue to seek approval for Cromolyn Sodium Nasal Solution, USP (40 mg/mL) in the 26 mL fill size only.

The information contained in this correspondence is confidential and as such should be handled in accordance with the provisions established in 21 CFR 314.430.

In accordance with 21 CFR 314.96(b), we certify that a true copy of this withdrawal letter has been forwarded to FDA's district office in Orlando, Florida.

If you have any questions or comments concerning this request, please contact me at the above address or at (813) 975-7700 ext. 7102.

Sincerely,

J. B. Hawk

Joseph B. Hawkins
Manager, Regulatory Affairs

CENTER FOR DRUG EVALUATION AND RESEARCH
MAR 14 2001
OGD

Enclosure

Pharmaceuticals, Inc. | 8500 Hidden River Parkway Tampa FL 33637 | 813 975 7700 Fax 813 975 7770

BIOAVAILABILITY

June 19, 2000

BAUSCH & LOMB

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

AA
FDA DRUG AMENDMENT

Re: ANDA 75-702
Cromolyn Sodium Nasal Solution, USP (40 mg/mL)
Gratuitous Amendment – Additional Fill Size

Dear Sir or Madam:

The purpose of this correspondence is to amend the above referenced application. Specifically, we are seeking approval for an additional fill size for the drug product. The reference listed drug for this application is marketed in 13 mL and 26 mL fill sizes. Our application, submitted September 13, 1999, contained information provided information for the 26 mL size only. We wish to provide information for the 13 mL fill size at this time.

This application contains 11 volumes. Volume 1 includes additional chemistry information needed to support the change and a summary of the in-vitro bioequivalence data which demonstrates the comparability of the new fill size to that of the innovator. The remaining volumes contain source data for each of the bioequivalence tests. An index of the information included in this amendment is provided following the 356h.

In accordance with 21 CFR 314.94 (d)(5), we certify that a true copy of the information contained in this application has been forwarded to FDA's Orlando District Office.

If you have any questions regarding this correspondence, please contact me at the above address or by telephone at (813) 975-7700 extension 7102.

CENTER FOR DRUG EVALUATION AND RESEARCH
RECEIVED
JUN 21 2000
OGD

Sincerely,

Joseph B. Hawkins
Manager, Regulatory Affairs

Enclosure

8500 Hidden River Parkway
Tampa FL 33637

813 975 7700
Fax 813 975 7757

May 1, 2001

BAUSCH & LOMB

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

ORIG AMENDMENT
N/Am

Re: ANDA 75-702
Cromolyn Sodium Nasal Solution, USP (40 mg/mL)
Telephone Amendment – Chemistry

Dear Sir or Madam:

The purpose of this correspondence is to respond to an April 25, 2001 telephone call from Ken Furnkranz and Mike Smela, regarding the above referenced application. In that conversation the Agency indicated that our response would be considered a telephone amendment.

To facilitate the Agency's review, each of the questions and our corresponding response is included in the text of this letter. Necessary supporting documentation for each response is provided in attachments to this amendment.

A1. The Agency asked us to evaluate/explain an out-of-trend assay value o) at the 78 week test station (page 43 of our March 29, 2001 amendment).

Response: We have reviewed the supporting data and the reported result .s an accurate reflection of the actual measured value (it isn't a typographical error). The review of documentation at the time of testing and, more recently in response to the Agency's question, did not disclose any reason (technician error, instrument calibration, etc.) to doubt the accuracy of the measurement. It is clear that the value, although within specification, is anomalous. This is supported by the value of % measured at the same time for the second sample stored under the same conditions. The trend for the remaining data suggests that the actual potency of the solution product continues to be about 100%.

A2. The Agency requested that we revise the Droplet Size specifications to microns for D_{50}, and NM nicron for D_{90}).

We believe that this correspondence provides a thorough response to the questions raised in the Agency's April 25, 2000 telephone correspondence. As such, we hope that a rapid review and subsequent product approval will be forthcoming. The information contained in this supplement is confidential and as such should be handled in accordance with the provisions established in 21 CFR 314.430.

In accordance with 21 CFR 314.96 (b), we certify that a true copy of the information contained in this amendment has been forwarded to FDA's Orlando District Office.

If you have any questions regarding this correspondence or need additional information, please contact Joe Hawkins by telephone at (813) 975-7700 ext. 7102, or by fax at (813) 975-7757.

Sincerely,

Joseph B. Hawkins
Manager, Regulatory Affairs

Enclosure

8500 Hidden River Parkway
Tampa FL 33637

813 975 7700
Fax 813 975 7757

BAUSCH
& LOMB

April 6, 2001

Mr. Gary Buehler
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
MPN II, HFD-600
7500 Standish Place
Rockville, MD 20857

Re: Controlled Correspondence
ANDA 75-702, Cromolyn Sodium Nasal Solution, USP (40 mg/mL)
Request for Reclassification of Amendment

Dear Mr. Buehler:

The purpose of this correspondence is to request reclassification of our March 29, 2001 response to the Agency's January 19, 2001, "not approvable" letter for the above referenced application. In that letter the Agency indicated that our response would be considered a MAJOR amendment. Virtually all of the significant issues raised in the Agency's letter resulted from an amendment submitted June 19, 2000, that added a 13 mL fill size to the application. In a letter submitted March 13, 2001, we requested that the Agency withdraw that amendment. We believe that our response now meets the Agency's criteria for classification as a minor amendment. It should be possible to review the remaining chemistry issues within one hour. We acknowledge the statement regarding withdrawal of portions of an application in the Agency's guidance for industry regarding the classification of amendments. That guidance indicates that this is generally not a basis for reclassification of an amendment. In light of other changes currently taking place in the Office of Generic Drugs, we believe this case merits consideration.

This is an important issue for Bausch & Lomb and your thoughtful consideration of our request is appreciated. Please do not hesitate to contact us if we can provide any additional information.

Sincerely,

J B. Hawk

Joseph B. Hawkins
Manager, Regulatory Affairs

8500 Hidden River Parkway
Tampa FL 33637

813 975 7700
Fax 813 975 7757

Response reclassified to MINOR. See Control # 01-189
M Smith 4/11/01

March 29, 2001

BAUSCH & LOMB

N/A 2 M

ORIG AMENDMENT

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

Re: ANDA 75-702
Cromolyn Sodium Nasal Solution, USP (40 mg/mL)
Major Amendment – Chemistry and Labeling Issues

Dear Sir or Madam:

The purpose of this correspondence is to respond to the Agency's January 19, 2001, "not approvable" letter for the above referenced application. In that letter the Agency indicated that our response would be considered a major amendment. A copy of the Agency's letter is provided in Attachment 1.

To facilitate the Agency's review, each of the questions and our corresponding response is included in the text of this letter. Necessary supporting documentation for each response is provided in attachments to this amendment.

A1.

s

Response:
fill :

A2. Regarding Droplet size testing of the drug product at release and on stability, you have revised the specifications for Droplet Size, however, there is no rationale for the established acceptance criteria. You should submit your reasons for establishing the specifications you are proposing based on results of Droplet Size evaluation of the exhibit batches).

Page(s) 2

Contain Trade Secret, Commercial/Confidential Information and are not releasable.

3/29/01

Lower specification:
Upper specification:

The target value (currently is based on data from the most recent filling equipment qualification and may be adjusted in the future, provided all containers are maintained within the range between the lower and upper specifications. These specifications ensure that the product consistently delivers the labeled number of sprays.

A10. Regarding the Fill Volume specifications for the package size, a minimum fill

Response:
fror

Bausch & Lomb Pharmaceuticals also acknowledges the following comments:

B1. The Agency's request for additional stability data generated on the stability lots since the last submission.

Response: Stability data for samples stored for 18 months at room temperature is provided in Attachment 2.

B2. Labeling deficiencies, if any, will also need to be addressed in your response.

Response: Revised Labeling is provided in Attachment B.

We believe that this correspondence provides a thorough response to the questions raised in the Agency's January 19, 2001 correspondence. As such, we hope that a rapid review and subsequent product approval will be forthcoming. The information contained in this supplement is confidential and as such should be handled in accordance with the provisions established in 21 CFR 314.430.

In accordance with 21 CFR 314.96 (b), we certify that a true copy of the information contained in this amendment has been forwarded to FDA's Orlando District Office.

If you have any questions regarding this correspondence or need additional information, please contact Joe Hawkins by telephone at (813) 975-7700 ext. 7102, or by fax at (813) 975-7757.

Sincerely,

Joseph B. Hawkins
Manager, Regulatory Affairs

Enclosure

Pharmaceuticals, Inc. 8500 Hidden River Parkway Tampa FL 33637 813 975 7700 Fax 813 975 7770

June 26, 2000

BAUSCH & LOMB

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

ORIG AMENDMENT
N/A C

Re: ANDA 75-702
Cromolyn Sodium Nasal Solution, USP (40 mg/mL)
Major Amendment – Chemistry and Labeling Issues

Dear Sir or Madam:

The purpose of this correspondence is to respond to the Agency's March 16, 2000, "not approvable" letter for the above referenced application. In that letter the Agency indicated that our response would be considered a major amendment. A copy of the Agency's letter is provided in Attachment 1.

To facilitate the Agency's review, each of the questions and our corresponding response is included in the text of this letter. Necessary supporting documentation for each response is provided in attachments to this amendment.

A.1.

vised

A.2.

A.3.

RECD
JUN 27 2000
OGD
EVALUATION AND RESEARCH

A.4.a. Regarding the tests and specifications for the drug product release: Specifications for Total Aerobic Count, Total Yeasts and Hold, and Individual Indicator Pathogens should be indicated on the Test and Specification Sheet. In addition, please add P. Cepacia as one of the individual indicator pathogens.

A.4.b. Regarding the tests and specifications for the drug product release: Droplet Size limits for the Nasal Spray should include a minimum of three specifications (e.g. D_{10}, D_{50} and D_{90}).

Response: The drug product release specifications have been revised as requested. The revised specifications are provided in Attachment 3 (page 19).

A.4.c. Regarding the tests and specifications for the drug product release: Please include the USP test (TLC) for related substances in addition to your test.

Response: The drug product release specifications have been revised as requested. The revised specifications are provided in Attachment 3 (page 19).

A.4.d. Regarding the tests and specifications for the drug product release: Please utilize the APHA color test, or correlate the APHA color with the BP test.

Response: A correlation study between BP and APHA color standards has been performed. This study suggests the following correlation of BP Reference Standard ranges to the APHA specification ranges:

BP Color Reference Standard	Associated APHA Values
Y1	1200-1600
Y2	900-1000
Y3	460-700
Y4	200-280
Y5	120-160
Y6	40-80
Y7	10-50

Each BP Color Reference Standard represents a range of APHA values because there is some subjective variability associated with the evaluation of these values. Since a correlation between the BP Color Reference Standard and APHA standards has been established, we will continue using the BP compendial method to determine color.

A.4.e. Regarding the tests and specifications for the drug product release: The Total Related Substances limit in the test should be tightened.

A.4.f. Regarding the tests and specifications for the drug product release: A Test and Specification for Fill Volume should be established.

Attachment 3 (page 23).

A.4.g. Regarding the tests and specifications for the drug product release: The Mean Spray Weight specifications appear excessively broad. There should also be a specification for individual spray weight, in addition to the mean spray weight.

Response: The drug product release specifications have been revised as requested. The revised specifications are provided in Attachment 3 (page 21).

A.4.h. Regarding the tests and specifications for the drug product release: Regarding the Quantity Delivered per Spray; if the drug product fails the 2nd tier test, then the batch will fail. There should be no provision for 3rd tier testing.

Response: The drug product release specifications have been revised as requested. The revised specifications are provided in Attachment 3 (page s21 & 22).

A.4.i. Regarding the tests and specifications for the drug product release: An additional test and specification for Quantity Delivered per Spray through container life should be performed to demonstrate that the spray pump delivers the appropriate dose at the end of container life (200 actuations).

Response: The drug product release specifications have been revised as requested. The revised specifications are provided in Attachment 3 (page 22).

A.4.j. Regarding the tests and specifications for the drug product release: Allowance of

There should be no significant loss of either during processing. The lower assay limit for both of these components should

Response: The drug product release specifications have been revised as requested. The revised specifications are provided in Attachment 3 (page 20).

A.5.a. The Marketed Drug Product Stability Protocol should be revised to reflect the following: All tests should be performed at the 24 month time point, since a tentative 24 month expiration dating period is proposed.

Response: The Marketed Stability Protocol provided in the original application (starting on page 1120) specified that all tests are to performed at the 24 month test station. The revised Marketed Stability Protocol provided in Attachment 4 still contains this requirement.

A.5.b. The Marketed Drug Product Stability Protocol should be revised to reflect the following: Please perform post-approval studies on the first 3 batches in both the inverted and upright positions (annual testing of upright samples is acceptable). Elimination of upright testing through a supplement to the ANDA may be appropriate after the first 3 batches are evaluated.

Response: The Marketed Stability Protocol has been revised to include testing of samples stored in both upright and horizontal positions. The revised protocol is provided in Attachment 4 (pages 25 through 32).

A.5.c. The Marketed Drug Product Stability Protocol should be revised to reflect the following: Specifications for Total Aerobic Count, Total Yeasts and Mold, and Individual Indicator Pathogens should be indicated on the Test and Specification Sheet. In addition, please add P. Cepacia as one of the individual indicator pathogens.

Response: The drug product stability specifications have been revised as requested. The revised Marketed Stability Protocol is provided in Attachment 4 (pages 28 & 32).

A.5.d. The Marketed Drug Product Stability Protocol should be revised to reflect the following: Droplet Size limits for the Nasal Spray should include a minimum of three specifications).

Response: The drug product stability specifications have been revised as requested. The revised Marketed Stability Protocol is provided in Attachment 4 (pages 26 & 30).

A.5.e. The Marketed Drug Product Stability Protocol should be revised to reflect the following: Please utilize the APHA color test, or correlate the APHA color with the UP test.

Response: A correlation study between BP and APHA color standards has been performed and is described in our response to question **A.4.d**. Since a correlation between the BP Color Reference Standard and APHA standards has been established, we will continue using the BP compendial method to determine color.

A.5.f. The Marketed Drug Product Stability Protocol should be revised to reflect the following: The Total Related Substances limit in the test should be tightened.

Response: The drug product stability specifications have been revised as requested. The revised Marketed Stability Protocol is provided in Attachment 4 (pages 26 & 30).

A.5.g. The Marketed Drug Product Stability Protocol should be revised to reflect the following: The Mean Spray Weight specifications appear excessively broad. There should also be a specification for individual spray weight, in addition to the mean spray weight.

Response: The drug product stability specifications have been revised as requested. The revised Marketed Stability Protocol is provided in Attachment 4 (pages 26 & 30).

A.5.h. The Marketed Drug Product Stability Protocol should be revised to reflect the following: Regarding the Quantity Delivered per Spray; if the drug product fails the 2nd tier test, then the batch fails. There should be no provision for 3rd tier testing.

Response: The drug product stability specifications have been revised as requested. The revised Marketed Stability Protocol is provided in Attachment 4 (pages 27 & 31).

A.5.i. The Marketed Drug Product Stability Protocol should be revised to reflect the following: An additional test and specification for Quantity Delivered per spray through container life on stability should be performed to demonstrate that the pump spray delivers the appropriate dose at the end of container life (200 actuations) on aged drug product.

Response: The drug product stability specifications have been revised as requested. The revised Marketed Stability Protocol is provided in Attachment 4 (pages 27 & 31).

A.6. Please provide revised drug substance acceptance specifications and drug product release and stability specifications considering the above deficiencies. Please also provide new Certificates of Analysis for the drug substance and drug product demonstrating compliance with the revised specifications.

Response: The drug substance specifications and the drug product release and stability specifications have been revised as requested. The revised specifications are provided in Attachments 2, 3 & 4. The additional testing requested by the Agency has been performed and a revised Certificate of Analysis for the drug product is enclosed in Attachment 5. Heavy metals test results for the exhibit batch drug substance lot are also enclosed in Attachment 5 (page 35). All other drug substance test results (provided in the original submission) meet the revised specifications.

Bausch & Lomb Pharmaceuticals also acknowledges the following comments:

1. That the firms referenced in the application relative to the manufacture and testing of the product must be in compliance with current GMP's at the time of approval.

2. The Agency's request for additional long-term stability data. A stability report which includes all data currently available is enclosed in Attachment 6.

3. Our response must also address the labeling deficiencies. Revised Labeling is provided in Attachment 7.

4. Our bioequivalence information is pending review. A response to the Agency's March 16, 2000 letter regarding Bioequivalence issues was submitted to the Office of Generic Drugs April 30, 2000.

We believe that this correspondence provides a thorough response to the questions raised in the Agency's March 16, 2000 letter. As such, we hope that a rapid review and subsequent product approval will be forthcoming. The information contained in this supplement is confidential and as such should be handled in accordance with the provisions established in 21 CFR 314.430.

In accordance with 21 CFR 314.96 (b), we certify that a true copy of the information contained in this amendment has been forwarded to FDA's Orlando District Office.

If you have any questions regarding this correspondence or need additional information, please contact Joe Hawkins by telephone at (813) 975-7700 ext. 7102, or by fax at (813) 975-7757.

Sincerely,

Joseph B. Hawkins
Manager, Regulatory Affairs

Enclosure

Pharmaceuticals, Inc. 8500 Hidden River Parkway Tampa FL 33637 813 975 7700 Fax 813 975 7770

May 26, 2000

BAUSCH & LOMB

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

NEW CORRESP
NC awarded & forwarded to ND 6/7/00

Re: ANDA 75-702
Cromolyn Sodium Nasal Solution, USP (40 mg/mL)
Telephone Amendment

Dear Sir or Madam:

The purpose of this correspondence is to amend the above referenced application. Specifically, we wish to correct the 356h form provided in our April 28, 2000 Bioequivalence Amendment.

The enclosed FDA Form 356h has been corrected to reference the appropriate listed drug (Nasalcrom® Cromolyn Sodium Nasal Solution, USP, marketed by Pharmacia & Upjohn Consumer Healthcare).

The information contained in this supplement is confidential and as such should be handled in accordance with the provisions established in 21 CFR 314.430.

In accordance with 21 CFR 314.96 (b), we certify that a true copy of the information contained in this amendment has been forwarded to FDA's Orlando District Office.

If you have any questions regarding this correspondence or need additional information, please contact Joe Hawkins by telephone at (813) 975-7700 ext. 7102, or by fax at (813) 975-7757.

Sincerely,

JB Hawk

Joseph B. Hawkins
Manager, Regulatory Affairs

Enclosure

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
MAY 30 2000
OGD

6-5-00

Pharmaceuticals, Inc. 8500 Hidden River Parkway Tampa FL 33637 813 975 7700 Fax 813 975 7770

ORIG AMENDMENT
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BAUSCH & LOMB

April 28, 2000

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: ANDA 75-702
Cromolyn Sodium Nasal Solution, 40 mg per mL
Bioequivalence Amendment

Dear Sir or Madam:

The purpose of this correspondence is to address the Agency's facsimile communications, dated March 16, 2000, for the above referenced application. Enclosed in Attachment A (in Volume 2, p. 170) of this submission is a copy of the March 16th OGD communications.

To facilitate the Agency's review, each of the questions and our corresponding response is included in the text of this letter. Necessary supporting documentation for each response is provided in attachments to this amendment.

1. **For the unit dose testing you state that the test was not blinded because of mechanical actuation of the bottle, mechanical weighing of the bottle, and the fact that the scintillation vial is also weighed. The assay result is checked against the 2 spray weights, so the chances for bias are essentially eliminated. Please submit the standard operating procedure (SOP) describing that blinding was not necessary.**

   Response: The procedures, standard operating procedures (SOPs), that describe the testing are contained in the submitted SOPs and C-spec in the original ANDA filing. SOP . . . (page 1034) describes the procedure for measuring spray weight. SOP (page 1063) and C-spec C-1536 (page 980) describes the measuring of spray weight using

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OGD
EVALUATION AND RESEARCH

2.a. Cascade Impaction: Please provide the SOP for this method including the flow rate and nature of throat.

Response: Enclosed in Attachment C is the Nasal Instrument Procedure "Determination of Droplet Size from Nasal Sprays by

test procedure is contained in this document.

2.b. Cascade Impaction: Was the drug deposited on stages 2-7 measured? If so, please provide the data.

Response: Table 3(b) of the ANDA original submission contained data for only the Throat, Stage 0, Stage 1 and the filter. Stages 2 and 3 were analyzed by testing, but the numbers were so small that they were not itemized in the submitted table. We have revised Table 3(b) in Attachment D to contain Stages 2 and 3. Although the testing was performed with all 8 stages included in the setup, stages 4 through 7 were not analyzed by Experimental testing showed recoveries for stages 4 – 7 to be below the Limit of Quantitation of the method used for alysis. Summary tables, and individual data for cascade impaction are also contained in Attachment D.

3.a. Spray Pattern: It is not clear if the same threshold was used for the test and reference products. How many samples were analyzed with a given threshold? What was the level of fluctuation between the various threshold levels? Please furnish the records to support the statement.

Response: The threshold was set at or all testing. This threshold value is listed at the top of the printout page. Refer to the resubmitted spray pattern calculations measuring through the center of the spray patterns (Attachment F).

3.b. Spray Pattern: Please provide a complete SOP for the method used for spray pattern testing. The method described in volume 3, page 986 does not include [redacted] System.

Response: Enclosed in Attachment E is the Nasal Instrument Procedure "Measurement of Spray Pattern of Cromolyn Sodium Nasal Solution USP (40mg/ml) 26ml fill size Using [redacted] System in Conjunction with the [redacted]. All information regarding the test procedure is contained in this document.

3.c. Spray Pattern: By definition, diameters should pass through the centers of spray patterns. Markings on photocopies of spray pattern for smallest and largest diameter do not go through the center of the spray patterns. Please recalculate the data making markings going through the center of the spray pattern rather than center of the plate.

Response: We have recalculated the spray pattern data so that diameters pass through the center of the spray pattern. Attachment F contains all the spray patterns, the tables of data, and the statistical analysis of the data.

3.d. Spray Pattern: Please submit color photographs representing placebo and active drug spray patterns.

Response: Enclosed in Attachment G are digital color print of the TLC plate sitting inside the light box, and [redacted] representing placebo and active drug spray patterns.

For visualization of the spray pattern on the plate, [redacted] at a wavelength of [redacted] was used to illuminate the plate bright green, leaving a dark pattern wherever the drug substance rests on the plate.

3.d. continued

4.a. Plume geometry data: What are the units of [illegible] used to calculate height and width? Were these parameters calculated based on the [illegible] shown in color photo. or marking on photocopies?

Response: The units of the [illegible] or the photographs are square inches. Enclosed in Attachment H of this submission is the Nasal Instrument Procedure [illegible] "Measurement of F [illegible] Photographs of Cromolyn Sodium Nasal Solution USP (40mg/ml) 26ml fill size to Determine Plume Geometry Using [illegible] System in Conjunction with the [illegible] The test procedure

[illegible] (2.54 cm) by the Leco measurement of a grid square (0.4 cm).

4.b. Plume geometry data: Quantitation of plume angle based on lines drawn on photocopies is inappropriate because on many patterns lines go through the plume images, rather than representing the periphery of these plume. Please revise the plume geometry data based on plumes shown in color photograph.

Response: In Response 4.a., Attachment H contains a detailed description of the method for measuring the plume angles with [illegible] System. Part 4.7 of the method describes the analysis of the plume angle. It is believed that the reviewer's comment regarding the inappropriate pattern lines refers to photographs in the later stages of the plume development. As the plume starts to degrade and fall down due to gravity, the plume angle is not affected by this downward motion of droplets and widening of the upper part of the plume. This can

4.b. continued

be clearly seen in the tangent lines from the tip of the actuator up the side of the plume. This does not change. Only the top of the plume widens in a mushroom shape due to this downward motion. We do not believe that this widening effect should be accounted for in the analysis of the plume angle. Consequently, we have not provided revised plume angle data since we believe the angles were appropriately calculated initially.

4.c. Plume geometry data: For some bottles plume height and width are not reported at all time delays. Please provide complete data sets.

Response: In response 4.a., Attachment H contains a detailed description of the method for measuring the plume height and width with the System. Attachment I contains the System printouts of the plumes calculating the height and width, tables of the data, and the statistical analysis. The complete data sets are provided. The data was arrived at by remeasuring the previously

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5. The innovator product is marketed in two fill-sizes: 13 a and 26 mL. Your correspondences dated October 14, 1999 and October 25, 1999 mention packaging configurations of 15 mL and 26 mL fill size. The correspondence dated October 21, 1399 mentions packaging configurations of . and 26 mL fill size. In the original submission, you provided priming retention data for . and 26 a fill sizes with a note that information regarding the L fill size may be ignored since this packaging configuration is not included in the application. Please explain these discrepancies.

Response: In a separate bioequivalence amendment, data will be provided for the package size. It was our initial intention to file for both packages, however, we were not able to accomplish this goal. The size will now be amended to the application. The ll size uses a 15 mL container.

6. **The procedure for blinding test and reference product bottles given on page 1113, Volume 3, is for desmopressin acetate nasal spray. Please provide the blinding procedure for cromolyn sodium nasal solution, which is the subject of this application.**

   Response: Enclosed in Attachment J is the blinding procedure for Cromolyn Sodium Nasal Solution.

We believe that this correspondence provides a thorough response to the questions raised in the Agency's March 16, 2000 Bioequivalence letter. The information contained in this amendment is confidential and as such should be handled in accordance with the provisions established in 21 CFR 314.430.

If you have any questions regarding this correspondence or need additional information, please contact Joe Hawkins by telephone at (813) 975-7700 ext. 7102, or by fax at (813) 975-7757.

Sincerely,

Joseph B. Hawkins
Manager, Regulatory Affairs

Enclosure

Pharmaceuticals, Inc. 8500 Hidden River Parkway Tampa FL 33637 813 975 7700 Fax 813 975 7770

BAUSCH & LOMB

October 25, 1999

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

Re: ANDA 75-702
Cromolyn Sodium Nasal Solution, USP (40 mg/mL)
Telephone Amendment

Dear Sir or Madam:

The purpose of this correspondence is to respond to an October 22, 1999 telephone request from Paras Patel in the Office of Generic Drugs. As requested, we are providing the following:

1. A revised form 356h which lists Nasalcrom® Nasal Spray, marketed by Pharmacia & Upjohn Consumer Healthcare, as the reference listed drug.
2. A waiver request for in vivo bioequivalence, pursuant to 21 CFR 320.22(b)(3).
3. A written explanation for the disposition of product not used in the packaging configurations for which we are seeking approval.

In accordance with 21 CFR 314.96 (b), we certify that a true copy of the information contained in this amendment has been forwarded to FDA's Orlando District Office.

The information contained in this supplement is confidential and as such should be handled in accordance with the provisions established in 21 CFR 314.430.

If you have any questions regarding this correspondence, please contact me at the above address or by telephone at (813) 975-7700 extension 7102.

Sincerely,

JB. Hawk

Joseph B. Hawkins
Manager,
Regulatory Affairs

Enclosure

22.99
2.1

Pharmaceuticals, Inc. 8500 Hidden River Parkway Tampa FL 33637 813 975 7700 Fax 813 975 7770

BAUSCH & LOMB

October 21, 1999

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

NEW CORRESP
NC

Re: ANDA 75-702
Cromolyn Sodium Nasal Solution, USP (40 mg/mL)
Telephone Amendment

Dear Sir or Madam:

The purpose of this correspondence is to respond to an October 20, 1999 telephone request from Paras Patel in the Office of Generic Drugs. Specifically, we are providing a concise summary of the packaged product accountability information already in the application.

A copy of the summary is provided following the 356h.

In accordance with 21 CFR 314.96 (b), we certify that a true copy of the information contained in this amendment has been forwarded to FDA's Orlando District Office.

The information contained in this supplement is confidential and as such should be handled in accordance with the provisions established in 21 CFR 314.430.

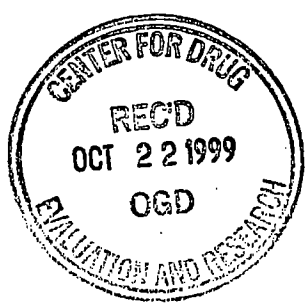
If you have any questions regarding this correspondence, please contact me at the above address or by telephone at (813) 975-7700 extension 7102.

Sincerely,

JB Hawkins

Joseph B. Hawkins
Manager,
Regulatory Affairs

Enclosure



Pharmaceuticals, Inc. | 8500 Hidden River Parkway Tampa FL 33637 | 813 975 7700 Fax 813 975 7770

BAUSCH & LOMB

October 14, 1999

75-702
NEW CORRESP
NC

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

Re: Cromolyn Sodium Nasal Solution, USP (40 mg/mL)
Gratuitous Amendment (Minor Corrections)

Dear Sir of Madam:

The purpose of this correspondence is to correct typographical/editorial errors noted during a review of our ANDA for our Cromolyn Sodium Nasal Solution submitted September 13, 1999.

Four revised pages are enclosed. Each page is numbered to indicate its proper location in the application. The pages replace those having the same page numbers in the original application submission.

In accordance with 21 CFR 314.96 (b), we certify that a true copy of the information contained in this amendment has been forwarded to FDA's Orlando District Office.

The information contained in this supplement is confidential and as such should be handled in accordance with the provisions established in 21 CFR 314.430.

If you have any questions regarding this correspondence, please contact me at the above address or by telephone at (813) 975-7700 extension 7102.

Sincerely,

J B. Hawk

Joseph B. Hawkins
Manager,
Regulatory Affairs

Enclosure

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
OCT 15 1999
OGD

(Attached is in A1.17)

Pharmaceuticals, Inc. | 8500 Hidden River Parkway Tampa FL 33637 | 813 975 7700 Fax 813 975 7770

NEW CORRESP

BAUSCH & LOMB

September 14, 1999

75-702

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

Re: Cromolyn Sodium Nasal Solution, USP (40 mg/mL)
September 13, 1999 ANDA Submission – Additional Information

Dear Sir or Madam:

This correspondence includes Information which was inadvertently omitted from our September 13, 1999 Abbreviated New Drug Application for Cromolyn Sodium Nasal Solution, USP. Specifically, we are providing the original of Volume 17, which contains photographs used for bioequivalence plume geometry evaluation. A copy of the volume was provided with the original submission.

If you have any questions regarding this correspondence, please contact me at the above address or by telephone at (813) 975-7700 extension 7102.

Sincerely,

Joseph B. Hawkins
Manager, Regulatory Affairs
8500 Hidden River Parkway
Tampa, Fl 33637

enclosure

1 copy

Pharmaceuticals, Inc. | 8500 Hidden River Parkway Tampa FL 33637 | 813 975 7700 Fax 813 975 7770

September 13, 1999

BAUSCH & LOMB

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855-2773

Re: Cromolyn Sodium Nasal Solution, USP (40 mg/mL)
ANDA Submission

Dear Sir or Madam:

In accordance with the provisions set forth in 21 CFR 314.94, we are submitting this abbreviated new drug application, in duplicate, for Cromolyn Sodium Nasal Solution, USP.

This application contains 17 volumes. An analytical methods validation package is provided under separate cover.

Standard operating procedures (SOP's) are provided in this application as an aid to the review process. Revisions may be made to these SOP's after appropriate in-house review and approval. Changes which influence the manufacture of Cromolyn Sodium Nasal Solution, USP, will be reported to the Agency as established in 21 CFR 314.70.

Bausch & Lomb Pharmaceuticals commits to work with the Agency to resolve any methods validation issues after approval.

In accordance with 21 CFR 314.94 (d)(5), we certify that a true copy of the information contained in this application has been forwarded to FDA's Orlando District Office.

If you have any questions regarding this correspondence, please contact me at the above address or by telephone at (813) 975-7700 extension 7102.

Sincerely,

Joseph B. Hawkins
Manager, Regulatory Affairs
8500 Hidden River Parkway
Tampa, Fl 33637

enclosure