CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 90-954

Name: Cromolyn Sodium Oral Solution, Concentrate, 100 mg/5mL, Unit-dose Ampules

Sponsor: Genera Pharmaceuticals, LLC

Approval Date: December 18, 2009

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 90-954

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 90-954

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 090954

Genera Pharmaceuticals, LLC
Attention: V. Ray Nathan, Ph.D., MBA
President
13734 Trento Place
San Diego, CA 92130

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated October 22, 2008, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Cromolyn Sodium Oral Solution, Concentrate, 100 mg/5mL, Unit-dose Ampules.

Reference is also made to your amendments dated May 4, July 24, August 7 and November 23, 2009.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Cromolyn Sodium Oral Solution Concentrate, 100 mg/5 mL, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug, Gastrocrom of Azur Pharma, Inc.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

We note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS, See 505-1(i).

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs

should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

Within 14 days of the date of this letter, submit updated content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the approved labeling. Upon receipt and verification, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission as "***Miscellaneous Correspondence - SPL for Approved ANDA 090954***".

Sincerely yours,

{See appended electronic signature page}

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-90954	ORIG-1	GENERA PHARMACEUTICALS LLC	CROMOLYN SODIUM

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

/s/

ROBERT L WEST
12/18/2009
Deputy Director, for Gary Buehler

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 90-954

LABELING REVIEWS

APPROVAL SUMMARY #1
LABELING REVIEW BRANCH

1. APPLICANT INFORMATION:

ANDA Number	90-954
Date of Submission	23 NOV2009
Applicant	Genera pharm (Catalent)
Drug Name	Cromolyn Sodium Oral Solution, Concentrate
Strength(s)	100 mg/5 mL unit dose ampules

Labels and Labeling Summary - FPL	
Container	5 mL- Unit dose ampules- Satisfactory Nov. 23, 2009 \\CDSESUB1\EVSPROD\ANDA090954\\0004\m1\us\labeling\viewing-graphic\final\pi.pdf
Pouch	8s- 5 mL- Satisfactory on Mov. 23, 2009
carton	\\CDSESUB1\EVSPROD\ANDA090954\\0005\m1\us\labeling\viewing-graphic\final\pouch.pdf \\CDSESUB1\EVSPROD\ANDA090954\\0005\m1\us\labeling\viewing-graphic\final\carton.pdf
Insert	Satisfactory in FPL Aug 7, 2009 \\CDSESUB1\EVSPROD\ANDA090954\\0004\m1\us\labeling\viewing-graphic\final\pi.pdf
Patient Leaflet	\\CDSESUB1\EVSPROD\ANDA090954\\0004\m1\us\labeling\viewing-graphic\final\pi.pdf

2. NOTE TO CHEMIST: None.

3. MODEL LABELING:

Reference Listed Drug	
RLD on the 356(h) form	Gastrocom
NDA Number	20-479
RLD established name	Cromolyn Sodium Oral Concentrate
Firm	Azur
Currently approved PI	S-005
AP Date	13 FEB 2003

4. REFERENCE LISTED DRUG PATENTS/EXCLUSIVITIES: See above.

Patent Data For NDA

Patent No	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None					

Exclusivity Data For NDA

Code/sup	Expiration	Description	*Labeling impact*
None		None	

5. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM: Manufactured by:

Catalent Pharma LLC, Solutions, Woodstock, IL 60098 …..Marketed by: Genera Pharmaceuticals, LL**C,** San Diego CA 92130. Genera does not appear to be the distributor now. The distributor has changed to PACK Pharmaceuticals, LLc in Buffalo Grove, IL

6. CONTAINER/CLOSURE; 5 mL Unit dose ampules LDPE.

7. INACTIVE INGREDIENTS

The description of the inactive ingredients in the insert labeling appears accurate according to the composition statement. Each 5 mL ampule of cromolyn sodium oral concentrate contains 100 mg cromolyn sodium, USP, in purified water. [Vol. A1.1 pg].

8. PACKAGING CONFIGURATIONS

RLD: 96 unit dose ampules (8 ampules per pouch)
ANDA: Same.

9. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

USP: Not a USP item.
RLD: Store at 20-25C (68- 77F). [See USP CRT]. Protect from light product.
ANDA: Same

10. DISPENSING STATEMENTS COMPARISON

USP: None :RLD:
ANDA (*Insert*):

11. BIOAVAILABILITY/BIOEQUIVALENCE:

12. (b) (4) is the way the firm states the established name. However, I have instructed the firm to revise it to include the dosage form as follows: Cromolyn Sodium Oral Solution Concentrate

---

Date of Review: 12/01/09 Date of Submission: 23 NOV 2009

Primary Reviewer: Angela Payne Date:

Team Leader: John Grace Date:

---

cc:

ANDA: 90-954
DUP/DIVISION FILE
HFD-613/Apayne/JGrace (no cc)
V:\FIRMSAM\catalent.genera\LTRS&REV\90954ap1labdrtsreview.doc
Review

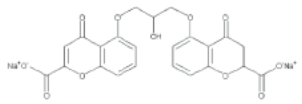
Cromolyn Sodium Oral Solution, Concentrate

℞ Only
Rev. 07/09
GEN 01B

For Oral Use Only – Not for Inhalation or Injection.

DESCRIPTION: Each 5 mL ampule of Cromolyn Sodium Oral Solution, Concentrate contains 100 mg cromolyn sodium, USP, in purified water. Cromolyn sodium is a hygroscopic, white powder having little odor. It may leave a slightly bitter aftertaste. Cromolyn Sodium Oral Solution, Concentrate is clear, colorless, and sterile. It is intended for oral use.

Chemically, cromolyn sodium is disodium 5,5'-[(2-hydroxytrimethylene) dioxy]bis[4-oxo-4H-1-benzopyran-2-carboxylate]. The empirical formula is $C_{23}H_{14}Na_2O_{11}$; the molecular weight is 512.34. Its chemical structure is:



Pharmacologic Category: Mast cell stabilizer

Therapeutic Category: Antiallergic

CLINICAL PHARMACOLOGY: In vitro and in vivo animal studies have shown that cromolyn sodium inhibits the release of mediators from sensitized mast cells. Cromolyn sodium acts by inhibiting the release of histamine and leukotrienes (SRS-A) from the mast cell. Cromolyn sodium has no intrinsic vasoconstrictor, antihistamine, or glucocorticoid activity.

Cromolyn sodium is poorly absorbed from the gastrointestinal tract. No more than 1% of an administered dose is absorbed by humans after oral administration, the remainder being excreted in the feces. Very little absorption of cromolyn sodium was seen after oral administration of 500 mg by mouth to each of 12 volunteers. From 0.28 to 0.50% of the administered dose was recovered in the first 24 hours of urinary excretion in 3 subjects. The mean urinary excretion of an administered dose over 24 hours in the remaining 9 subjects was 0.45%.

CLINICAL STUDIES: Four randomized, controlled clinical trials were conducted with Cromolyn Sodium Oral Solution, Concentrate in patients with either cutaneous or systemic mastocytosis; two of which utilized a placebo-controlled crossover design, one utilized an active controlled (chlorpheniramine plus cimetidine) crossover design, and one utilized a placebo-controlled parallel group design. Due to the rare nature of this disease, only 36 patients qualified for study entry, of whom 32 were considered evaluable. Consequently, formal statistical analyses were not performed. Clinically significant improvement in gastrointestinal symptoms (diarrhea, abdominal pain) were seen in the majority of patients with some improvement also seen for cutaneous manifestations (urticaria, pruritus, flushing) and cognitive function. The benefit seen with Cromolyn Sodium Oral Solution, Concentrate 200 mg QID was similar to chlorpheniramine (4 mg QID) plus cimetidine (300 mg QID) for both cutaneous and systemic symptoms of mastocytosis.

Clinical improvement occurred within 2-6 weeks of treatment initiation and persisted for 2-3 weeks after treatment withdrawal. Cromolyn Sodium Oral Solution, Concentrate did not affect urinary histamine levels or peripheral eosinophilia, although neither of these variables appeared to correlate with disease severity. Positive clinical benefits were also reported for 37 of 51 patients who received Cromolyn Sodium Oral Solution, Concentrate in United States and foreign humanitarian programs.

Cromolyn Sodium Oral Solution, Concentrate

GEN01B

INDICATIONS AND USAGE: Cromolyn Sodium Oral Solution, Concentrate is indicated in the management of patients with mastocytosis. Use of this product has been associated with improvement in diarrhea, flushing, headaches, vomiting, urticaria, abdominal pain, nausea, and itching in some patients.

CONTRAINDICATIONS: Cromolyn Sodium Oral Solution, Concentrate is contraindicated in those patients who have shown hypersensitivity to cromolyn sodium.

WARNINGS: The recommended dosage should be decreased in patients with decreased renal or hepatic function. Severe anaphylactic reactions may occur rarely in association with cromolyn sodium administration.

PRECAUTIONS: In view of the biliary and renal routes of excretion of Cromolyn Sodium Oral Solution, Concentrate, consideration should be given to decreasing the dosage of the drug in patients with impaired renal or hepatic function.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: In carcinogenicity studies in mice, hamsters, and rats, cromolyn sodium had no neoplastic effects at intraperitoneal doses up to 150 mg/kg three days per week for 12 months in mice, at intraperitoneal doses up to 53 mg/kg three days per week for 15 weeks followed by 17.5 mg/kg three days per week for 37 weeks in hamsters, and at subcutaneous doses up to 75 mg/kg six days per week for 18 months in rats. These doses in mice, hamsters, and rats are less than the maximum recommended daily oral dose in adults and children on a mg/m² basis.

Cromolyn sodium showed no mutagenic potential in Ames Salmonella/microsome plate assays, mitotic gene conversion in Saccharomyces cerevisiae and in an in vitro cytogenetic study in human peripheral lymphocytes.

In rats, cromolyn sodium showed no evidence of impaired fertility at subcutaneous doses up to 175 mg/kg in males (approximately equal to the maximum recommended daily oral dose in adults on a mg/m² basis) and 100 mg/kg in females (less than the maximum recommended daily oral dose in adults on a mg/m²basis).

Pregnancy: Pregnancy Category B. In reproductive studies in pregnant mice, rats, and rabbits, cromolyn sodium produced no evidence of fetal malformations at subcutaneous doses up to 540 mg/kg in mice (approximately equal to the maximum recommended daily oral dose in adults on a mg/m² basis) and 164 mg/kg in rats (less than the maximum recommended daily oral dose in adults on a mg/m² basis) or at intravenous doses up to 485 mg/kg in rabbits (approximately 4 times the maximum recommended daily oral dose in adults on a mg/m² basis). There are, however, no adequate and well controlled studies in pregnant women.

Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Drug Interaction During Pregnancy: In pregnant mice, cromolyn sodium alone did not cause significant increases in resorptions or major malformations at subcutaneous doses up to 540 mg/kg (approximately equal to the maximum recommended daily oral dose in adults on a mg/m² basis). Isoproterenol alone increased both resorptions and major malformations (primarily cleft palate) at a subcutaneous dose of 2.7 mg/kg (approximately 7 times the maximum recommended daily inhalation dose in adults on a mg/m² basis). The incidence of major malformations increased further when cromolyn sodium at a subcutaneous dose of 540 mg/kg was added to isoproterenol at a subcutaneous dose of 2.7 mg/kg. No such interaction was observed in rats or rabbits.

PHARMACIST – DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

Patient Instructions

Cromolyn Sodium Oral Solution, Concentrate

For Oral Use Only – Not for Inhalation or Injection.

How to Use Cromolyn Sodium Oral Solution, Concentrate:
As with all prescription drugs, follow the directions for dosage that your physician recommends.
The effect of Cromolyn Sodium Oral Solution, Concentrate therapy is dependent upon its administration at REGULAR intervals, for as long as recommended by your physician.

Usual Starting Dose:

Adults and Adolescents (13 Years and Older):
Two ampules four times daily, taken one-half hour before meals and at bedtime.

Children 2-12 Years:
One ampule four times daily, taken one-half hour before meals and at bedtime.

Note:
Your physician may decide to increase OR decrease your dosage to achieve optimum results with Cromolyn Sodium Oral Solution, Concentrate. However, do not change your dose or stop taking Cromolyn Sodium Oral Solution, Concentrate without first consulting your physician.

Care & Storage:
Cromolyn Sodium Oral Solution, Concentrate should be stored between 20°-25°C (68°-77°F) and protected from light. Do not use if it contains a precipitate (particles or cloudiness) or becomes discolored. Keep out of the reach of children.

Store ampules in foil pouch until ready for use.

Recycling Information: Cromolyn Sodium Oral Solution, Concentrate ampules are made with a low density polyethylene plastic (recycling material code: ♳LDPE).

(over)

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Cromolyn Sodium Oral Solution, Concentrate is administered to a nursing woman.

Pediatric Use: In adult rats no adverse effects of cromolyn sodium were observed at oral doses up to 6144 mg/kg (approximately 25 times the maximum recommended daily oral dose in adults on a mg/m² basis). In neonatal rats, cromolyn sodium increased mortality at oral doses of 1000 mg/kg or greater (approximately 9 times the maximum recommended daily oral dose in infants on a mg/m² basis) but not at doses of 300 mg/kg or less (approximately 3 times the maximum recommended daily oral dose in infants on a mg/m² basis). Plasma and kidney concentrations of cromolyn after oral administration to neonatal rats were up to 20 times greater than those in older rats. In term infants up to six months of age, available clinical data suggest that the dose should not exceed 20 mg/kg/day. The use of this product in pediatric patients less than two years of age should be reserved for patients with severe disease in which the potential benefits clearly outweigh the risks.

Geriatric Use: Clinical studies of Cromolyn Sodium Oral Solution, Concentrate did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS: Most of the adverse events reported in mastocytosis patients have been transient and could represent symptoms of the disease. The most frequently reported adverse events in mastocytosis patients who have received Cromolyn Sodium Oral Solution, Concentrate during clinical studies were headache and diarrhea, each of which occurred in 4 of the 87 patients. Pruritus, nausea, and myalgia were each reported in 3 patients and abdominal pain, rash, and irritability in 2 patients each. One report of malaise was also recorded.

Other Adverse Events: Additional adverse events have been reported during studies in other clinical conditions and from worldwide postmarketing experience. In most cases the available information is incomplete and attribution to the drug cannot be determined. The majority of these reports involve the gastrointestinal system and include: diarrhea, nausea, abdominal pain, constipation, dyspepsia, flatulence, glossitis, stomatitis, vomiting, dysphagia, esophagospasm.

Other less commonly reported events (the majority representing only a single report) include the following:

Skin:	pruritus, rash, urticaria/angioedema, erythema/ burning, photosensitivity
Musculoskeletal:	arthralgia, myalgia, stiffness/weakness of legs
Neurologic:	headache, dizziness, hypoesthesia, paresthesia, migraine, convulsions, flushing
Psychiatric:	psychosis, anxiety, depression, hallucinations, behavior change, insomnia, nervousness
Heart Rate:	tachycardia, premature ventricular contractions (PVCs), palpitations
Respiratory:	pharyngitis, dyspnea

Cromolyn Sodium Oral Solution, Concentrate

Miscellaneous:	fatigue, edema, unpleasant taste, chest pain, postprandial lightheadedness and lethargy, dysuria, urinary frequency, purpura, hepatic function test abnormal, polycythemia, neutropenia, pancytopenia, tinnitus, lupus erythematosus (LE) syndrome

DOSAGE AND ADMINISTRATION: NOT FOR INHALATION OR INJECTION. SEE DIRECTIONS FOR USE.

The usual starting dose is as follows:

Adults and Adolescents (13 Years and Older): Two ampules four times daily, taken one-half hour before meals and at bedtime.

Children 2-12 Years: One ampule four times daily, taken one-half hour before meals and at bedtime.

Pediatric Patients Under 2 Years: Not recommended.

If satisfactory control of symptoms is not achieved within two to three weeks, the dosage may be increased but should not exceed 40 mg/kg/day. Patients should be advised that the effect of Cromolyn Sodium Oral Solution, Concentrate therapy is dependent upon its administration at regular intervals, as directed.

Maintenance Dose: Once a therapeutic response has been achieved, the dose may be reduced to the minimum required to maintain the patient with a lower degree of symptomatology. To prevent relapses, the dosage should be maintained.

Administration: Cromolyn Sodium Oral Solution, Concentrate should be administered as a solution at least 1/2 hour before meals and at bedtime after preparation according to the following directions:

1. Break open ampule(s) and squeeze liquid contents of ampule(s) into a glass of water.
2. Stir solution.
3. Drink all of the liquid.

HOW SUPPLIED: Cromolyn Sodium Oral Solution, Concentrate is an unpreserved, colorless solution supplied in a low density polyethylene plastic unit dose ampule with 8 ampules per foil pouch.

Each 5 mL ampule contains 100 mg cromolyn sodium, USP, in purified water.

NDC 16571-150-70	96 ampules x 5 mL (12 pouches x 8 ampules)

Cromolyn Sodium Oral Solution, Concentrate should be stored between 20° – 25°C (68° – 77°F) [see USP Controlled Room Temperature] and protected from light. Do not use if it contains a precipitate or becomes discolored. Keep out of the reach of children.

Store ampules in foil pouch until ready for use.

Distributed by:
PACK Pharmaceuticals.LLC
Buffalo Grove, IL 60089 USA

Manufactured by:
Catalent Pharma Solutions, LLC
Woodstock, IL 60098 USA

Rev. 07/09
GEN 01B

PHARMACIST – DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

Directions for Use:

1. Open foil pouch by tearing at serrated edge as shown.

2. Remove ampule(s) from the strip.

3. Open the ampule by twisting off the tabbed top section.

4. Squeeze liquid contents into a glass of water. Stir solution. Drink all of the liquid. Discard the empty ampule.

Distributed by:
PACK Pharmaceuticals, LLC
1110 W. Lake Cook Rd., Ste. 152
Buffalo Grove, IL 60089
Manufactured by:
Catalent Pharma Solutions, LLC
2200 Lakeshore Dr.
Woodstock, IL 60098 USA
Rev. 07/09
GEN 01B

Contains: 96 (12 pouches x
8 - five mL unit dose ampules)

Sterile

PACK PHARMACEUTICALS, LLC

NDC#16571-150-70

Cromolyn Sodium
Oral Solution, Concentrate
100 mg/5 mL

FOR ORAL SOLUTION ONLY –
NOT FOR INHALATION OR INJECTION

Rx Only
Must Be Diluted

Store ampules in foil pouch
until ready to use

Distributed by:
PACK Pharmaceuticals, LLC
Buffalo Grove, IL 60089 USA

Manufactured by:
Catalent Pharma Solutions, LLC
Woodstock, IL 60098 USA

DESCRIPTION: Each 5 mL ampule contains 100 mg cromolyn sodium, USP, in purified water.

NOTE: See package circular for full prescribing information including contraindications, warnings and precautions.

Cromolyn Sodium Oral Solution, Concentrate should be stored between 20° - 25°C (68° - 77°F) [see USP Controlled Room Temperature] and protected from light. Do not use if it contains a precipitate or becomes discolored. Keep out of the reach of children.

ITEM NUMBER CODE - FPO
STW-XXXXXXX

Catalent

(b) (4)

Cromolyn Sodium
Oral Solution, Concentrate
100 mg/5 mL

Distributed by:
PACK Pharmaceuticals, LLC
Buffalo Grove, IL 60089 USA

Manufactured by:
Catalent Pharma Solutions, LLC
Woodstock, IL 60098 USA

Lot:
Exp.:

3 16571 15070 0

CPS

Cromolyn Sodium
Oral Solution, Concentrate
100 mg/5 mL

FOR ORAL SOLUTION ONLY –
NOT FOR INHALATION OR INJECTION

Rx Only
Must Be Diluted

Store ampules in foil pouch
until ready to use

Distributed by:
PACK Pharmaceuticals, LLC
Buffalo Grove, IL 60089 USA

Manufactured by:
Catalent Pharma Solutions, LLC
Woodstock, IL 60098 USA

DESCRIPTION: Each 5 mL ampule contains 100 mg cromolyn sodium, USP, in purified water.

NOTE: See package circular for full prescribing information including contraindications, warnings and precautions.

Cromolyn Sodium Oral Solution, Concentrate should be stored between 20° - 25°C (68° - 77°F) [see USP Controlled Room Temperature] and protected from light. Do not use if it contains a precipitate or becomes discolored. Keep out of the reach of children.

ITEM NUMBER CODE - FPO
STW-XXXXXXX

Rev. 09/09

Cromolyn Sodium
Oral Solution, Concentrate
100 mg/5 mL

Contains: 96 (12 pouches x
8 - five mL unit dose ampules)

Sterile

PACK PHARMACEUTICALS, LLC

NDC#16571-150-70

Cromolyn Sodium
Oral Solution, Concentrate
100 mg/5 mL

FOR ORAL SOLUTION ONLY –
NOT FOR INHALATION OR INJECTION

Store ampules in foil pouch
until ready to use

Distributed by:
PACK Pharmaceuticals, LLC
Buffalo Grove, IL 60089 USA

Manufactured by:
Catalent Pharma Solutions, LLC
Woodstock, IL 60098 USA

Rx Only

(b) (4)

(b) (4)

(b) (4)

NOTES:

(b) (4)

DRAFT

SEP 30 2009

Catalent

IMPERIAL UNITS – 3RD ANGLE PROJECTION
TOLERANCES UNLESS OTHERWISE SPECIFIED
DECIMAL DIMS ± .06 [1.5mm] FRACTIONAL DIMS ± 1/16 [1.5mm]

TITLE:
LAYOUT VIAL 5mL

(b) (4)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-90954	ORIG-1	GENERA PHARMACEUTICALS LLC	CROMOLYN SODIUM

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/s/

ANGELA M PAYNE
12/02/2009

JOHN F GRACE
12/02/2009

Telephone Fax

ANDA 90-954

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
Angela.payne@fda.hhs.gov

TO: Genera Pharma (Catalent)

TEL: 1-619-246-5700

ATTN: V. Ray Nathan,

FAX 1-888-479-3683

FROM: Mrs. Angela Payne

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Cromolyn Sodium Oral Solution, Concentrate.

Pages (including cover): 4

SPECIAL INSTRUCTIONS:

See attached labeling comments.

REVIEW OF PROFESSIONAL LABELING #2
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 90-954 Date of Submission: 07 AUG 2009

Applicant's Name: Genera Pharm (Catalent)

Established Name: Cromolyn Sodium Oral Solution, Concentrate 100 mg/5 mL, Unit Dose vials

---

Labeling Deficiencies:

1. CONTAINER: Please add the manufacturer or distributor information to the container. On the TAB end of your container please delete "cromolyn sodium oral solution concentrate" and add "Must be diluted". If space permits on front or back please add the word sterile.

2. POUCH 8 ampules:

a. Place a coma in "Cromolyn Sodium Oral Solution, Concentrate".

b. Add "Must be diluted".

c. "FOR ORAL SOLUTION ONLY- NOT FOR INHALATION OR INJECTION" should be prominently displayed in capital letters.

d. Delete **"8 ampules"** that appears prominently in bold print on the right side of the labeling.

e. Revise "1 pouch x 8 ampules" to read " ..8- five mL ampules". You may relocate this net quantity statement to appear towards the bottom of the label.

3. CARTON 96 (12 pouches x 8-5mLampules):

a. Add "Sterile".

b. Add "Must Be Diluted". below the banner towards the right side of the front and back panels.

c. Revise the net content statement to Contains: 96 (12 pouches X 8 - five mL unit dose ampules).

d. It is not necessary to place the net content in bold print. Please revise to give it less prominence.

e. Please delete the following: " (b) (4) just below "Rx Only" on the front and back panels. The net quantity statement already exists at the top corners of the top panel and front panels.

f. See comments under POUCH.

4. INSERT: Satisfactory

5. PATIENT LEAFLE**T:** Satisfactory.

Revise your labels and labeling, as instructed above, and submit final print electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – ANDA.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling and the latest approved labeling for the reference listed drug (or your last submission) with all differences annotated and explained.

{See appended electronic signature page}

_____

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-90954	ORIG-1	GENERA PHARMACEUTICAL LLC	CROMOLYN SODIUM

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/s/

JOHN F GRACE
09/10/2009
for Wm Peter Rickman

REVIEW OF PROFESSIONAL LABELING #2
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 90-954 Date of Submission: 07 AUG 2009

Applicant's Name: Genera Pharm (Catalent)

Established Name: Cromolyn Sodium Oral Solution, Concentrate 100 mg/5 mL, Unit Dose vials

---

Labeling Deficiencies:

1. CONTAINER: Please add the manufacturer or distributor information to the container. On the TAB end of your container please delete "cromolyn sodium oral solution concentrate" and add "Must be diluted". If space permits on front or back please add the word sterile.

2. POUCH 8 ampules:

a. Place a coma in "Cromolyn Sodium Oral Solution, Concentrate".

b. Add "Must be diluted".

c. "FOR ORAL SOLUTION ONLY- NOT FOR INHALATION OR INJECTION" should be prominently displayed in capital letters.

d. Delete **"8 ampules"** that appears prominently in bold print on the right side of the labeling.

e. Revise "1 pouch x 8 ampules" to read " ..8- five mL ampules". You may relocate this net quantity statement to appear towards the bottom of the label.

3. CARTON 96 (12 pouches x 8-5mLampules):

a. Add "Sterile".

b. Add "Must Be Diluted". below the banner towards the right side of the front and back panels.

c. Revise the net content statement to Contains: 96 (12 pouches X 8 - five mL unit dose ampules).

d. It is not necessary to place the net content in bold print. Please revise to give it less prominence.

e. Please delete the following: "(b) (4)", just below "Rx Only" on the front and back panels. The net quantity statement already exists at the top corners of the top panel and front panels.

f. See comments under POUCH.

4. INSERT: Satisfactory

5. PATIENT LEAFLE**T:** Satisfactory.

Revise your labels and labeling, as instructed above, and submit final print electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – ANDA.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily

or weekly updates of new documents posted on the CDER web site at the following address - http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling and the latest approved labeling for the reference listed drug (or your last submission) with all differences annotated and explained.

FOR THE RECORD
LABELING REVIEW BRANCH

1. APPLICANT INFORMATION:

ANDA Number	90-954
Date of Submission	
Applicant	Genera pharm
Drug Name	Cromolyn Sodium Oral Solution, Concentrate
Strength(s)	100 mg/5 mL unit dose ampules

Labels and Labeling Summary
Container
Pouch carton Insert
Patient Leaflet

2. NOTE TO CHEMIST:

3. MODEL LABELING:

Reference Listed Drug	
RLD on the 356(h) form	Gastrocom
NDA Number	20-479
RLD established name	Cromolyn Sodium Oral Concentrate
Firm	Azur
Currently approved PI	S-005
AP Date	13 FEB 2003

4. REFERENCE LISTED DRUG PATENTS/EXCLUSIVITIES: See above.

Patent Data For NDA

Patent No	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None					

Exclusivity Data For NDA

Code/sup	Expiration	Description	*Labeling impact*
None		None	

5. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM: Manufactured by: Catalent Pharma LLC, Solutions, Woodstock, IL 60098 …..Marketed by: Genera Pharmaceuticals, LL**C,**San Diego CA 92130. Genera does not appear to be the distributor now. The distributor has changed to PACK Pharmaceuticals, LLc in Buffalo Grove, IL

6. CONTAINER/CLOSURE; 5 mL Unit dose ampules LDPE.

7. INACTIVE INGREDIENTS

The description of the inactive ingredients in the insert labeling appears accurate according to the composition statement. Each 5 mL ampule of cromolyn sodium oral concentrate contains 100 mg cromolyn sodium, USP, in purified water. [Vol. A1.1 pg].

8. PACKAGING CONFIGURATIONS

RLD: 96 unit dose ampules (8 ampules per pouch)
ANDA: Same.

9. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

USP: Not a USP item.
RLD: Store at 20-25C (68- 77F). [See USP CRT]. Protect from light product.
ANDA: Same

10. DISPENSING STATEMENTS COMPARISON

USP: None :RLD:
ANDA (*Insert*):

11. BIOAVAILABILITY/BIOEQUIVALENCE:

12. (b) (4) is the way the firm states the established name. However, I have instructed the firm to revise it to include the dosage form as follows: Cromolyn Sodium Oral Solution Concentrate

---

Date of Review: 9/2/09 Date of Submission: 07 AUG 2009

Primary Reviewer: Angela Payne Date:

Team Leader: John Grace Date:

---

cc:

ANDA: 90-954
DUP/DIVISION FILE
HFD-613/Apayne/JGrace (no cc)
V:\FIRMSAM\catalent.genera\LTRS&REV\90954na2labdrtsreview.doc
Review

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-90954	ORIG-1	GENERA PHARMACEUTICAL LLC	CROMOLYN SODIUM

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

/s/

ANGELA M PAYNE
09/02/2009

JOHN F GRACE
09/10/2009

REVIEW OF PROFESSIONAL LABELING #1
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 90-954 Date of Submission: 21 NOV 2008 (original)

Applicant's Name: Genera Pharm (Catalent)

Established Name: Cromolyn Sodium Oral Solution, Concentrate 100 mg/5 mL, Unit Dose vials

---

Labeling Deficiencies:

1. CONTAINER: Please resubmit with visual text. Please note established name revision.

2. POUCH 8 ampules:

a. The established name should read as follows on all labels and labeling: Cromolyn Sodium Oral Solution, Concentrate.

b. In addition delete ",USP".

c. Relocate the declaration of strength so that it follows immediately after the established name and displays as follows: 100 mg/5 mL.

d. Add "Sterile" and "Unit dose" on the label. Add the Rx Only

e. Add "Must be diluted".

f. "FOR ORAL SOLUTION ONLY- NOT FOR INHALATION OR INJECTION" should be prominently displayed and should be place not to far from the established name and strength. It should be displayed each time the name is cited on each panel.

g. "Ampoules" in the storage statement should read "ampules".

h. Please include the contents statements 1 pouch X 8 ampules

i. You label this section as your container. Please revise to accurately describe the unit. This section should be the pouch and the container is the immediate container and would be the ampule itself.

3. CARTON 96 (X __X__ampules):

a. On one of the panels you have "USP". Since this is not a USP item at this time delete "USP".

b. Where you cite the established name please include the strength.

c. Please include the content statement i.e. Carton contains 96 unit dose ampules (12 pouches X 8 ampules).

d. Relocate the text on the back panel to the front panel.

4. INSERT: See comment regarding the established name..

5. PATIENT LEAFLE**T:** See comment under insert.

Revise your labels and labeling, as instructed above, and submit final print electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – ANDA.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling and the latest approved labeling for the reference listed drug (or your last submission) with all differences annotated and explained.

FOR THE RECORD
LABELING REVIEW BRANCH

1. APPLICANT INFORMATION:

ANDA Number	90-954
Date of Submission	
Applicant	Genera pharm
Drug Name	Cromolyn Sodium Oral Solution Concentrate
Strength(s)	100 mg/5 mL unit dose ampules

Labels and Labeling Summary
Container
Pouch carton Insert
Patient Leaflet

2. NOTE TO CHEMIST:

3. MODEL LABELING:

Reference Listed Drug	
RLD on the 356(h) form	Gastrocom
NDA Number	20-479
RLD established name	Cromolyn Sodium Oral Concentrate
Firm	Azur
Currently approved PI	S-005
AP Date	13 FEB 2003

4. REFERENCE LISTED DRUG PATENTS/EXCLUSIVITIES: See above.

Patent Data For NDA

Patent No	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None					

Exclusivity Data For NDA

Code/sup	Expiration	Description	*Labeling impact*
None		None	

5. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM: Manufactured by:
Catalent Pharma Solutions, Woodstock, IL 60098 …..Marketed by: Genera Pharmaceuticals, LL**C,**San Diego CA 92130

6. CONTAINER/CLOSURE; 5 mL Unit dose ampules LDPE.

7. INACTIVE INGREDIENTS

The description of the inactive ingredients in the insert labeling appears accurate according to the composition statement. Each 5 mL ampule of cromolyn sodium oral concentrate contains 100 mg cromolyn sodium, USP, in purified water. [Vol. A1.1 pg].

8. PACKAGING CONFIGURATIONS

RLD: 96 unit dose ampules (8 ampules per pouch)
ANDA: Same.

9. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

USP: Not a USP item.
RLD: Store at 20-25C (68- 77F). [See USP CRT]. Protect from light product.
ANDA: Same

10. DISPENSING STATEMENTS COMPARISON

USP: None :RLD:
ANDA (*Insert*):

11. BIOAVAILABILITY/BIOEQUIVALENCE:

12. Cromolyn Sodium Oral Concentrate is the way the firm states the established name. However, I have instructed the firm to revise it to include the dosage form as follows: Cromolyn Sodium Oral Solution Concentrate

---

Date of Review: 5/12/09 Date of Submission: 21 NOV 2008

Primary Reviewer: Angela Payne Date:

Team Leader: John Grace Date:

---

cc:

ANDA: 90-954
DUP/DIVISION FILE
HFD-613/Apayne/JGrace (no cc)
V:\FIRMSAM\genera\LTRS&REV\90954na1labdfsreview.doc
Review

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

/s/

Angela Payne
5/12/2009 02:16:14 PM
LABELING REVIEWER

John Grace
5/18/2009 09:30:06 AM
LABELING REVIEWER

Telephone Fax

ANDA 90-954

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
Angela.payne@fda.hhs.gov

TO: Genera Pharma (Catalent)

TEL: 1-619-246-5700

ATTN: V.Ray Nathan,

FAX 1-888-479-3683

FROM: Mrs. Angela Payne

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Cromolyn Sodium Oral Solution, Concentrate.

Pages (including cover): 4

SPECIAL INSTRUCTIONS:

See attached labeling comments.

REVIEW OF PROFESSIONAL LABELING #1
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 90-954 Date of Submission: 21 NOV 2008 (original)

Applicant's Name: Genera Pharm (Catalina)

Established Name: Cromolyn Sodium Oral Solution, Concentrate 100 mg/5 mL, Unit Dose vials

---

Labeling Deficiencies:

1. CONTAINER: Please resubmit with visual text. Please note established name revision.

2. POUCH 8 ampules:

a. The established name should read as follows on all labels and labeling: Cromolyn Sodium Oral Solution ,Concentrate.

b. In addition delete ",USP".

c. Relocate the declaration of strength so that it follows immediately after the established name and displays as follows: 100 mg/5 mL.

d. Add "Sterile" and "Unit dose" on the label. Add the Rx Only

e. Add "Must be diluted".

f. "FOR ORAL SOLUTION ONLY- NOT FOR INHALATION OR INJECTION" should be prominently displayed and should be place not to far from the established name and strength. It should be displayed each time the name is cited on each panel.

g. "Ampoules" in the storage statement should read "ampules".

h. Please include the contents statements 1 pouch X 8 ampules

i. You label this section as your container. Please revise to accurately describe the unit. This section should be the pouch and the container is the immediate container and would be the ampule itself.

3. CARTON 96 (X __X__ampules):

a. On one of the panels you have "USP". Since this is not a USP item at this time delete "USP".

b. Where you cite the established name please include the strength.

c. Please include the content statement i.e. Carton contains 96 unit dose ampules (12 pouches X 8 ampules).

d. Relocate the text on the back panel to the front panel.

4. INSERT: See comment regarding the established name..

5. PATIENT LEAFLE**T:** See comment under insert.

Revise your labels and labeling, as instructed above, and submit final printed or draft electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – ANDA.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of

new documents posted on the CDER web site at the following address - http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling and the latest approved labeling for the reference listed drug (or your last submission) with all differences annotated and explained.

{See appended electronic signature page}

_____

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
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/

John Grace
5/18/2009 09:29:47 AM
for Wm Peter Rickman

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 90-954

CHEMISTRY REVIEWS

V:\Chemistry Division I\Team 2\TL Folder\ANDA\Final\90954N00R02.doc

ANDA 90-954

Cromolyn Sodium Oral Concentrate, 100 mg/5 mL (20 mg/mL)

Genera Pharmaceuticals, LLC

Eugene L. Schaefer, Ph.D.
Division of Chemistry I

Review #2

Table of Contents

Chemistry Review Data Sheet

1. ANDA 90-954

2. REVIEW #: 2

3. REVIEW DATE: 09/01/2009 REVISED: 09/04/09

4. REVIEWER: Eugene L. Schaefer, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Volumes/SD#	Document Date
Original ANDA	eCTD 0000/SD#1	10/22/2008
Expedited Review/Request	SD#2	10/24/2008
MC*	A2.1/SD#3	11/03/2008
RTF Amendment	eCTD 0001/SD#4	11/21/2008

*DMF holder's letter designating US agent

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed *	Volumes/SD#	Document Date
Microbiology amendment	eCTD 0002SD#5	05/04/2009
*Minor amendment	eCTD 0003/SD#6	07/24/2009
Labeling amendment	eCTD 0004/SD#7	08/07/2009

7. NAME & ADDRESS OF APPLICANT:

Name:	Genera Pharmaceuticals, LLC
Address:	13734 Trento Place San Diego, CA 92130
Representative:	V. Ray Nathan, Ph.D., MBA, President
Telephone:	619-246-5700
Fax:	888-479-3683

Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: None
b) Non-Proprietary Name (USAN): Cromolyn Sodium
c) Code Name/# (ONDC only):
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type:
- Submission Priority:

9. LEGAL BASIS FOR SUBMISSION:

Gastrocrom®, Azur Pharma, Inc., NDA 20479

10. PHARMACOLOGIC CATEGORY:

Mastocytosis; improvement of diarrhea, flushing, headaches, vomiting, urticaria, abdominal pain, nausea, and itching

11. DOSAGE FORM: Oral Concentrate

12. STRENGTH/POTENCY: 100 mg/5 mL (20 mg/mL)

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: _X__Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

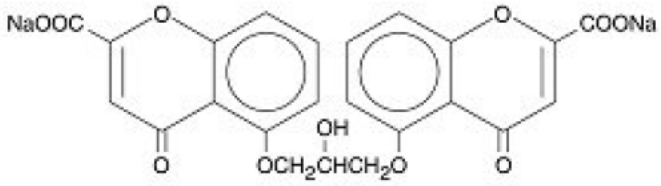
_____SPOTS product – Form Completed

__X__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: Disodium 5,5'-[(2-hydroxy-l ,3-propanediyl)bis(oxy)]bis[4-oxo-4H-1-benzopyran-2-carboxylate

Molecular Structure:



Molecular Formula: $C_{23}H_{14}Na_2O_{11}$
Molecular Weight: 512.34 g/mol

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER (LoA Date)	ITEM REFERENCED	CODE [1]	STATUS [2]	DATE REVIEW COMPLETED	COMMENTS
		(b) (4)	Cromolyn Sodium, USP	1	Adequate	9/1/09	
			(b) (4)	4			
				4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
None		

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Acceptable	06/08/09	Theodore Garnett, Ph.D.
EES	Acceptable	12/11/08	S.Ferguson
Methods Validation	Not needed		
Labeling	Pending *		
Bioequivalence	Acceptable	01/08/09	Ke Ren, Ph.D.
EA	Acceptable	03/10/09	Eugene L. Schaefer, Ph.D.
Radiopharmaceutical	N/A		

* See Approval Routing Summary for Final Endorsement.

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ____ Yes __X__ No If no, explain reason(s) below:

The application was granted expedited review.

The Chemistry Review for ANDA 90-954

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The ANDA is not ready for approval because labeling is pending. See Approval Routing Summary for Final Endorsement.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

Genera commits to re-assess compliance with (b) (4) if they change ingredient suppliers in the post approval period including implementing revised controls, if appropriate. (Review #1, Section P.4)

Genera has provided a stability commitment.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Each 5 mL ampule of cromolyn sodium oral concentrate contains 100 mg cromolyn sodium, USP, in purified water. Cromolyn sodium is a hygroscopic, white powder having little odor. It may leave a slightly bitter aftertaste. Cromolyn sodium oral concentrate is clear, colorless, and sterile. It is intended for oral use.

Chemically, cromolyn sodium is disodium 5,5'-[(2-hydroxytrimethylene) dioxy]bis[4-oxo-4H-1-benzopyran-2-carboxylate]. The empirical formula is $C_{23}H_{14}Na_2O_{11}$; the molecular weight is 512.34.

B. Description of How the Drug Product is Intended to be Used

Pharmacologic Category: Mast cell stabilizer

Therapeutic Category: Antiallergic

Cromolyn sodium acts by inhibiting the release of histamine and leukotrienes (SRS-A) from the mast cell.

Maximum daily dose:

The labeling says the dosage should not exceed 40 mg/kg/day. Therefore, the MDD depends on the weight of the patient. If we assume a patient weight of 75 kg, the MDD would be 3000 mg = 3 g. 75 kg is slightly higher than the typical average weight of 70 kg.

C. Basis for Approvability or Not-Approval Recommendation

Labeling is pending. See Approval Routing Summary for Final Endorsement.

The chemistry deficiencies have been remedied. Microbiology, Establishment Evaluation and Bioequivalence are acceptable. Methods Validation is not needed.

24 Pages have been Withheld as b4 (CCI/TS) immediately following this page

CHEMISTRY REVIEW TEMPLATE

Chemistry Assessment Section

cc: ANDA 90-954

Endorsements:

HFD-625/ELSchaefer, Chemist/9-4-09

HFD-625/BCai, Team Leader/

HFD-617/EChuh, Project Manager

V:\Chemistry Division I\Team 2\TL Folder\ANDA\Final\90954N00R02.doc

TYPE OF LETTER: Labeling is pending. Otherwise the ANDA is ready for approval. See Approval Routing Summary for Final Endorsement.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-90954	ORIG-1	GENERA PHARMACEUTICAL LLC	CROMOLYN SODIUM
ANDA-90954	ORIG-1	GENERA PHARMACEUTICAL LLC	CROMOLYN SODIUM

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

/s/

EUGENE L SCHAEFER
09/24/2009

BING CAI
09/24/2009

EUNJUNG E CHUH
09/25/2009

ANDA 90-954

Cromolyn Sodium Oral Concentrate, 100 mg/5 mL (20 mg/mL)

Genera Pharmaceuticals, LLC

Eugene L. Schaefer, Ph.D.
Division of Chemistry I

Review #1

Table of Contents

Chemistry Review Data Sheet

1. ANDA 90-954

2. REVIEW #: 1

3. REVIEW DATE: 3/17/2009 REVISED: 3/19/2009

4. REVIEWER: Eugene L. Schaefer, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Volumes	Document Date
None		

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Volumes	Document Date
Original ANDA	eCTD 0000	10/22/2008
MC*	A2.1	11/03/2008
RTF Amendment	eCTD 0001	11/21/2008

*DMF holder's letter designating US agent

7. NAME & ADDRESS OF APPLICANT:

Name:	Genera Pharmaceuticals, LLC
Address:	13734 Trento Place San Diego, CA 92130
Representative:	V. Ray Nathan, Ph.D., MBA, President
Telephone:	619-246-5700
Fax:	888-479-3683

Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: None
b) Non-Proprietary Name (USAN): Cromolyn Sodium
c) Code Name/# (ONDC only):
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type:
- Submission Priority:

9. LEGAL BASIS FOR SUBMISSION:

Gastrocrom®, Azur Pharma, Inc., NDA 20479

10. PHARMACOLOGIC CATEGORY:

Mastocytosis; improvement of diarrhea, flushing, headaches, vomiting, urticaria, abdominal pain, nausea, and itching

11. DOSAGE FORM: Oral Concentrate

12. STRENGTH/POTENCY: 100 mg/5 mL (20 mg/mL)

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: _X__Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

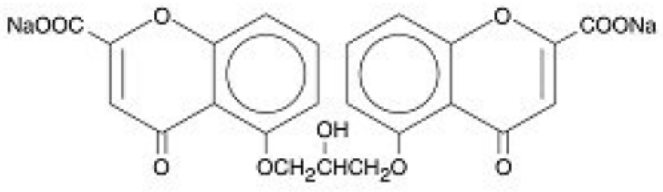
_____SPOTS product – Form Completed

__X__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: Disodium 5,5'-[(2-hydroxy-l ,3-propanediyl)bis(oxy)]bis[4-oxo-4H-1-benzopyran-2-carboxylate

Molecular Structure:



Molecular Formula: $C_{23}H_{14}Na_2O_{11}$
Molecular Weight: 512.34 g/mol

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER (LoA Date)	ITEM REFERENCED	CODE [1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	Cromolyn Sodium, USP	3	Adequate	8/18/08	By Raman Murali. No CMC information has been submitted to the DMF since then, as of 3/12/09.
	III		(b) (4)	4			
	III			4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
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3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
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[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

Chemistry Review Data Sheet

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
None		

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Deficient	03/11/09*	Theorore Garnett, Ph.D.
EES	Acceptable**	12/11/08	S.Ferguson
Methods Validation	Not needed		
Labeling	Pending		
Bioequivalence	Acceptable	01/08/09	Ke Ren, Ph.D.
EA	Acceptable	03/10/09	Eugene L. Schaefer, Ph.D.
Radiopharmaceutical	N/A		

* Deficiencies were faxed 3/11/09.

** I have verified that the correct facilities are on the EER.

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ____ Yes __X__ No If no, explain reason(s) below:

The application was granted expedited review.

The Chemistry Review for ANDA 90-954

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The ANDA is not ready for approval. A minor amendment is being requested.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

Genera commits to re-assess compliance with [redacted] (b) (4) if they change ingredient suppliers in the post approval period including implementing revised controls, if appropriate. (Review #1, Section P.4)

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Chemically, cromolyn sodium is disodium 5,5'-[(2-hydroxytrimethylene) dioxy]bis[4-oxo-4H-1-benzopyran-2-carboxylate]. The empirical formula is $C_{23}H_{14}Na_2O_{11}$; the molecular weight is 512.34.

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Therapeutic Category: Antiallergic

Cromolyn sodium acts by inhibiting the release of histamine and leukotrienes (SRS-A) from the mast cell.

Maximum daily dose:

The labeling says the dosage should not exceed 40 mg/kg/day. Therefore, the MDD depends on the weight of the patient. If we assume a patient weight of 75 kg, the MDD would be 3000 mg = 3 g. 75 kg is slightly higher than the typical average weight of 70 kg.

C. Basis for Approvability or Not-Approval Recommendation

There are chemistry deficiencies. Microbiology is deficient. Labeling is pending.

Establishment Evaluation and Bioequivalence are acceptable. Methods Validation is not needed.

29 Pages have been Withheld as b4 (CCI/TS) immediately following this page

CHEMISTRY REVIEW TEMPLATE

Chemistry Assessment Section

cc: ANDA 90-954
ANDA DUP

Endorsements:

HFD-625/ELSchaefer, Chemist

HFD-625/RSRandad, Acting Team Leader/3/20/2009

HFD-617/EChuh, Project Manager

V:\Chemistry Division I\Team 2\TL Folder\ANDA\90954N00R01.DOC

TYPE OF LETTER: NOT APPROVABLE - MINOR

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/s/

Eugene Schaefer
3/26/2009 03:03:05 PM
CHEMIST

Esther Chuh
3/27/2009 08:13:28 AM
CHEMIST

Ramnarayan Randad
3/27/2009 08:24:18 AM
CHEMIST

COMPLETE RESPONSE -- MINOR

ANDA 90-954

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Genera Pharmaceuticals, LLC TEL: (619) 246-5700

ATTN: V. Ray Nathan FAX: (888) 479-3683

FROM: Esther Chuh FDA CONTACT PHONE: (240) 276-8530

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated October 22, 2008, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Cromolyn Sodium Oral Concentrate, 100 mg/5 mL.

Reference is also made to your amendment dated November 21, 2008.

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format. This will improve document availability to review staff.

We have completed the review of your ANDA and have determined that we cannot approve this application in its present form. We have described below our reasons for this action and, where possible, our recommendations to address these issues in the following attachments (_5___ pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. Upon OGD's acceptance for filing of your ANDA, it was determined that an adequate amount of information was submitted to allow for review of your Bioequivalence and Microbiology data. You will be notified in a separate communication of any further deficiencies identified during our review of your Bioequivalence and Microbiology data If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 90-954

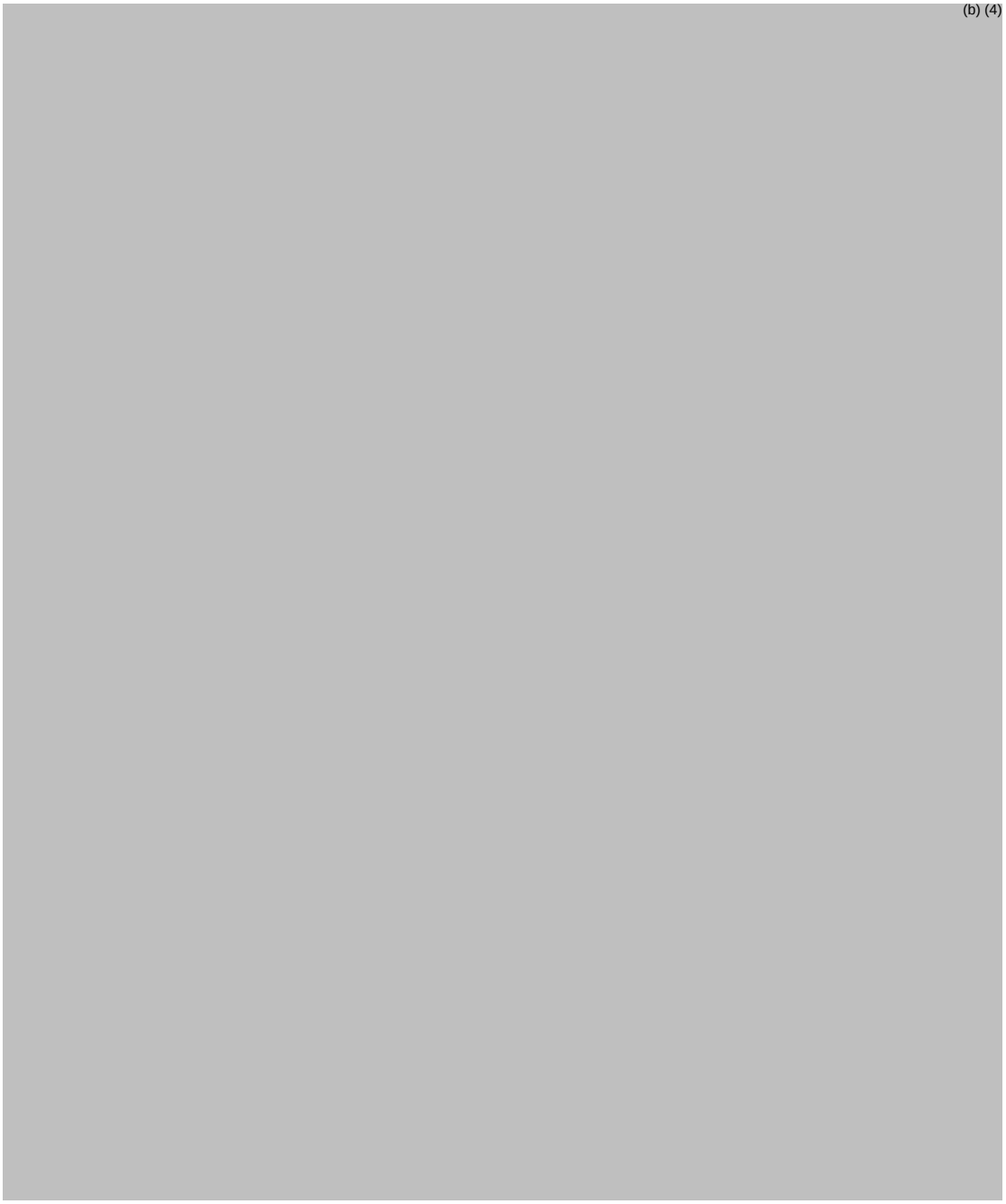
APPLICANT: Genera Pharmaceuticals, LLC

DRUG PRODUCT: Cromolyn Sodium Oral Concentrate, 100 mg/5 mL (20 mg/mL)

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

(b) (4)



6. For the drug substance and drug product HPLC Related Substances methods:

8. From the executed batch record for Lot No. 04208A, and from the Proposed Commercial Batch Record, we conclude that the ANDA batch size was (b) (4) kg, made up in (b) (4) of (b) (4) kg each, and the commercial batch size will be (b) (4) kg, made up in (b) (4) of (b) (4) kg each. From Sections 2.3.P.3, 3.2.P.2.3 and 3.2.P.3.2 we conclude that (b) (4) % of the intended ANDA batch was filled, and the amount filled corresponds to (b) (4) % of the intended commercial batch size.

However, there are inconsistencies in these three sections. Please confirm that our conclusions are correct, and please revise these sections to remove the inconsistencies.

9. Please revise the drug product release and stability specifications as follows:

   a. Please add a quantitative color test.

   b. Please add a second Identification test.

   c. Please designate the limits "(b) (4) mL" for Volume in Container as (b) (4), and set Mean limits that are tighter.

   d. Please tighten the pH limits range.

   e. Please add individual limits for the impurities (b) (4) .

   f. Please tighten the limit for Related Compounds (TLC) to NMT (b) (4) %, to agree with 3.2.P.5.6, Section 1.3.

(b) (4)

10. (b) (4)

11. (b) (4)

12. 3.2.P.8.1 Section 1.2 says photostability testing was performed with and without an (b) (4) device. Please confirm that this is a typographic error.

13. The drug product stability specifications should include the condition of the container, concerning visible deterioration or interaction with the product.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. Sterility Assurance has not been demonstrated for this drug product. Please reply to the comments provided to you by facsimile on March 11, 2009.

2. Please provide any additional stability data that may be available.

3. Your labeling information is pending review. Deficiencies, if any, will be communicated separately.

Sincerely yours,

{See appended electronic signature page}

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

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/s/

Paul Schwartz
3/27/2009 09:54:38 AM
Signed for R. Patel

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 90-954

BIOEQUIVALENCE REVIEWS

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	90-954
Drug Product Name	Cromolyn Sodium Oral Concentrate
Strength(s)	100 mg/5 mL (20 mg/mL)
Applicant Name	Genera Pharmaceuticals, LLC
Address	13734 Trento Place San Diego, CA 92130
Applicant's Point of Contact	V.Ray Nathan, PhD., MBA
Contact's Telephone Number	1-619-246-5700
Contact's Fax Number	1-888-479-3683
Original Submission Date(s)	DATE OF APPLICATION: October 20, 2008 DATE (RECEIVED) ACCEPTABLE FOR FILING: November 21, 2008
Submission Date(s) of Amendment(s) Under Review	N/A
Reviewer	Ke Ren. Ph.D.
OUTCOME DECISION	**COMPLETE**

1 EXECUTIVE SUMMARY

This application, submitted by Genera Pharmaceutical LLC, requests a waiver of *in vivo* bioequivalence (BE) study for its Cromolyn Sodium Oral Concentrate, 100 mg/5 mL, under 21 CFR § 320.22 (b) (3). The reference listed drug (RLD) is Gastrocrom ® Oral Concentrate, 100 mg/5 mL, manufactured by Azur Pharma. (NDA #20-479, approved February 29, 1996).

The test drug product is an oral concentrate which contains the same active and inactive ingredients in the same concentration as the RLD. Based on the information provided, the DBE *grants* Genera Pharmaceutical LLC the waiver of *in vivo* BE study requirements for its Cromolyn Sodium Oral Concentrate, 100 mg/5 mL, based on criteria set forth in Section 21 CFR § 320.22 (b) (3).

The application is **acceptable** with no deficiencies.

2 TABLE OF CONTENTS

3 SUBMISSION SUMMARY

3.1 Drug Product Information

Test Product	Cromolyn Sodium Oral Concentrate, 100 mg /5 mL
Reference Product*	Gastrocrom ® Oral Concentrate, 100 mg/5 mL
RLD Manufacturer*	Azur Pharma
NDA No.*	20-479
RLD Approval Date*	February 29, 1996
Indication[1]	Gastrocrom ® is indicated in the management of patients with mastocytosis. Use of this product has been associated with improvement in diarrhea, flushing, headaches, vomiting, urticaris, abdominal pain, nausea and itching in some patients.

* The Orange Book (Online version 2008).

3.2 PK/PD Information[1,2]

Bioavailability	Cromolyn sodium is poorly absorbed from the gastrointestinal tract. Systemic bioavailability of oral cromolyn is approximately 1%, the remainder being excreted in the feces.
Food Effect	RLD labeling states that Gastrocrom ® should be administered as a solution at least 0.5 hour before meals.
Tmax	Not known
Mechanism	*In vitro* and *in vivo* animal studies have shown that cromolyn sodium inhibits the release of mediators from sensitized mast cells. Cromolyn sodium acts by inhibiting the release of histamine and leukotrienes

[1] http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=729#nlm34090-1
[2] http://www.clinicalpharmacology-ip.com/Forms/Monograph/monograph.aspx?cpnum=153&sec=monphar

	(SRS-A) from the mast cell. Cromolyn sodium has no intrinsic vasoconstrictor, antihistamine, or glucocorticoid activity.
Excretion	Very little absorption of cromolyn sodium was seen after oral administration of 500 mg by mouth to each of 12 volunteers. From 0.28 to 0.50% of the administered dose was recovered in the first 24 hours of urinary excretion in 3 subjects. The mean urinary excretion of an administered dose over 24 hours in the remaining 9 subjects was 0.45%. Roughly 98% of the dose is eliminated unchanged in the feces.
Half-life	Not Known
Drug Specific Issues (if any)	1) The recommended dosage should be decreased in patients with decreased renal or hepatic function. Severe anaphylactic reactions may occur rarely in association with cromolyn sodium administration. 2) Cromolyn sodium is classified as pregnancy category B. 3) Cromolyn sodium is not a bronchodilator; it is contraindicated (ineffective) for the treatment of acute bronchospasm or status asthmaticus. 4) Oral preparations of cromolyn contain lactose. Patients with lactase deficiency should take appropriate precautions with use.

3.3 OGD Recommendations for Drug Product

Analytes to measure (in plasma/serum/blood):	N/A
Bioequivalence based on:	21 CFR § 320.22 (b) (3)
Waiver request of in-vivo testing:	Yes
Summary of OGD or DBE History	DBE approved AND (b) (4) (b) (4) The criteria for waiver of the in-vivo bioequivalence study requirements for the test product per 21 CFR 320.22 (b)(3), in that the product: (i) Is an oral solution. (ii) Contains an active drug ingredient in the same concentration and dosage form as a drug product that is the subject of an approved full new drug application. (iii) Contains no inactive ingredient or other change in formulation from the listed reference drug product that may significantly affect absorption of the active drug ingredient.

3.4 Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	No	--
Single-dose fed	No	--
Steady-state	No	--
In vitro dissolution	No	--
Waiver requests	YES	1
BCS Waivers	No	--
Clinical Endpoints	No	--
Failed Studies	No	--
Amendments	No	--

3.5 Formulation

Ingredients	Cromolyn Sodium Oral Concentrate	Gastrocrom ®
Cromolyn Sodium, USP	(b) (4)	
Water for Injection, USP		

Reviewers' Comments on the Formulation

1. The test product, Cromolyn Sodium Oral Concentrate, 100 mg/5 ml, contains the same active and inactive ingredients in the same concentration and dosage form as the reference product, Gastrocrom® (Cromolyn Sodium, USP) Oral Concentrate.

2. Comparative pH data for the RLD, test and approved ANDA (b) (4) product:

Specification	Current ANDA 90-954	Approved ANDA (b) (4)	NDA 20-479[4]
pH	(b) (4)	(b) (4)	(b) (4)

The test product, approved ANDA (b) (4) product and RLD have the similar pH range.

3. Gastrocrom® Oral Concentrate is an unpreserved sterile solution supplied in a clear plastic unit dose ampule with 8 ampules per foil pouch. The proposed Cromolyn Sodium Oral Concentrate is also supplied in a clear plastic unit dose ampule. Both oral concentrate amplues are made with a low density polyethylene plastic.

[3] (b) (4)

[4] DFS N 020479 SCS 004 AC 25-Nov-2002 from Dr. Vibhakar J. Shah

4. The test product meets the criteria for waiver of the *in vivo* bioequivalence study requirements per Section 21 CFR § 320.22 (b) (3).

3.6 Waiver Request(s)

Strengths for which waivers are requested	Cromolyn Sodium Oral Concentrate, 100 mg/5 ml
Regulation cited	21 CFR 320.22(b)(3)
Proportional to strength tested in vivo?	N/A
Waivers granted?	**WAIVER GRANTED**
If not then why?	

3.7 Comments

1. The test drug product is an oral concentrate intended solely for oral administration.

2. The test drug product contains the same amount of active and inactive ingredients in the same strength and dosage form as the currently approved RLD.

3. The test product meets the criteria for waiver of the *in vivo* bioequivalence study requirements per Section 21 CFR § 320.22 (b) (3).

3.8 Recommendations

The Division of Bioequivalence (DBE) agrees that the information submitted by Genera Pharmaceuticals LLC demonstrates that its test product, Cromolyn Sodium Oral Concentrate, 100 mg/5 ml, meets the requirements of Section 21 CFR § 320.22 (b) (3). The DBE recommends the waiver of *in vivo* bioequivalence testing be granted for the test product.

The Division of Bioequivalence deems the test product, Cromolyn Sodium Oral Concentrate, 100 mg/5 ml, manufactured by Genera Pharmaceutical LLC, to be bioequivalent to the reference listed product, Gastrocrom®, 100 mg /5 mL, manufactured by Azur Pharma.

3.9 Comments for Other OGD Disciplines

None.

BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA:	90-954
APPLICANT:	Genera Pharmaceuticals, LLC.
DRUG PRODUCT:	Cromolyn Sodium Oral Concentrate, 100 mg/5 mL (20 mg/mL)

The Division of Bioequivalence has completed its review acknowledged on the cover page and has no further questions at this time.

Please note that the bioequivalence comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

{See appended electronic signature page}

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

3.10 Outcome Page

ANDA: 90-954

Reviewer: Ren, Ke **Date Completed:**

Verifier: **Date Verified:**

Division: Division of Bioequivalence

Description: Cromolyn Sodium Oral Concentrate, 100 mg/5 mL (20 mg/mL), Genera Pharmaceuticals, LLC.

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
7132	10/22/2008	Other	Waiver Oral Solution	1	1
				Bean Total:	1

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/s/

Ke Ren
1/8/2009 09:37:35 AM
BIOPHARMACEUTICS

Bing Li
1/8/2009 10:26:26 AM
BIOPHARMACEUTICS

Hoainhon T. Nguyen
1/8/2009 12:33:32 PM
BIOPHARMACEUTICS
For Dale P. Conner, Pharm. D., Director, Division of Bioequivalence I

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 90-954

MICROBIOLOGY REVIEWS

Product Quality Microbiology Review

May 20, 2009

ANDA: 90-954

Drug Product Name
Proprietary: N/A
Non-proprietary: Cromolyn Sodium Oral Concentrate
Drug Product Priority Classification:

Review Number: 2

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
05/04/2009	05/04/2009	N/A	05/05/2009

Submission History (for amendments only):

Submission Date (s)	Microbiology Review #	Review Date(s)
10/22/2008*	1	01/12/2009
11/21/2008	1	01/12/2009

*RFT

Applicant/Sponsor
Name: Genera Pharmaceuticals, LLC
Address: 13734 Trento Plance, San Diego, CA 92130
Representative: V. Ray Nathan, President
Telephone: (619) 246-5700

Name of Reviewer: Theodore Garnett, Ph.D.

Conclusion: This submission **is recommended** for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original ANDA

2. SUBMISSION PROVIDES FOR: Initial marketing of sterile drug product.

3. MANUFACTURING SITE:
Catalent Pharma Solutions, LLC
2200 Lake Shore Drive
Woodstock, IL 60098

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Cromolyn Sodium Oral Concentrate (20 mg/mL) is a sterile, oral solution consisting of 100 mg/5 mL Cromolyn Sodium, USP. The product is filled into 5 mL low-density polyethylene (LPDE) containers/ampoules. The product container-closure is both (b) (4).

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: Mastocytosis; improvement of diarrhea, flushing, headaches, vomiting, urticaria, abdominal pain, nausea, and itching.

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: This is an electronic submission.

filename: 90-954a1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability –

The submission **is recommended** for approval on the basis of sterility assurance.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable –

N/A

II. Summary of Microbiology Assessments

(b) (4)

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block

Microbiologist / Theodore Garnett, Ph.D.
Microbiology Team Leader/Lynne Ensor, Ph.D.

C. CC Block

cc: Field Copy

5 Pages have been Withheld as b4 (CCI/TS) immediately following this page

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/s/

Theodore O Garnett
6/8/2009 03:10:50 PM
MICROBIOLOGIST

Mark Anderson
6/8/2009 03:17:37 PM
MICROBIOLOGIST

Checked for correct file and linking; both OK

Lynne Ensor
6/8/2009 08:16:32 PM
MICROBIOLOGIST

Product Quality Microbiology Review

January 12, 2009

ANDA: 90-954

Drug Product Name
Proprietary: N/A
Non-proprietary: Cromolyn Sodium Oral Concentrate
Drug Product Priority Classification:

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
10/22/2008*	10/22/2008	N/A	1/7/2009
11/21/2008	11/24/2008	N/A	1/7/2009

*RFT

Submission History (for amendments only): N/A

Applicant/Sponsor
Name: Genera Pharmaceuticals, LLC
Address: 13734 Trento Plance, San Diego, CA 92130
Representative: V. Ray Nathan, President
Telephone: (619) 246-5700

Name of Reviewer: Theodore Garnett, Ph.D.

Conclusion: This submission **is not recommended** for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original ANDA

2. SUBMISSION PROVIDES FOR: Initial marketing of sterile drug product.

3. MANUFACTURING SITE:
Catalent Pharma Solutions, LLC
2200 Lake Shore Drive
Woodstock, IL 60098

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Cromolyn Sodium Oral Concentrate (20 mg/mL) is a sterile, oral solution consisting of 100 mg/5 mL Cromolyn Sodium, USP. The product is filled into 5 mL low-density polyethylene (LPDE) containers/ampoules. The product container-closure is both (b) (4).

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: Mastocytosis; improvement of diarrhea, flushing, headaches, vomiting, urticaria, abdominal pain, nausea, and itching.

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: This is an electronic submission.

filename: 90-954.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – The submission **is not recommended** for approval on the basis of sterility assurance. Specific comments and deficiencies are provided in the "Product Quality Microbiology Assessment" and "List of Microbiology Deficiencies and Comments" sections.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A

II.

(b) (4)

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block

Microbiologist / Theodore Garnett, Ph.D.
Microbiology Team Leader/Lynne Ensor, Ph.D.

C. CC Block

cc: Field Copy

13 Pages have been Withheld as b4 (CCI/TS) immediately following this page

7. Please state the maximum [redacted (b) (4)] for production and indicate whether it is validated through the [redacted (b) (4)] simulations.

8. Please provide data to validate the product's sterility test.

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,

{See appended electronic signature page}

Lynne A. Ensor, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

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/s/

Theodore O Garnett
3/9/2009 09:39:56 AM
MICROBIOLOGIST

Mark Anderson
3/9/2009 10:43:19 AM
MICROBIOLOGIST

Checked for correct file and linking; all OK

Lynne Ensor
3/11/2009 07:04:57 AM
MICROBIOLOGIST

FAX – Microbiology Deficiencies Enclosed

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville MD 20855-2773 (240-276-8408)

TO: Genera Pharmaceuticals, LLC		**FROM:** Bonnie McNeal
V. Ray Nathan		Microbiology Project Manager
PHONE: 619-246-5700		**PHONE:** (240) 276-8831
FAX: 888-479-3683		**FAX:** (240) 276-8725

Total number of pages, excluding this cover sheet: **3**

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format. This will improve document availability to review staff.

Microbiology Deficiencies:

Enclosed are the microbiology deficiencies for ANDA 90-954 for Cromolyn Sodium Oral Concentrate. The submissions reviewed were submitted on October 22, and November 21, 2008. Please respond to this communication as quickly as possible. This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review. The response to this communication will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT-RESPONSE TO MICROBIOLOGY DEFICIENCIES should appear prominently in your cover letter.

Should you also have other outstanding deficiencies, for review purposes, please attempt to consolidate your responses into a single submission for this application.

If you have questions, feel free to call Bonnie McNeal or Mark Anderson.

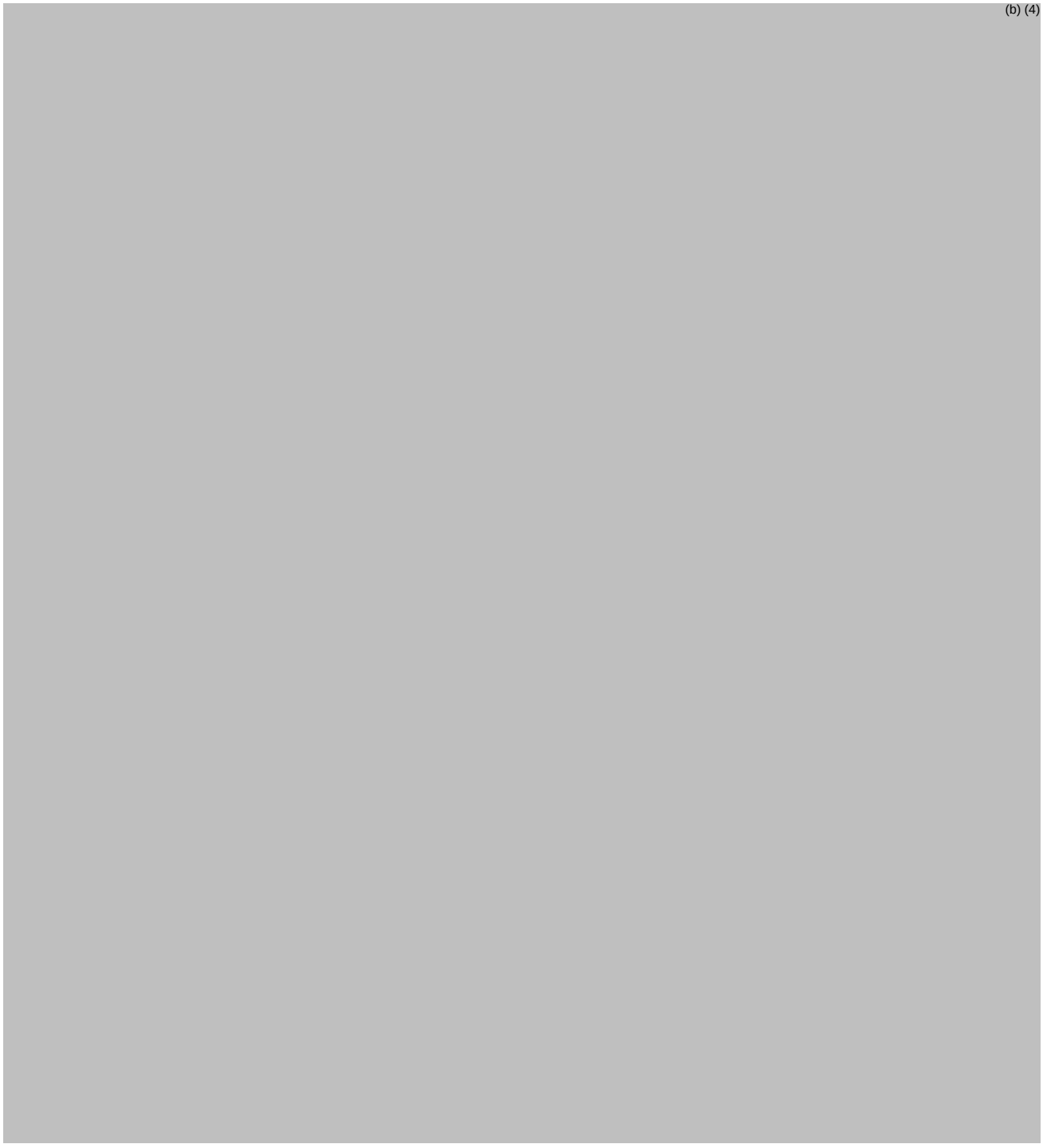
3. LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS:

ANDA: 90-954 APPLICANT: Genera Pharmaceuticals, LLC

DRUG PRODUCT: Cromolyn Sodium Oral Concentrate

Microbiology Deficiencies:

(b) (4)



8. Please provide data to validate the product's sterility test.

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,

{See appended electronic signature page}

Lynne A. Ensor, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

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/s/

Lynne Ensor
3/11/2009 07:05:34 AM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 90-954

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

OGD APPROVAL ROUTING SUMMARY

ANDA # 090954 Applicant Genera Pharmaceuticals, LLC
Drug Cromolyn Sodium Oral Concentrate Strength(s) 100 mg/5 mL (20 mg/mL)

APPROVAL ☒ **TENTATIVE APPROVAL** ☐ **SUPPLEMENTAL APPROVAL (NEW STRENGTH)** ☐ **OTHER** ☐

REVIEWER: **DRAFT Package** **FINAL Package**

1. **Martin Shimer** Date 21 Sept 2009 Date _____
Chief, Reg. Support Branch Initials MHS Initials _____
Contains GDEA certification: Yes ☒ No ☐ Determ. of Involvement? Yes ☐ No ☐
(required if sub after 6/1/92) Pediatric Exclusivity System
RLD = _____ NDA# _____
Patent/Exclusivity Certification: Yes ☒ No ☐ Date Checked _____
If Para. IV Certification- did applicant Nothing Submitted ☐
Notify patent holder/NDA holder Yes ☐ No ☐ Written request issued ☐
Was applicant sued w/in 45 days: Yes ☐ No ☐ Study Submitted ☐
Has case been settled: Yes ☐ No ☐ Date settled:
Is applicant eligible for 180 day
Generic Drugs Exclusivity for each strength: Yes ☐ No ☒
Date of latest Labeling Review/Approval Summary _____
Any filing status changes requiring addition Labeling Review Yes ☐ No ☒
Type of Letter: Full Approval.
Comments: ANDA submitted on 11/22/2008, BOS=Gastrocrom NDA 20479, no relevant patent certification provided. RTR issued on 10/28/2009. ANDA ack for filing on 11/21/2008 (LO dated 12/2/2008). There are no remaining unexpired patents or exclusivities which protect the RLD. This ANDA is eligible for immediate Full Approval.

2. Project Manager, Esther Chuh Team 2 Date 9/17/2009 Date _____
Review Support Branch Initials EC Initials _____

Original Rec'd date 11/21/2008
Date Acceptable for Filing 11/21/2008
Patent Certification (type) I
Date Patent/Exclus.expires n/a
Citizens' Petition/Legal Case Yes ☐ No ☒
(If YES, attach email from PM to CP coord)
First Generic Yes ☒ No ☐
Priority Approval Yes ☐ No ☒
(If yes, prepare Draft Press Release, Email it to Cecelia Parise)
Acceptable Bio reviews tabbed Yes ☐ No ☒
Bio Review Filed in DFS: Yes ☒ No ☐
Suitability Petition/Pediatric Waiver

EER Status Pending ☐ Acceptable ☒ OAI ☐
Date of EER Status 12/11/2008
Date of Office Bio Review 1/8/2009
Date of Labeling Approv. Sum 12/2/2009
Date of Sterility Assur. App. 6/8/2009
Methods Val. Samples Pending Yes ☐ No ☒
MV Commitment Rcd. from Firm Yes ☐ No ☐
Modified-release dosage form: Yes ☐ No ☒
Interim Dissol. Specs in AP Ltr: Yes ☐

Pediatric Waiver Request Accepted ☐ Rejected ☐ Pending ☐
Previously reviewed and tentatively approved ☐ Date _____
Previously reviewed and CGMP def. /NA Minor issued ☐ Date _____
Comments:

3. Labeling Endorsement
Reviewer: Labeling Team Leader:
Date 12/2/2009 Date 12/2/2009
Name/Initials Angela Payne Name/Initials John Grace

Comments:
Labeling was found acceptable, signed in DARRTS 12/2/2009.

4. David Read **(PP IVs Only)** Pre-MMA Language included ☐ Date _____
OGD Regulatory Counsel, Post-MMA Language Included ☐ Initials _____
Comments:

5. Div. Dir./Deputy Dir. Date 12/03/09
Chemistry Div. I Initials PS

Comments:CMC is OK; API is USP

6. Frank Holcombe **First Generics Only** Date12/17/09
Assoc. Dir. For Chemistry Initials RR
Comments: (First generic drug review)
CMC is acceptable; for Frank,

7. Vacant Date_____
Deputy Dir., DLPS Initials_____

8. Peter Rickman Date12/18/2009
Director, DLPS Initials wpr
Para.IV Patent Cert: Yes☐ No☒;Pending Legal Action: Yes ☐No ☒;Petition: Yes☐ No☒
Comments: BOS=Gastrocrom NDA 20479; There are no remaining unexpired patents or exclusivities which protect the RLD; Labeling acceptable 12/2/2009, TL sign-off 12/2/2009; Bio acceptable 1/8/2009; Micro 6/8/2009; EER acceptable 12/11/2008. This ANDA is eligible for Full Approval.

OR

8. Robert L. West Date _____
Deputy Director, OGD Initials _____
Para.IV Patent Cert: Yes☐ No☐; Pending Legal Action: Yes☐ No☐; Petition: Yes☐ No☐
Press Release Acceptable ☐
Comments:

9. Gary Buehler Date _____
Director, OGD Initials _____
Comments:
First Generic Approval ☐ PD or Clinical for BE ☐ Special Scientific or Reg.Issue ☐
Press Release Acceptable ☐

10. Project Manager, SELECT PM NAME Team TEAM # Date_____

Review Support Branch Initials _____
_____Date PETS checked for first generic drug (just prior to notification to firm)

Applicant notification:
_____Time notified of approval by phone
_____Time approval letter faxed

FDA Notification:
_____Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.
_____Date Approval letter copied to \\CDS014\DRUGAPP\ directory.

EER DATA:

APPEARS THIS WAY ON ORIGINAL

COMIS TABLE:

APPEARS THIS WAY ON ORIGINAL

ORANGE BOOK PRINT OFF:

APPEARS THIS WAY ON ORIGINAL

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-90954	ORIG-1	GENERA PHARMACEUTICALS LLC	CROMOLYN SODIUM

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

/s/

NITIN K PATEL
12/18/2009

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 90-954

Genera Pharmaceuticals, LLC
Attention: V. Ray Nathan, Ph.D.
13734 Trento Place
San Diego, CA 92130

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is made to our "Refuse to Receive" letter dated October 28, 2008 and your amendment dated November 21, 2008.

NAME OF DRUG: Cromolyn Sodium Oral Concentrate, 100 mg/5 mL

DATE OF APPLICATION: October 20, 2008

DATE (RECEIVED) ACCEPTABLE FOR FILING: November 21, 2008

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Esther Chuh
Project Manager
(240) 276-8530

Sincerely yours,

{See appended electronic signature page}

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
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/

Martin Shimer
12/2/2008 11:58:54 AM
Signing for Wm Peter Rickman

RESPONSE TO REFUSE TO RECEIVE
EXPETITED REVIEW GRANTED 10/24/2008

ANDA CHECKLIST FOR CTD or eCTD FORMAT
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION FOR FILING

For More Information on Submission of an ANDA in Electronic Common Technical Document (eCTD) Format please go to: http://www fda.gov/cder/regulatory/ersr/ectd.htm
***For a Comprehensive Table of Contents Headings and Hierarchy please go to:**
http://www fda.gov/cder/regulatory/ersr/5640CTOC-v1.2.pdf
**** For more** CTD and eCTD informational links **see the final page of the ANDA Checklist**
***** A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage** http://www.fda.gov/cder/ogd/ *****

ANDA #: 90-954 **FIRM NAME**: GENERA PHARMACEUTICALS LLC

PIV: NO **Electronic or Paper Submission:** ELECTRONIC (GATEWAY)

RELATED APPLICATION(S): NA

First Generic Product Received? NO

Bio Assignments:		
☒ **BPH**	☐ **BCE**	☒ **Micro Review (Yes)**
☐ **BST**	☐ **BDI**	

DRUG NAME: CROMOLYN SODIUM
DOSAGE FORM: ORAL CONCENTRATE ,
100 MG/5 ML (b) (4)
Random Queue: 2
Chem Team Leader: Smela, Michael Chem PM: Esther Chuh Labeling Reviewer: Angela Payne
Bio PM: Lizzie Sanchez (Acting Bio PM)

Letter Date: OCTOBER 20, 2008 **Received Date**: OCTOBER 22, 2008

Comments: EC- 1 YES **On Cards:** YES
Therapeutic Code: 6011800 MISCELLANOUS RESPIRATORY

Archival copy: ELECTRONIC (GATEWAY) **Sections** I
Review copy: NA E-Media Disposition: NO
Not applicable to electronic sections

PART 3 Combination Product Category N Not a Part3 Combo Product
(Must be completed for ALL Original Applications) Refer to the Part 3 Combination Algorithm

Reviewing CSO/CST Saundra T. Middleton Date 11/25/2008	**Recommendation:** ☒ **FILE** ☐ **REFUSE to RECEIVE**
Supervisory Concurrence/Date: _____	**Date:** _____

ADDITIONAL COMMENTS REGARDING THE ANDA:

Note: Genera has requested expedited review. Expedited review granted, see next page.

You have failed to provide [redacted] validation data in your application. [redacted] validation is required for drug products that are [redacted] You should consult the *Guidance for Industry for the Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products* (November 1994) for guidance on [redacted] validation study. Submitted 11/21/2008 - see also e-mail from Jesse Wells below.

The exhibit batch in Module 3 needs to be in a legible format. There are many pages in the exhibit batch that are not legible, please resubmit a readable copy of the exhibit batch. Submitted 11/21/2008.

Please provide the following:

1. A batch reconciliation detailing the proposed production yield as well as the theoretical and actual yields for each executed batch size. Submitted 11/21/2008.

2. Current Good Manufacturing Practices (cGMP) in accord with 21 CFR Parts 210 and 211 from the **holder** of the ANDA. Submitted 11/21/2008.

3. You have failed to provide a letter from the DMF holder, [redacted] as the U.S. Agent with authority to grant access to the DMF. Please provide authorization from the DMF holder in support of this application. Submitted a response on 11/3/2008 from [redacted] and a response on 11/21/2008 from Genera.

FW: Request for expedite review of 90-954 - Cromolyn Sodium Oral Concentrate, 100 mg/5 mL - Message (Rich Text)

File Edit View Insert Format Tools Actions Help Adobe PDF

Reply | Reply to All | Forward

From: West, Robert L
To: CDER-DDR600
Cc: Middleton, Saundra T; Shimer, Martin; Ames, Timothy W
Subject: FW: Request for expedite review of 90-954 - Cromolyn Sodium Oral Concentrate, 100 mg/5 mL
Sent: Fri 10/24/2008 2:05 PM

Genera Pharmaceuticals ANDA 90-954 for Cromolyn Sodium Oral Concentrate appears to meet our criteria for "expedited review" status as outlined in MaPP 5240.3.

Please grant this ANDA "expedited review" status in COMIS.

Thank you,

Bob

From: Middleton, Saundra T
Sent: Friday, October 24, 2008 7:16 AM
To: West, Robert L
Cc: Shimer, Martin
Subject: FW: Request for expedite review of 90-954 - Cromolyn Sodium Oral Concentrate, 100 mg/5 mL

Revised e-mail...

Hi Bob,

Please see the attached request for expedite review for the ANDA submitted by Genera Pharmaceuticals, LLC for Cromolyn Sodium Oral Concentrate, 100 mg/5 mL in LDPE containers dated October 20, 2008 that cites MAPP 5240.3 and the G.I.V.E. as reason for the request. Please evaluate and decide if expedite should be granted for this ANDA. There are currently no approved generics or patents for this product.

We currently (b) (4) ANDAs for this product.

Thanks,

Saundra

90954.EXP.PDF.pdf
(38 KB)

MODULE 1
ADMINISTRATIVE

ACCEPTABLE

1.1	**1.1.2 Signed and Completed Application Form (356h) (original signature)** (Check Rx/OTC Status) RX YES	☒
1.2	**Cover Letter** Dated: OCTOBER 22, 2008	☒
1.2.1	**Form FDA 3674 (PDF) YES**	☒
*	**Table of Contents (paper submission only)** YES	☒
1.3.2	**Field Copy Certification (original signature)** NA **(N/A for E-Submissions)**	☒
1.3.3	**Debarment Certification-GDEA (Generic Drug Enforcement Act)/Other:** 1. Debarment Certification (original signature) YES 2. List of Convictions statement (original signature)	☒
1.3.4	**Financial Certifications** Bioavailability/Bioequivalence Financial Certification (Form FDA 3454) NA Disclosure Statement (Form FDA 3455, submit copy to Regulatory Branch Chief) NA **Form FDA 3674 YES**	☐
1.3.5	**1.3.5.1 Patent Information** Patents listed for the RLD in the Electronic Orange Book Approved Drug Products with Therapeutic Equivalence Evaluations **1.3.5.2 Patent Certification** 1. Patent number(s) No patents 2. Paragraph: (Check all certifications that apply) MOU ☐ PI ☒ PII ☐ PIII ☐ PIV ☐ (Statement of Notification) ☐ 3. Expiration of Patent(s): a. Pediatric exclusivity submitted? b. Expiration of Pediatric Exclusivity? 4. Exclusivity Statement: YES	☒
1.4.1	**References** Letters of Authorization 1. DMF letters of authorization a. Type II DMF authorization letter(s) or synthesis for Active Pharmaceutical Ingredient YES - Type II (b) (4) b. Type III DMF authorization letter(s) for container closure **YES** 2. US Agent Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) NA	☒
1.12.11	**Basis for Submission** NDA# : 20-479 Ref Listed Drug: GASTROCROM Firm: AZUR PHARMA, INC. ANDA suitability petition required? NA If Yes, then is change subject to PREA (change in dosage form, route or active ingredient) see section 1.9.1	☒

MODULE 1 (Continued)
ADMINISTRATIVE

ACCEPTABLE

1.12.12	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use **YES** 2. Active ingredients **YES** 3. Inactive ingredients **YES** 4. Route of administration **YES** 5. Dosage Form **YES** 6. Strength **YES**	☒
1.12.14	**Environmental Impact Analysis Statement** YES	☒
1.12.15	**Request for Waiver** Request for Waiver of In-Vivo BA/BE Study(ies): YES	☒
1.14.1	**Draft Labeling (Mult Copies N/A for E-Submissions)** **1.14.1.1** 4 copies of draft (each strength and container) **1.14.1.2** 1 side by side labeling comparison of containers and carton with all differences annotated and explained **YES** **1.14.1.3** 1 package insert (content of labeling) submitted electronically **YES** ***Was a proprietary name request submitted? no (If yes, send email to Labeling Reviewer indicating such.)	☒
1.14.3	**Listed Drug Labeling** **1.14.3.1** 1 side by side labeling (package and patient insert) comparison with all differences annotated and explained **YES** **1.14.3.3** 1 RLD label and 1 RLD container label **YES**	☒

MODULE 2
SUMMARIES ACCEPTABLE

2.3	**Quality Overall Summary (QOS)** **E-Submission: PDF YES** **Word Processed e.g., MS Word YES** A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage http://www fda.gov/cder/ogd/ **Question based Review (QbR) YES** **2.3.S** **Drug Substance (Active Pharmaceutical Ingredient) YES** **2.3.S.1 General Information** **2.3.S.2 Manufacture** **2.3.S.3 Characterization** **2.3.S.4 Control of Drug Substance** **2.3.S.5 Reference Standards or Materials** **2.3.S.6 Container Closure System** **2.3.S.7 Stability** **2.3.P** **Drug Product YES** **2.3.P.1 Description and Composition of the Drug Product** **2.3.P.2 Pharmaceutical Development** **2.3.P.2.1 Components of the Drug Product** **2.3.P.2.1.1 Drug Substance** **2.3.P.2.1.2 Excipients** **2.3.P.2.2 Drug Product** **2.3.P.2.3 Manufacturing Process Development** **2.3.P.2.4 Container Closure System** **2.3.P.3 Manufacture** **2.3.P.4 Control of Excipients** **2.3.P.5 Control of Drug Product** **2.3.P.6 Reference Standards or Materials** **2.3.P.7 Container Closure System** **2.3.P.8 Stability**	☒
2.7	**Clinical Summary (Bioequivalence) - NA** **Model Bioequivalence Data Summary Tables** **E-Submission: PDF** **Word Processed e.g., MS Word** **2.7.1 Summary of Biopharmaceutic Studies and Associated Analytical Methods** **2.7.1.1 Background and Overview** Table 1. Submission Summary Table 4. Bioanalytical Method Validation Table 6. Formulation Data **2.7.1.2 Summary of Results of Individual Studies** Table 5. Summary of In Vitro Dissolution **2.7.1.3 Comparison and Analyses of Results Across Studies** Table 2. Summary of Bioavailability (BA) Studies Table 3. Statistical Summary of the Comparative BA Data **2.7.1.4 Appendix** **2.7.4.1.3 Demographic and Other Characteristics of Study Population** Table 7. Demographic Profile of Subjects Completing the Bioequivalence Study **2.7.4.2.1.1 Common Adverse Events** Table 8. Incidence of Adverse Events in Individual Studies	☐

MODULE 3

3.2.S DRUG SUBSTANCE ACCEPTABLE

3.2.S.1	**General Information** **3.2.S.1.1 Nomenclature** **3.2.S.1.2 Structure** **3.2.S.1.3 General Properties**	☒
3.2.S.2	**Manufacturer** **3.2.S.2.1** **Manufacturer(s) (This section includes contract manufacturers and testing labs)** **Drug Substance (Active Pharmaceutical Ingredient)** 1. Name and Full Address(es)of the Facility(ies) **YES** 2. Function or Responsibility **YES** 3. Type II DMF number for API (b) (4) 4. CFN or FEI numbers	☒
3.2.S.3	**Characterization**	☒
3.2.S.4	**Control of Drug Substance (Active Pharmaceutical Ingredient)** **3.2.S.4.1 Specification** Testing specifications and data from drug substance manufacturer(s) **YES** **3.2.S.4.2 Analytical Procedures YES** **3.2.S.4.3 Validation of Analytical Procedures** 1. Spectra and chromatograms for reference standards and test samples **YES** 2. Samples-Statement of Availability and Identification of: a. Drug Substance **YES** b. Same lot number(s) **YES** **3.2.S.4.4 Batch Analysis** 1. COA(s) specifications and test results from drug substance mfgr(s) **YES** 2. Applicant certificate of analysis **YES** **3.2.S.4.5 Justification of Specification**	☒
3.2.S.5	**Reference Standards or Materials**	☒
3.2.S.6	**Container Closure Systems – IN DMF**	☒
3.2.S.7	**Stability – IN DMF**	☒

MODULE 3

3.2.P DRUG PRODUCT ACCEPTABLE

3.2.P.1	**Description and Composition of the Drug Product** 1. Unit composition **YES** 2. Inactive ingredients and amounts are appropriate per IIG **YES – SEE BELOW**	☒
3.2.P.2	**Pharmaceutical Development** Pharmaceutical Development Report **YES**	☒
3.2.P.3	**Manufacture** **3.2.P.3.1 Manufacture(s)** (Finished Dosage Manufacturer and Outside Contract Testing Laboratories) 1. Name and Full Address(es)of the Facility(ies) **YES** 2. CGMP Certification: YES 3. Function or Responsibility **YES** 4. CFN or FEI numbers **YES** **3.2.P.3.2 Batch Formula YES** **3.2.P.3.3 Description of Manufacturing Process and Process Controls** 1. Description of the Manufacturing Process **YES** 2. Master Production Batch Record(s) for largest intended production runs (no more than (b) (4) pilot batch) with equipment specified (b) (4) L 3. If sterile product: Aseptic fill / Terminal sterilization 4. Reprocessing Statement **YES** **3.2.P.3.4 Controls of Critical Steps and Intermediates** **3.2.P.3.5 Process Validation and/or Evaluation** 1. Microbiological sterilization validation NO see e-mail below from George Arhin 2. (b) (4) validation (if (b) (4)) NO – see e-mail below:	☒

RE: ANDA 90-954 - Message (Rich Text)

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Reply | Reply to All | Forward

You replied on 11/25/2008 6:54 AM.

From: Wells, Jesse
To: Middleton, Saundra T; Arhin, George
Cc:
Subject: RE: ANDA 90-954
Sent: Tue 11/25/2008 6:53 AM

Saundra,

I took a look at the (b) (4) validation studies and it looks like they provide enough to get them in the door, though there may be micro deficiencies when it gets reviewed.

From: Middleton, Saundra T
Sent: Tuesday, November 25, 2008 6:45 AM
To: Arhin, George
Cc: Wells, Jesse
Subject: RE: ANDA 90-954

Hi George and Jesse,

The firm has responded to the RTR letter requesting (b) (4) validation via eCTD. Could either of you take a look at the 11/21/2008 response and let me know if their response is adequate.

Thanks a bunch.

Saundra

From: Arhin, George
Sent: Monday, October 27, 2008 6:41 AM
To: Middleton, Saundra T
Cc: Wells, Jesse
Subject: RE: ANDA 90-954

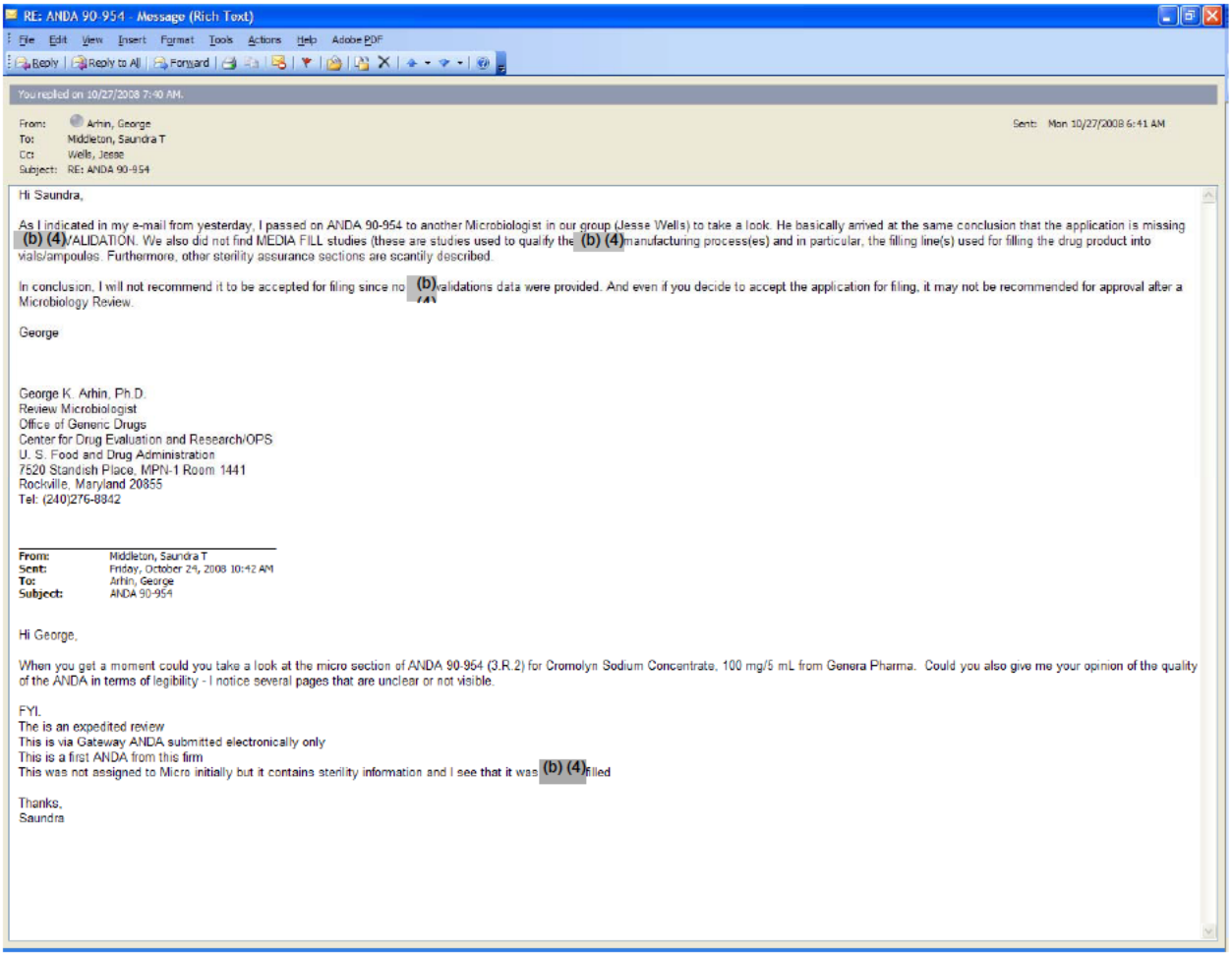
Hi Saundra,

As I indicated in my e-mail from yesterday, I passed on ANDA 90-954 to another Microbiologist in our group (Jesse Wells) to take a look. He basically arrived at the same conclusion that the application is missing (b) (4) VALIDATION. We also did not find MEDIA FILL studies (these are studies used to qualify the (b) (4) manufacturing process(es) and in particular, the filling line(s) used for filling the drug product into vials/ampoules. Furthermore, other sterility assurance sections are scantily described.

In conclusion, I will not recommend it to be accepted for filing since no (b) (4) validations data were provided. And even if you decide to accept the application for filing, it may not be recommended for approval after a Microbiology Review.

George

start 6:54 AM



RE: ANDA 90-954 - Message (Rich Text)

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Reply | Reply to All | Forward

You replied on 10/27/2008 7:40 AM.

From: Arhin, George
To: Middleton, Saundra T
Cc: Wells, Jesse
Subject: RE: ANDA 90-954

Sent: Mon 10/27/2008 6:41 AM

Hi Saundra,

As I indicated in my e-mail from yesterday, I passed on ANDA 90-954 to another Microbiologist in our group (Jesse Wells) to take a look. He basically arrived at the same conclusion that the application is missing (b) (4) VALIDATION. We also did not find MEDIA FILL studies (these are studies used to qualify the (b) (4) manufacturing process(es) and in particular, the filling line(s) used for filling the drug product into vials/ampoules. Furthermore, other sterility assurance sections are scantily described.

In conclusion, I will not recommend it to be accepted for filing since no (b) (4) validations data were provided. And even if you decide to accept the application for filing, it may not be recommended for approval after a Microbiology Review.

George

George K. Arhin, Ph.D.
Review Microbiologist
Office of Generic Drugs
Center for Drug Evaluation and Research/OPS
U. S. Food and Drug Administration
7520 Standish Place, MPN-1 Room 1441
Rockville, Maryland 20855
Tel: (240)276-8842

From: Middleton, Saundra T
Sent: Friday, October 24, 2008 10:42 AM
To: Arhin, George
Subject: ANDA 90-954

Hi George,

When you get a moment could you take a look at the micro section of ANDA 90-954 (3.R.2) for Cromolyn Sodium Concentrate, 100 mg/5 mL from Genera Pharma. Could you also give me your opinion of the quality of the ANDA in terms of legibility - I notice several pages that are unclear or not visible.

FYI.
The is an expedited review
This is via Gateway ANDA submitted electronically only
This is a first ANDA from this firm
This was not assigned to Micro initially but it contains sterility information and I see that it was (b) (4) filled

Thanks,
Saundra

3.2.P.4	**Controls of Excipients (Inactive Ingredients)** Source of inactive ingredients identified **YES** **3.2.P.4.1 Specifications** 1. Testing specifications (including identification and characterization) **YES** 2. Suppliers' COA (specifications and test results) **YES** **3.2.P.4.2 Analytical Procedures** **3.2.P.4.3 Validation of Analytical Procedures** **3.2.P.4.4 Justification of Specifications** Applicant COA	☒

MODULE 3

3.2.P DRUG PRODUCT

ACCEPTABLE

3.2.P.5	**Controls of Drug Product** **3.2.P.5.1 Specification(s) YES** **3.2.P.5.2 Analytical Procedures YES** **3.2.P.5.3 Validation of Analytical Procedures** Samples - Statement of Availability and Identification of: 1. Finished Dosage Form **YES** 2. Same lot numbers **YES** **3.2.P.5.4 Batch Analysis** Certificate of Analysis for Finished Dosage Form **YES** **3.2.P.5.5 Characterization of Impurities** **3.2.P.5.6 Justification of Specifications**	☒
3.2.P.7	**Container Closure System** 1. Summary of Container/Closure System (if new resin, provide data) **YES** 2. Components Specification and Test Data **YES** 3. Packaging Configuration and Sizes **YES** 4. Container/Closure Testing **YES** 5. Source of supply and suppliers address **YES**	☒
3.2.P.8	**3.2.P.8.1 Stability (Finished Dosage Form)** 1. Stability Protocol submitted **YES** 2. Expiration Dating Period **YES – 24 MONTHS** **3.2.P.8.2 Post-approval Stability and Conclusion** Post Approval Stability Protocol and Commitments **YES** **3.2.P.8.3 Stability Data** 1. 3 month accelerated stability data **YES** 2. Batch numbers on stability records the same as the test batch **YES**	☒

MODULE 3

3.2.R Regional Information

ACCEPTABLE

3.2.R (Drug Substance)	**3.2.R.1.S Executed Batch Records for drug substance (if available) NO** **3.2.R.2.S Comparability Protocols NA** **3.2.R.3.S Methods Validation Package NA** Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☒

3.2.R (Drug Product)	**3.2.R.1.P.1** **Executed Batch Records** Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures) Batch Reconciliation and Label Reconciliation **YES** Theoretical Yield (b) (4) Actual Yield (b) (4) Packaged Yield (b) (4) **3.2.R.1.P.2 Information on Components YES** **3.2.R.2.P Comparability Protocols NO** **3.2.R.3.P Methods Validation Package** NA Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☒

Taken from November 21, 2008 amendment:

CONFIDENTIAL

FOOD AND DRUG ADMINISTRATION ABBREVIATED NEW DRUG APPLICATION

CROMOLYN SODIUM ORAL CONCENTRATE GENERA PHARMACEUTICALS, LLC

BATCH RECONCILIATION SUMMARY

Batch Reconciliation Summary:

The batch reconciliation details for the exhibit batch and proposed commercial batch size of Cromolyn Sodium Oral Concentrate is provided below:

Batch reconciliation of Cromolyn Sodium Oral Concentrate

	Exhibit Batch	Proposed Commercial Batch
Batch size (Kg)		(b) (4)
Theoretical Batch size (Units)		
Number Manufactured (Units)		
Volume of Solution Discarded Purge (Kg) Tank Excess (Kg)		
Quantity of Solution Filled (Kg)		
Potential Solution Filled (Kg)		
Product Yield[1]		
Theoretical Yield		

[1] Product Yield is actual units filled divided by potential product produced.

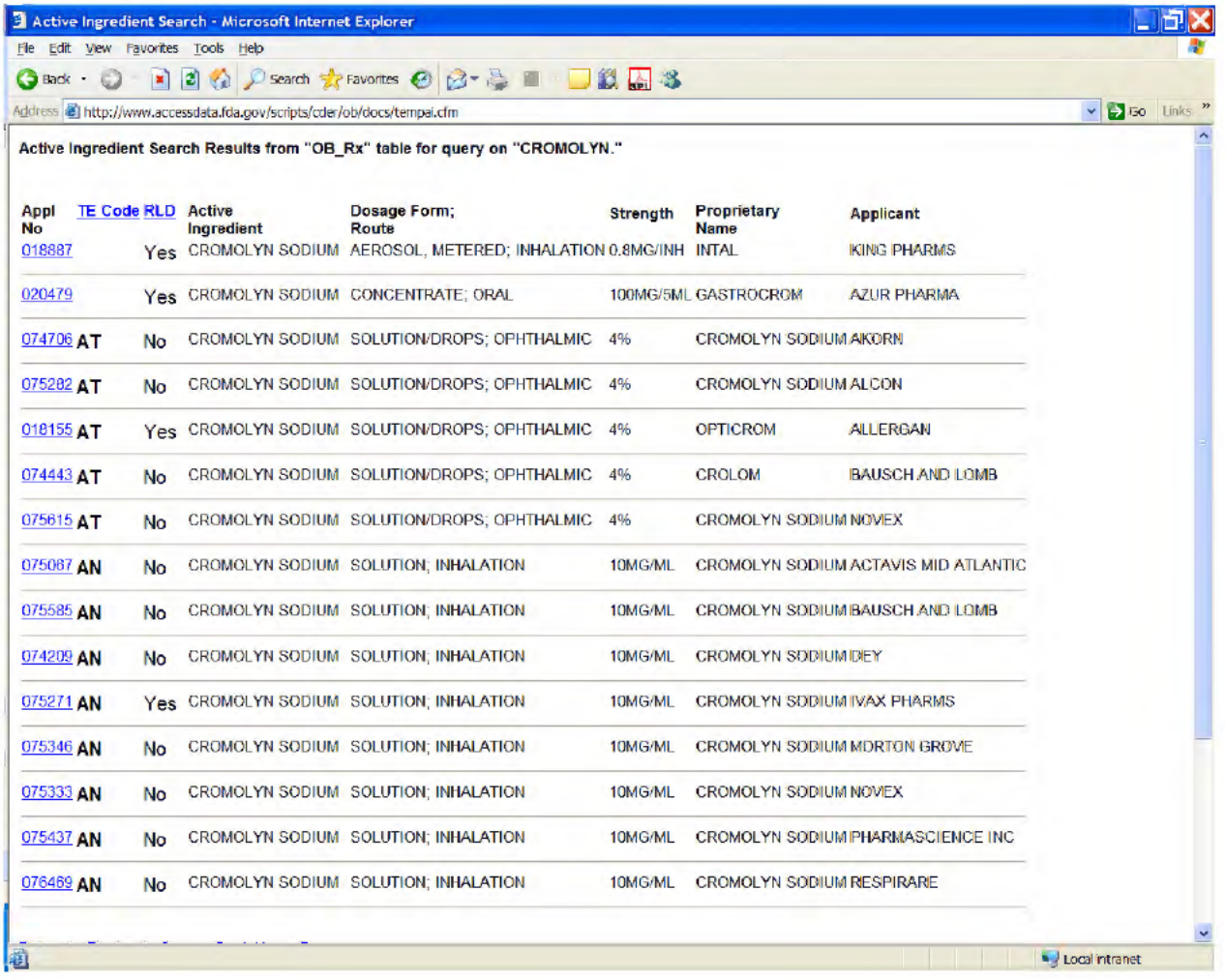
MODULE 5
CLINICAL STUDY REPORTS ACCEPTABLE

5.2	**Tabular Listing of Clinical Studies - NA**	☐
5.3.1 (complete study data)	**Bioavailability/Bioequivalence** **1. Formulation data same?** a. Comparison of all Strengths (check proportionality of multiple strengths) b. Parenterals, Ophthalmics, Otics and Topicals per 21 CFR 314.94 (a)(9)(iii)-(v) **2. Lot Numbers of Products used in BE Study(ies):** **3. Study Type: IN-VIVO PK STUDY(IES)** (Continue with the appropriate study type box below)	☐

	5.3.1.2 Comparative BA/BE Study Reports 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. Summary Bioequivalence tables: Table 10. Study Information Table 12. Dropout Information Table 13. Protocol Deviations **5.3.1.3** **In Vitro-In-Vivo Correlation Study Reports** 1. Summary Bioequivalence tables: Table 11. Product Information Table 16. Composition of Meal Used in Fed Bioequivalence Study **5.3.1.4** **Reports of Bioanalytical and Analytical Methods for Human Studies** 1. Summary Bioequivalence table: Table 9. Reanalysis of Study Samples Table 14. Summary of Standard Curve and QC Data for Bioequivalence Sample Analyses Table 15. SOPs Dealing with Bioanalytical Repeats of Study Samples **5.3.7** **Case Report Forms and Individual Patient Listing**	☐
5.4	**Literature References**	☐
	Possible Study Types:	
Study Type	**IN-VIVO BE STUDY(IES) with PK ENDPOINTS** (i.e., fasting/fed/sprinkle) NA 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted: YES SENT TO EDR 3. In-Vitro Dissolution: NO	☐
Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** NO 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria: 90% CI of the proportional difference in success rate between test and reference must be within (-0.20, +0.20) for a binary/dichotomous endpoint. For a continuous endpoint, the test/reference ratio of the mean result must be within (0.80, 1.25). 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted	☐
Study Type	**IN-VITRO BE STUDY(IES)** (i.e., in vitro binding assays) NO 1. Study(ies) meets BE criteria (90% CI of 80-125) 2. EDR Email: Data Files Submitted: 3. In-Vitro Dissolution:	☐

Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** 1. Solutions (Q1/Q2 sameness): a. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming) 2. Suspensions (Q1/Q2 sameness): a. In-Vivo PK Study 1. Study(ies) meets BE Criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted b. In-Vivo BE Study with Clinical End Points 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria (90% CI within +/- 20% of 80-125) 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted c. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming)	☐
Study Type	**IN-VIVO BE STUDY(IES) with PD ENDPOINTS** (e.g., topical corticosteroid vasoconstrictor studies) 1. Pilot Study (determination of ED50) 2. Pivotal Study (study meets BE criteria 90%CI of 80-125)	☐
Study Type	**TRANSDERMAL DELIVERY SYSTEMS** 1. In-Vivo PK Study 1. Study(ies) meet BE Criteria (90% CI of 80-125, C max, AUC) 2. In-Vitro Dissolution 3. EDR Email: Data Files Submitted 2. Adhesion Study 3. Skin Irritation/Sensitization Study	☐

Updated 8/11/2008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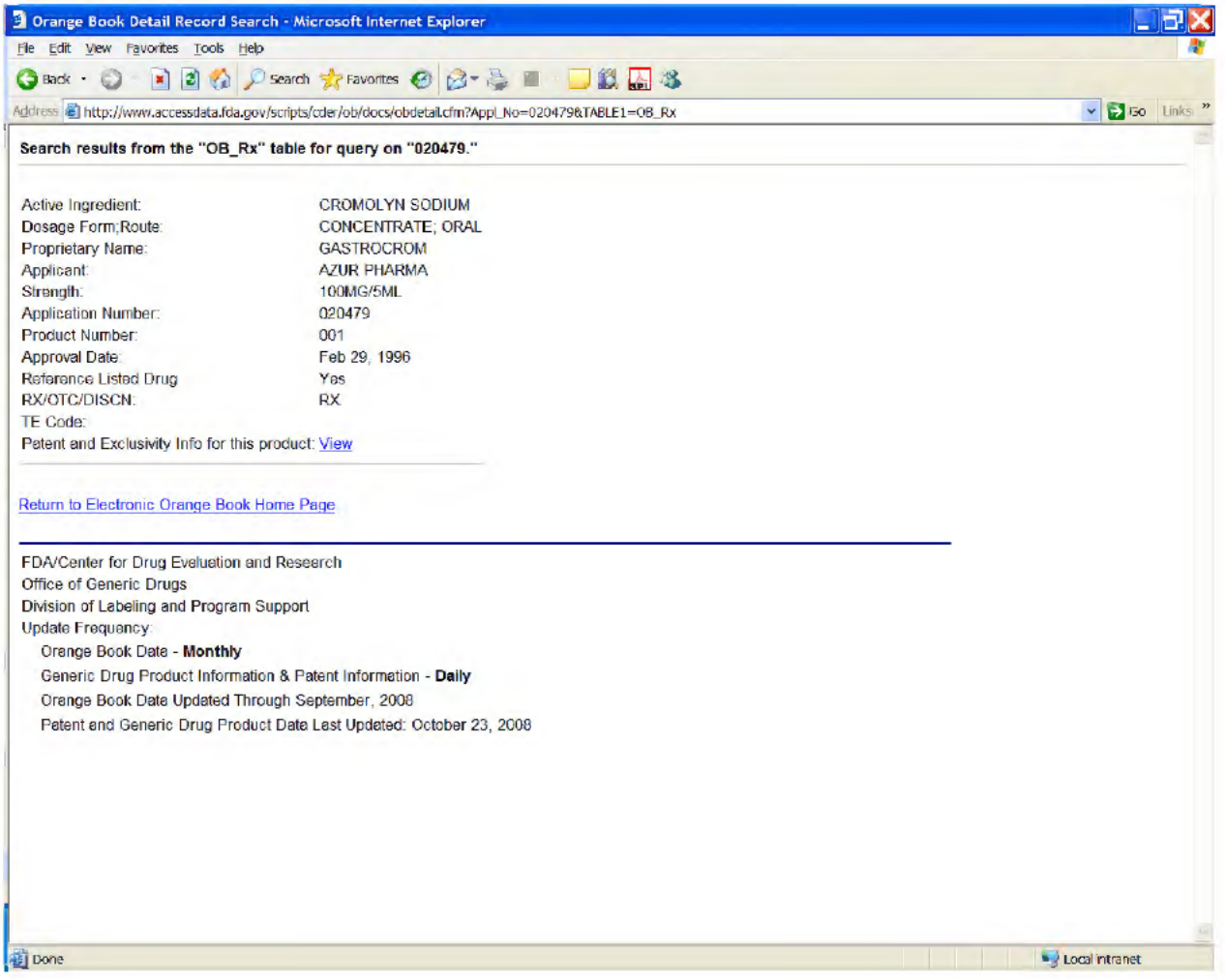
Go Links
Active Ingredient Search Results from "OB_Rx" table for query on "CROMOLYN."
Appl No
TE Code
RLD
Active Ingredient
Dosage Form; Route
Strength
Proprietary Name
Applicant
018887 Yes CROMOLYN SODIUM AEROSOL, METERED; INHALATION 0.8MG/INH INTAL KING PHARMS
020479 Yes CROMOLYN SODIUM CONCENTRATE; ORAL 100MG/5ML GASTROCROM AZUR PHARMA
074706 AT No CROMOLYN SODIUM SOLUTION/DROPS; OPHTHALMIC 4% CROMOLYN SODIUM AKORN
075282 AT No CROMOLYN SODIUM SOLUTION/DROPS; OPHTHALMIC 4% CROMOLYN SODIUM ALCON
018155 AT Yes CROMOLYN SODIUM SOLUTION/DROPS; OPHTHALMIC 4% OPTICROM ALLERGAN
074443 AT No CROMOLYN SODIUM SOLUTION/DROPS; OPHTHALMIC 4% CROLOM BAUSCH AND LOMB
075615 AT No CROMOLYN SODIUM SOLUTION/DROPS; OPHTHALMIC 4% CROMOLYN SODIUM NOVEX
075087 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM ACTAVIS MID ATLANTIC
075585 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM BAUSCH AND LOMB
074209 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM DEY
075271 AN Yes CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM IVAX PHARMS
075346 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM MORTON GROVE
075333 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM NOVEX
075437 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM PHARMASCIENCE INC
076469 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM RESPIRARE
Local intranet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File Edit View Favorites Tools Help
Back Search Favorites
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Go Links
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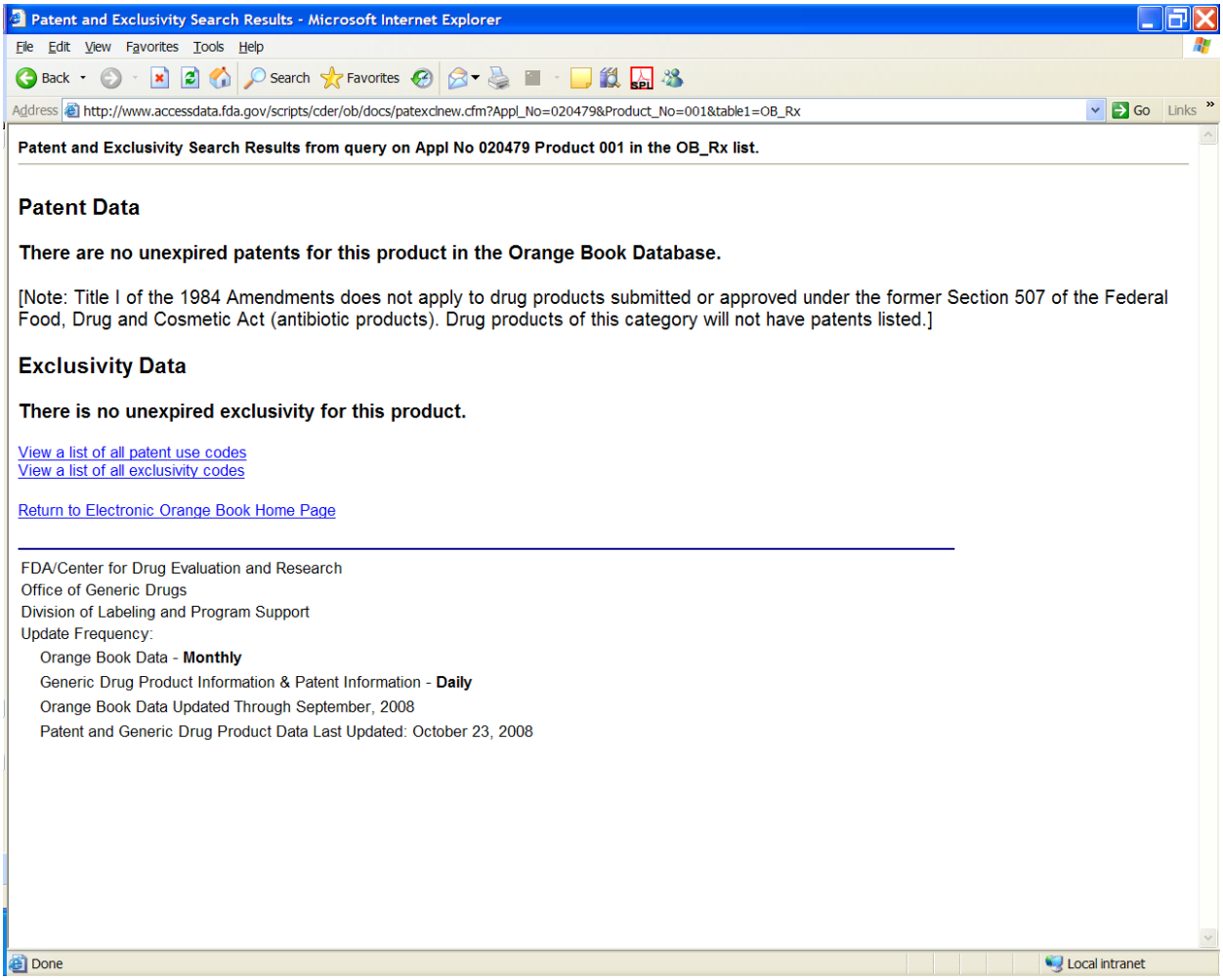
Active Ingredient: CROMOLYN SODIUM
Dosage Form;Route: CONCENTRATE; ORAL
Proprietary Name: GASTROCROM
Applicant: AZUR PHARMA
Strength: 100MG/5ML
Application Number: 020479
Product Number: 001
Approval Date: Feb 29, 1996
Reference Listed Drug Yes
RX/OTC/DISCN: RX
TE Code:
Patent and Exclusivity Info for this product: View
Return to Electronic Orange Book Home Page
FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Date - Monthly
Generic Drug Product Information & Patent Information - Daily
Orange Book Date Updated Through September, 2008
Patent and Generic Drug Product Date Last Updated: October 23, 2008
Done
Local intranet

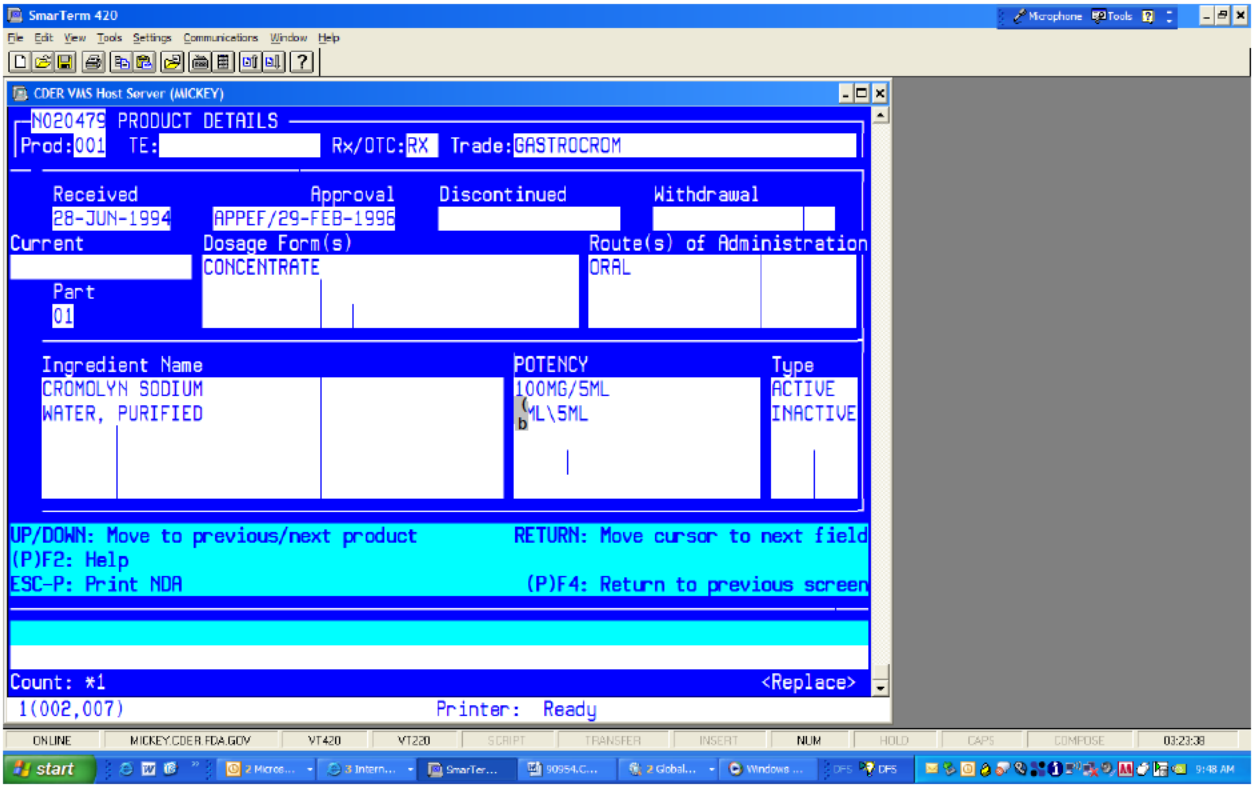

Patent and Exclusivity Search Results - Microsoft Internet Explorer
File Edit View Favorites Tools Help
Back Search Favorites
Address http://www.accessdata.fda.gov/scripts/cder/ob/docs/patexclnew.cfm?Appl_No=020479&Product_No=001&table1=OB_Rx
Go Links
Patent and Exclusivity Search Results from query on Appl No 020479 Product 001 in the OB_Rx list.
Patent Data
There are no unexpired patents for this product in the Orange Book Database.
[Note: Title I of the 1984 Amendments does not apply to drug products submitted or approved under the former Section 507 of the Federal Food, Drug and Cosmetic Act (antibiotic products). Drug products of this category will not have patents listed.]
Exclusivity Data
There is no unexpired exclusivity for this product.
View a list of all patent use codes
View a list of all exclusivity codes
Return to Electronic Orange Book Home Page
FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - Monthly
Generic Drug Product Information & Patent Information - Daily
Orange Book Data Updated Through September, 2008
Patent and Generic Drug Product Data Last Updated: October 23, 2008
Done
Local intranet

DESCRIPTION AND COMPOSITION OF THE DRUG PRODUCT

What are the components and composition of the final product? What is the function(s) of each excipient?

.

Component	Quality Standard	Function	Cromolyn Sodium Oral Concentrate 100 mg/ 5 mL
Cromolyn Sodium	USP	Drug Substance	(b) (4) mg/mL1
Water for Injection	USP	(b) (4)	(b) (4)
Total Volume		5.0 mL	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N020479 PRODUCT DETAILS
Prod:001 TE: Rx/OTC:RX Trade:GASTROCROM
Received
28-JUN-1994
Approval
APPEF/29-FEB-1996
Discontinued
Withdrawal
Current
Dosage Form(s)
CONCENTRATE
Route(s) of Administration
ORAL
Part
01
Ingredient Name
CROMOLYN SODIUM
WATER, PURIFIED
POTENCY
100MG/5ML
ML\5ML
Type
ACTIVE
INACTIVE
UP/DOWN: Move to previous/next product
RETURN: Move cursor to next field
(P)F2: Help
ESC-P: Print NDA
(P)F4: Return to previous screen
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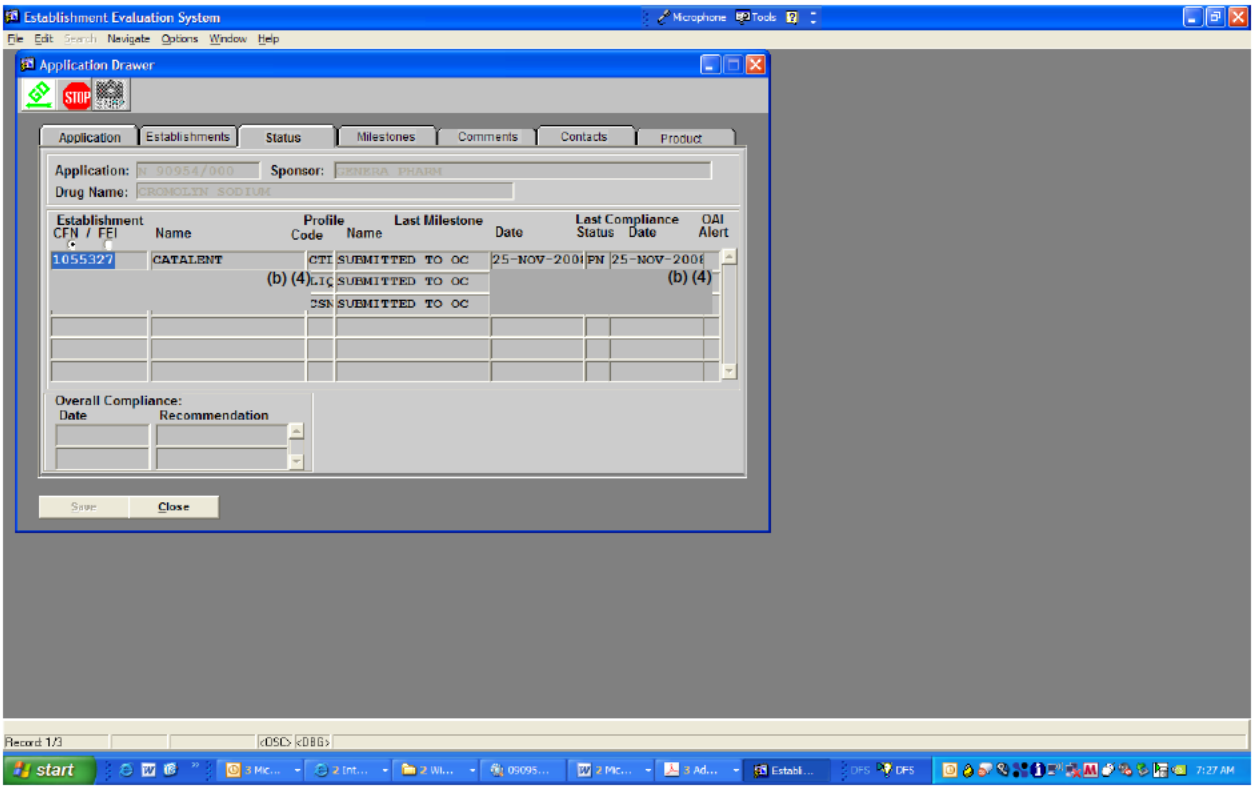
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Establishments
Status
Milestones
Comments
Contacts
Product
Application:
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Establishment CFN / FEI
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Profile Code
Last Milestone Name
Date
Last Compliance Status
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(b) (4)
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(b) (4)
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Overall Compliance:
Date
Recommendation
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Close
Record: 1/3
start

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

/s/

Martin Shimer

12/2/2008 11:58:02 AM

[redacted] (b) (4)

rec. via fax - mtf - S. Middleton 11/12/08

November 3, 2008

MC

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park, North II
7500 Standish Place, Room 150
Rockville, MD 20855-2733
ATTN: Ms. Saundra Middleton

RE: Genera Pharmaceuticals ANDA No. 90-954 / Sodium Cromoglycate

Dear Ms. Middleton:

As requested, attached please find the DMF Holder's authorization letter designating [redacted] (b) (4) as the US Agent with authority to grant access to the DMF.

Please feel free to contact me should you have any further questions at 908-981-5873.

Regards,

[redacted] (b) (4)

CC: Genera Pharmaceuticals
Ray Nathan

Encl.

[redacted] (b) (4)

RECEIVED
NOV 04 2008
OGD

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 90-954

Genera Pharmaceuticals, LLC
Attention: V. Ray Nathan, Ph.D.
13734 Trento Place
San Diego, CA 92130

Dear Sir:

Please refer to your abbreviated new drug application (ANDA) dated October 20, 2008, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Cromolyn Sodium Oral Concentrate, 100 mg/5 mL.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to receive this ANDA under 21 CFR 314.101(d)(3) for the following reasons:

You have failed to provide (b) (4) validation data in your application. (b) (4) validation is required for drug products that are (b) (4) filled. You should consult the *Guidance for Industry for the Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products* (November 1994) for guidance on (b) (4) validation study.

The exhibit batch in Module 3 needs to be in a legible format. There are many pages in the exhibit batch that are not legible, please resubmit a readable copy of the exhibit batch.

Please provide the following:

1. A batch reconciliation detailing the proposed production yield as well as the theoretical and actual yields for each executed batch size.

2. Current Good Manufacturing Practices (cGMP) in accord with 21 CFR Parts 210 and 211 from the **holder** of the ANDA.

3. You have failed to provide a letter from the DMF holder, (b) (4) as the U.S. Agent with authority to grant access to the DMF. Please provide authorization from the DMF holder in support of this application.

Thus, it will not be received as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

Upon receipt of this communication, you may either amend your application to correct the deficiencies or withdraw your application under 21 CFR 314.99. If you have any questions please call:

Saundra T. Middleton
Project Manager
(240) 276-8421

Sincerely yours,

{See appended electronic signature page}

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
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/

Martin Shimer
10/28/2008 06:57:19 AM
Signing for Wm Peter Rickman

ANDA CHECKLIST FOR CTD or eCTD FORMAT
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION FOR FILING

For More Information on Submission of an ANDA in Electronic Common Technical Document (eCTD) Format please go to: http://www fda.gov/cder/regulatory/ersr/ectd.htm
***For a Comprehensive Table of Contents Headings and Hierarchy please go to:**
http://www fda.gov/cder/regulatory/ersr/5640CTOC-v1.2.pdf
**** For more** CTD and eCTD informational links **see the final page of the ANDA Checklist**
*** **A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage** http://www.fda.gov/cder/ogd/ ***

ANDA #: 90-954 **FIRM NAME**: GENERA PHARMACEUTICALS LLC

PIV: NO **Electronic or Paper Submission:** ELECTRONIC (GATEWAY)

RELATED APPLICATION(S): NA

First Generic Product Received? NO

Bio Assignments:		
☒ **BPH**	☐ **BCE**	☒ **Micro Review (Yes)**
☐ **BST**	☐ **BDI**	

DRUG NAME: CROMOLYN SODIUM
DOSAGE FORM: ORAL CONCENTRATE , 100 MG/5 ML (20 MG/ML)
Random Queue: 2
Chem Team Leader: Smela, Michael Chem PM: Esther Chuh Labeling Reviewer: Angela Payne
Bio PM: Lizzie Sanchez (Acting Bio PM)

Letter Date: OCTOBER 20, 2008 **Received Date**: OCTOBER 22, 2008

Comments: EC- 1 YES **On Cards:** YES
Therapeutic Code: 6011800 MISCELLANOUS RESPIRATORY

Archival copy: ELECTRONIC (GATEWAY) **Sections** I
Review copy: NA E-Media Disposition: NO
Not applicable to electronic sections

PART 3 Combination Product Category N Not a Part3 Combo Product
(Must be completed for ALL Original Applications) Refer to the Part 3 Combination Algorithm

Reviewing CSO/CST Saundra T. Middleton	**Recommendation:**
Date 10/27/2008	☐ **FILE** ☒ **REFUSE to RECEIVE**
Supervisory Concurrence/Date: _____	**Date:** _____

ADDITIONAL COMMENTS REGARDING THE ANDA:

Note: Genera has requested expedited review. Expedited review granted, see next page.

You have failed to provide (b) (4) validation data in your application. (b) (4) validation is required for drug products that are (b) (4) filled. You should consult the *Guidance for Industry for the Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products* (November 1994) for guidance on (b) (4) validation study.

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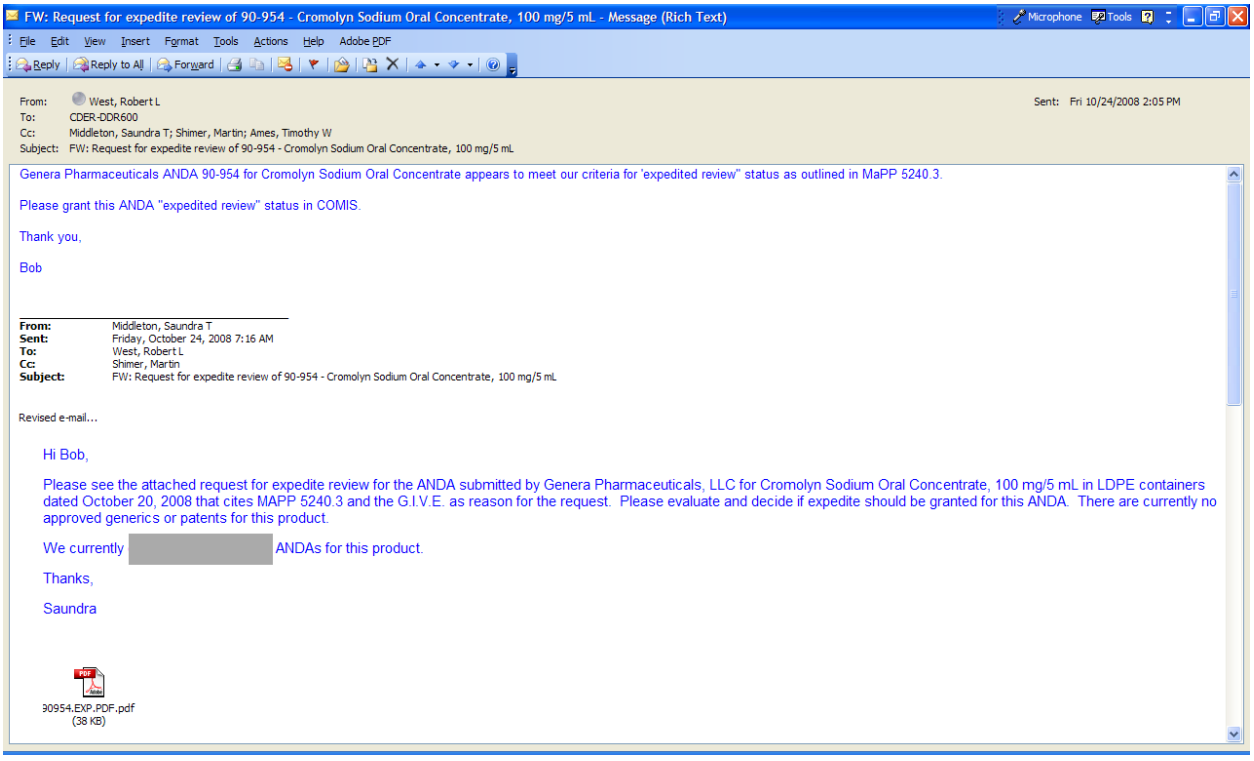
Please provide the following:

1. A batch reconciliation detailing the proposed production yield as well as the theoretical and actual yields for each executed batch size.

2. Current Good Manufacturing Practices (cGMP) in accord with 21 CFR Parts 210 and 211 from the **holder** of the ANDA.



FW: Request for expedite review of 90-954 - Cromolyn Sodium Oral Concentrate, 100 mg/5 mL - Message (Rich Text)

File Edit View Insert Format Tools Actions Help Adobe PDF

Reply | Reply to All | Forward

From: West, Robert L
To: CDER-DDR600
Cc: Middleton, Saundra T; Shimer, Martin; Ames, Timothy W
Subject: FW: Request for expedite review of 90-954 - Cromolyn Sodium Oral Concentrate, 100 mg/5 mL
Sent: Fri 10/24/2008 2:05 PM

Genera Pharmaceuticals ANDA 90-954 for Cromolyn Sodium Oral Concentrate appears to meet our criteria for 'expedited review" status as outlined in MaPP 5240.3.

Please grant this ANDA "expedited review" status in COMIS.

Thank you,

Bob

From: Middleton, Saundra T
Sent: Friday, October 24, 2008 7:16 AM
To: West, Robert L
Cc: Shimer, Martin
Subject: FW: Request for expedite review of 90-954 - Cromolyn Sodium Oral Concentrate, 100 mg/5 mL

Revised e-mail...

Hi Bob,

Please see the attached request for expedite review for the ANDA submitted by Genera Pharmaceuticals, LLC for Cromolyn Sodium Oral Concentrate, 100 mg/5 mL in LDPE containers dated October 20, 2008 that cites MAPP 5240.3 and the G.I.V.E. as reason for the request. Please evaluate and decide if expedite should be granted for this ANDA. There are currently no approved generics or patents for this product.

We currently (b) (4) ANDAs for this product.

Thanks,

Saundra

90954.EXP.PDF.pdf
(38 KB)

MODULE 1
ADMINISTRATIVE

ACCEPTABLE

1.1	**1.1.2 Signed and Completed Application Form (356h) (original signature)** (Check Rx/OTC Status) RX YES	☒
1.2	**Cover Letter** Dated: OCTOBER 22, 2008	☒
1.2.1	**Form FDA 3674 (PDF) YES**	☒
*	**Table of Contents (paper submission only)** YES	☒
1.3.2	**Field Copy Certification (original signature)** NA **(N/A for E-Submissions)**	☒
1.3.3	**Debarment Certification-GDEA (Generic Drug Enforcement Act)/Other:** 1. Debarment Certification (original signature) YES 2. List of Convictions statement (original signature)	☒
1.3.4	**Financial Certifications** Bioavailability/Bioequivalence Financial Certification (Form FDA 3454) NA Disclosure Statement (Form FDA 3455, submit copy to Regulatory Branch Chief) NA **Form FDA 3674 YES**	☐
1.3.5	**1.3.5.1 Patent Information** Patents listed for the RLD in the Electronic Orange Book Approved Drug Products with Therapeutic Equivalence Evaluations **1.3.5.2 Patent Certification** 1. Patent number(s) No patents 2. Paragraph: (Check all certifications that apply) MOU ☐ PI ☒ PII ☐ PIII ☐ PIV ☐ (Statement of Notification) ☐ 3. Expiration of Patent(s): a. Pediatric exclusivity submitted? b. Expiration of Pediatric Exclusivity? 4. Exclusivity Statement: YES	☒
1.4.1	**References** Letters of Authorization 1. DMF letters of authorization a. Type II DMF authorization letter(s) or synthesis for Active Pharmaceutical Ingredient YES - Type II (b) (4) b. Type III DMF authorization letter(s) for container closure **YES** 2. US Agent Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) NA	☒
1.12.11	**Basis for Submission** NDA# : 20-479 Ref Listed Drug: GASTROCROM Firm: AZUR PHARMA, INC. ANDA suitability petition required? NA If Yes, then is change subject to PREA (change in dosage form, route or active ingredient) see section 1.9.1	☒

MODULE 1 (Continued)
ADMINISTRATIVE

ACCEPTABLE

1.12.12	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use **YES** 2. Active ingredients **YES** 3. Inactive ingredients **YES** 4. Route of administration **YES** 5. Dosage Form **YES** 6. Strength **YES**	☒
1.12.14	**Environmental Impact Analysis Statement** YES	☒
1.12.15	**Request for Waiver** Request for Waiver of In-Vivo BA/BE Study(ies): YES	☒
1.14.1	**Draft Labeling (Mult Copies N/A for E-Submissions)** **1.14.1.1** 4 copies of draft (each strength and container) **1.14.1.2** 1 side by side labeling comparison of containers and carton with all differences annotated and explained **YES** **1.14.1.3** 1 package insert (content of labeling) submitted electronically **YES** ***Was a proprietary name request submitted? no (If yes, send email to Labeling Reviewer indicating such.)	☒
1.14.3	**Listed Drug Labeling** **1.14.3.1** 1 side by side labeling (package and patient insert) comparison with all differences annotated and explained **YES** **1.14.3.3** 1 RLD label and 1 RLD container label **YES**	☒

MODULE 2
SUMMARIES ACCEPTABLE

2.3	**Quality Overall Summary (QOS)** **E-Submission: PDF YES** **Word Processed e.g., MS Word YES** A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage http://www fda.gov/cder/ogd/ **Question based Review (QbR) YES** **2.3.S** **Drug Substance (Active Pharmaceutical Ingredient) YES** **2.3.S.1 General Information** **2.3.S.2 Manufacture** **2.3.S.3 Characterization** **2.3.S.4 Control of Drug Substance** **2.3.S.5 Reference Standards or Materials** **2.3.S.6 Container Closure System** **2.3.S.7 Stability** **2.3.P** **Drug Product YES** **2.3.P.1 Description and Composition of the Drug Product** **2.3.P.2 Pharmaceutical Development** **2.3.P.2.1 Components of the Drug Product** **2.3.P.2.1.1 Drug Substance** **2.3.P.2.1.2 Excipients** **2.3.P.2.2 Drug Product** **2.3.P.2.3 Manufacturing Process Development** **2.3.P.2.4 Container Closure System** **2.3.P.3 Manufacture** **2.3.P.4 Control of Excipients** **2.3.P.5 Control of Drug Product** **2.3.P.6 Reference Standards or Materials** **2.3.P.7 Container Closure System** **2.3.P.8 Stability**	☒
2.7	**Clinical Summary (Bioequivalence) - NA** **Model Bioequivalence Data Summary Tables** **E-Submission: PDF** **Word Processed e.g., MS Word** **2.7.1 Summary of Biopharmaceutic Studies and Associated Analytical Methods** **2.7.1.1 Background and Overview** Table 1. Submission Summary Table 4. Bioanalytical Method Validation Table 6. Formulation Data **2.7.1.2 Summary of Results of Individual Studies** Table 5. Summary of In Vitro Dissolution **2.7.1.3 Comparison and Analyses of Results Across Studies** Table 2. Summary of Bioavailability (BA) Studies Table 3. Statistical Summary of the Comparative BA Data **2.7.1.4 Appendix** **2.7.4.1.3 Demographic and Other Characteristics of Study Population** Table 7. Demographic Profile of Subjects Completing the Bioequivalence Study **2.7.4.2.1.1 Common Adverse Events** Table 8. Incidence of Adverse Events in Individual Studies	☐

MODULE 3

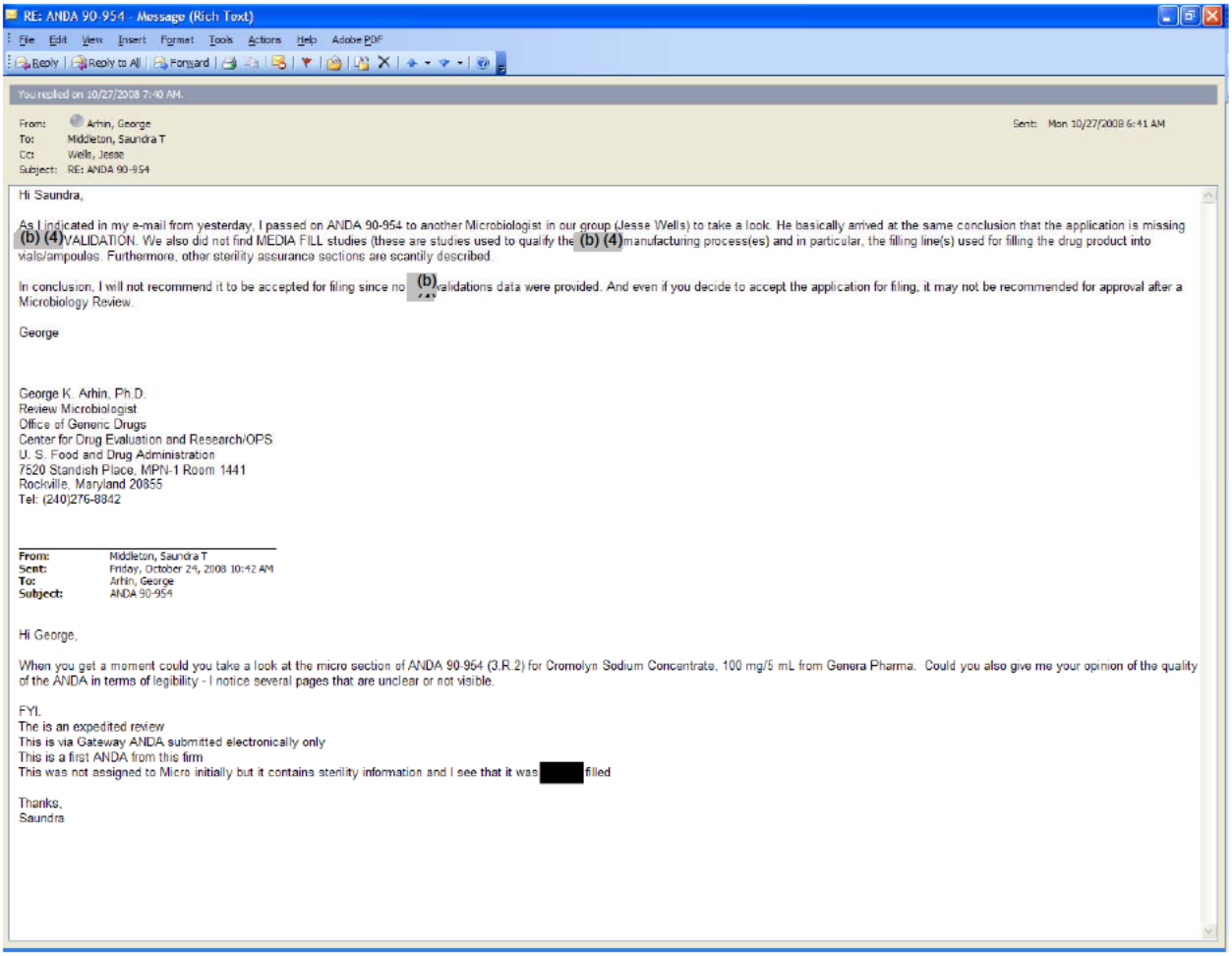
3.2.S DRUG SUBSTANCE ACCEPTABLE

3.2.S.1	**General Information** **3.2.S.1.1 Nomenclature** **3.2.S.1.2 Structure** **3.2.S.1.3 General Properties**	☒
3.2.S.2	**Manufacturer** **3.2.S.2.1** **Manufacturer(s) (This section includes contract manufacturers and testing labs)** **Drug Substance (Active Pharmaceutical Ingredient)** 1. Name and Full Address(es)of the Facility(ies) **YES** 2. Function or Responsibility **YES** 3. Type II DMF number for API (b) (4) 4. CFN or FEI numbers	☒
3.2.S.3	**Characterization**	☒
3.2.S.4	**Control of Drug Substance (Active Pharmaceutical Ingredient)** **3.2.S.4.1 Specification** Testing specifications and data from drug substance manufacturer(s) **YES** **3.2.S.4.2 Analytical Procedures YES** **3.2.S.4.3 Validation of Analytical Procedures** 1. Spectra and chromatograms for reference standards and test samples **YES** 2. Samples-Statement of Availability and Identification of: a. Drug Substance **YES** b. Same lot number(s) **YES** **3.2.S.4.4 Batch Analysis** 1. COA(s) specifications and test results from drug substance mfgr(s) **YES** 2. Applicant certificate of analysis **YES** **3.2.S.4.5 Justification of Specification**	☒
3.2.S.5	**Reference Standards or Materials**	☒
3.2.S.6	**Container Closure Systems – IN DMF**	☒
3.2.S.7	**Stability – IN DMF**	☒

MODULE 3

3.2.P DRUG PRODUCT ACCEPTABLE

3.2.P.1	**Description and Composition of the Drug Product** 1. Unit composition **YES** 2. Inactive ingredients and amounts are appropriate per IIG **YES – SEE BELOW**	☒
3.2.P.2	**Pharmaceutical Development** Pharmaceutical Development Report **YES**	☒
3.2.P.3	**Manufacture** **3.2.P.3.1 Manufacture(s)** (Finished Dosage Manufacturer and Outside Contract Testing Laboratories) 1. Name and Full Address(es)of the Facility(ies) **YES** 2. CGMP Certification: YES 3. Function or Responsibility **YES** 4. CFN or FEI numbers **YES** **3.2.P.3.2 Batch Formula YES** **3.2.P.3.3 Description of Manufacturing Process and Process Controls** 1. Description of the Manufacturing Process **YES** 2. Master Production Batch Record(s) for largest intended production runs (no more than (b) (4) pilot batch) with equipment specified (b) (4) 3. If sterile product: Aseptic fill / Terminal sterilization 4. Reprocessing Statement **YES** **3.2.P.3.4 Controls of Critical Steps and Intermediates** **3.2.P.3.5 Process Validation and/or Evaluation** 1. Microbiological sterilization validation NO see e-mail below from George Arhin 2 (b) (4) validation (if (b) (4) NO – see e-mail below:	☒



RE: ANDA 90-954 - Message (Rich Text)

File Edit View Insert Format Tools Actions Help Adobe PDF

Reply | Reply to All | Forward

You replied on 10/27/2008 7:40 AM.

From: Arhin, George
To: Middleton, Saundra T
Cc: Wells, Jesse
Subject: RE: ANDA 90-954

Sent: Mon 10/27/2008 6:41 AM

Hi Saundra,

As I indicated in my e-mail from yesterday, I passed on ANDA 90-954 to another Microbiologist in our group (Jesse Wells) to take a look. He basically arrived at the same conclusion that the application is missing (b) (4) VALIDATION. We also did not find MEDIA FILL studies (these are studies used to qualify the (b) (4) manufacturing process(es) and in particular, the filling line(s) used for filling the drug product into vials/ampoules. Furthermore, other sterility assurance sections are scantily described.

In conclusion, I will not recommend it to be accepted for filing since no (b) validations data were provided. And even if you decide to accept the application for filing, it may not be recommended for approval after a Microbiology Review.

George

George K. Arhin, Ph.D.
Review Microbiologist
Office of Generic Drugs
Center for Drug Evaluation and Research/OPS
U. S. Food and Drug Administration
7520 Standish Place, MPN-1 Room 1441
Rockville, Maryland 20855
Tel: (240)276-8842

From: Middleton, Saundra T
Sent: Friday, October 24, 2008 10:42 AM
To: Arhin, George
Subject: ANDA 90-954

Hi George,

When you get a moment could you take a look at the micro section of ANDA 90-954 (3.R.2) for Cromolyn Sodium Concentrate, 100 mg/5 mL from Genera Pharma. Could you also give me your opinion of the quality of the ANDA in terms of legibility - I notice several pages that are unclear or not visible.

FYI.
The is an expedited review
This is via Gateway ANDA submitted electronically only
This is a first ANDA from this firm
This was not assigned to Micro initially but it contains sterility information and I see that it was [redacted] filled

Thanks,
Saundra

3.2.P.4	**Controls of Excipients (Inactive Ingredients)** Source of inactive ingredients identified **YES** **3.2.P.4.1 Specifications** 1. Testing specifications (including identification and characterization) **YES** 2. Suppliers' COA (specifications and test results) **YES** **3.2.P.4.2 Analytical Procedures** **3.2.P.4.3 Validation of Analytical Procedures** **3.2.P.4.4 Justification of Specifications** Applicant COA	☒

MODULE 3

3.2.P DRUG PRODUCT

ACCEPTABLE

3.2.P.5	**Controls of Drug Product** **3.2.P.5.1 Specification(s) YES** **3.2.P.5.2 Analytical Procedures YES** **3.2.P.5.3 Validation of Analytical Procedures** Samples - Statement of Availability and Identification of: 1. Finished Dosage Form **YES** 2. Same lot numbers **YES** **3.2.P.5.4 Batch Analysis** Certificate of Analysis for Finished Dosage Form **YES** **3.2.P.5.5 Characterization of Impurities** **3.2.P.5.6 Justification of Specifications**	☒
3.2.P.7	**Container Closure System** 1. Summary of Container/Closure System (if new resin, provide data) **YES** 2. Components Specification and Test Data **YES** 3. Packaging Configuration and Sizes **YES** 4. Container/Closure Testing **YES** 5. Source of supply and suppliers address **YES**	☒
3.2.P.8	**3.2.P.8.1 Stability (Finished Dosage Form)** 1. Stability Protocol submitted **YES** 2. Expiration Dating Period **YES – 24 MONTHS** **3.2.P.8.2 Post-approval Stability and Conclusion** Post Approval Stability Protocol and Commitments **YES** **3.2.P.8.3 Stability Data** 1. 3 month accelerated stability data **YES** 2. Batch numbers on stability records the same as the test batch **YES**	☒

MODULE 3

3.2.R Regional Information

ACCEPTABLE

3.2.R (Drug Substance)	**3.2.R.1.S Executed Batch Records for drug substance (if available) NO** **3.2.R.2.S Comparability Protocols NA** **3.2.R.3.S Methods Validation Package NA** Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☒

3.2.R (Drug Product)	**3.2.R.1.P.1** **Executed Batch Records** Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures) Batch Reconciliation and Label Reconciliation **YES** Theoretical Yield (b) (4) Actual Yield (b) (4) Packaged Yield (b) (4) **3.2.R.1.P.2 Information on Components YES** **3.2.R.2.P Comparability Protocols NO** **3.2.R.3.P Methods Validation Package** NA Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☒

MODULE 5

CLINICAL STUDY REPORTS

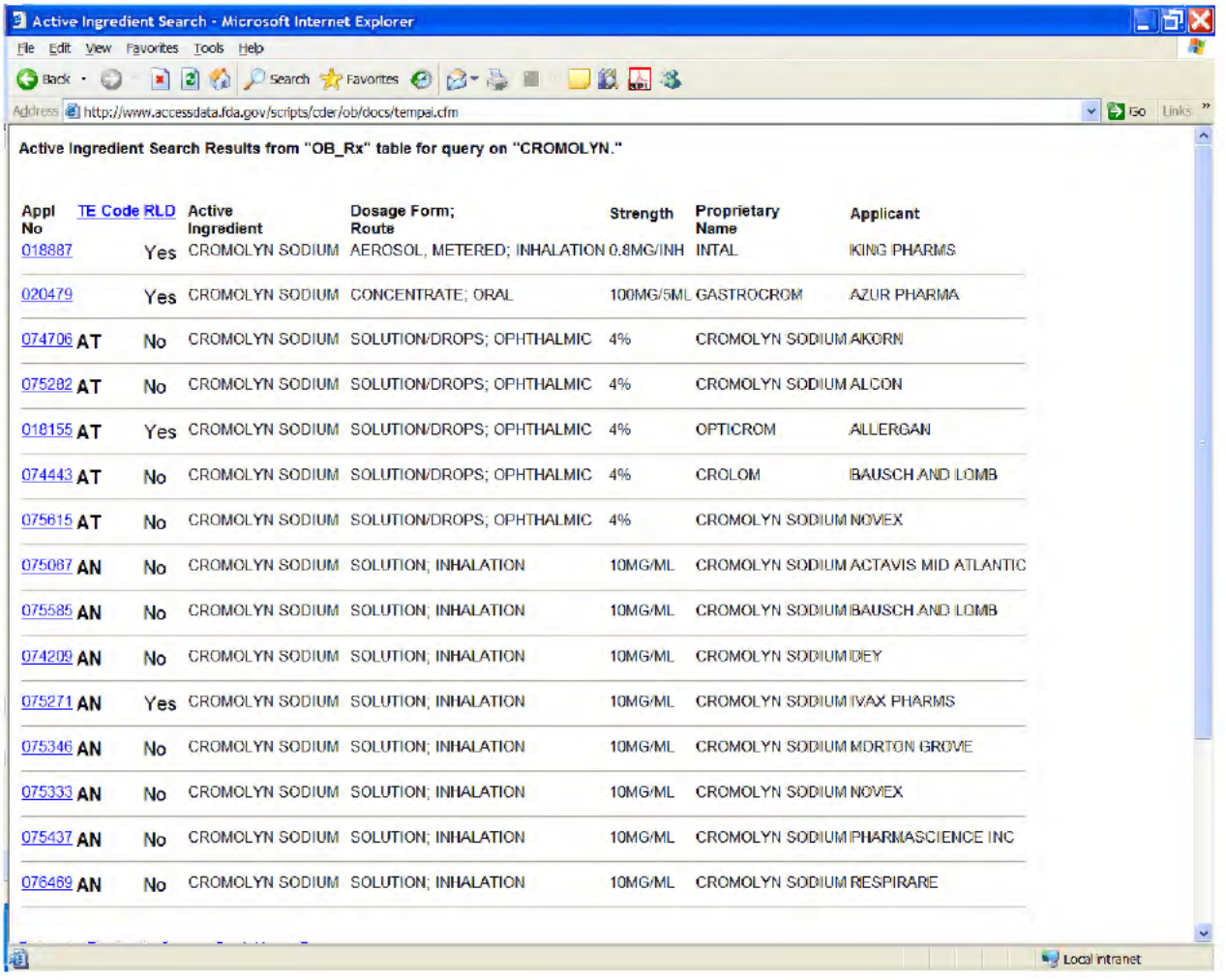
ACCEPTABLE

5.2	**Tabular Listing of Clinical Studies - NA**	☐
5.3.1 (complete study data)	**Bioavailability/Bioequivalence** **1. Formulation data same?** a. Comparison of all Strengths (check proportionality of multiple strengths) b. Parenterals, Ophthalmics, Otics and Topicals per 21 CFR 314.94 (a)(9)(iii)-(v) **2. Lot Numbers of Products used in BE Study(ies):** **3. Study Type: IN-VIVO PK STUDY(IES)** (Continue with the appropriate study type box below)	☐

	5.3.1.2 Comparative BA/BE Study Reports 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. Summary Bioequivalence tables: Table 10. Study Information Table 12. Dropout Information Table 13. Protocol Deviations **5.3.1.3** **In Vitro-In-Vivo Correlation Study Reports** 1. Summary Bioequivalence tables: Table 11. Product Information Table 16. Composition of Meal Used in Fed Bioequivalence Study **5.3.1.4** **Reports of Bioanalytical and Analytical Methods for Human Studies** 1. Summary Bioequivalence table: Table 9. Reanalysis of Study Samples Table 14. Summary of Standard Curve and QC Data for Bioequivalence Sample Analyses Table 15. SOPs Dealing with Bioanalytical Repeats of Study Samples **5.3.7** **Case Report Forms and Individual Patient Listing**	☐
5.4	**Literature References**	☐
	Possible Study Types:	
Study Type	**IN-VIVO BE STUDY(IES) with PK ENDPOINTS** (i.e., fasting/fed/sprinkle) NA 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted: YES SENT TO EDR 3. In-Vitro Dissolution: NO	☐
Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** NO 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria: 90% CI of the proportional difference in success rate between test and reference must be within (-0.20, +0.20) for a binary/dichotomous endpoint. For a continuous endpoint, the test/reference ratio of the mean result must be within (0.80, 1.25). 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted	☐
Study Type	**IN-VITRO BE STUDY(IES)** (i.e., in vitro binding assays) NO 1. Study(ies) meets BE criteria (90% CI of 80-125) 2. EDR Email: Data Files Submitted: 3. In-Vitro Dissolution:	☐

Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** 1. Solutions (Q1/Q2 sameness): a. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming) 2. Suspensions (Q1/Q2 sameness): a. In-Vivo PK Study 1. Study(ies) meets BE Criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted b. In-Vivo BE Study with Clinical End Points 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria (90% CI within +/- 20% of 80-125) 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted c. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming)	☐
Study Type	**IN-VIVO BE STUDY(IES) with PD ENDPOINTS** (e.g., topical corticosteroid vasoconstrictor studies) 1. Pilot Study (determination of ED50) 2. Pivotal Study (study meets BE criteria 90%CI of 80-125)	☐
Study Type	**TRANSDERMAL DELIVERY SYSTEMS** 1. In-Vivo PK Study 1. Study(ies) meet BE Criteria (90% CI of 80-125, C max, AUC) 2. In-Vitro Dissolution 3. EDR Email: Data Files Submitted 2. Adhesion Study 3. Skin Irritation/Sensitization Study	☐

Updated 8/11/2008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Appl No
TE Code
RLD
Active Ingredient
Dosage Form; Route
Strength
Proprietary Name
Applicant
018887 Yes CROMOLYN SODIUM AEROSOL, METERED; INHALATION 0.8MG/INH INTAL KING PHARMS
020479 Yes CROMOLYN SODIUM CONCENTRATE; ORAL 100MG/5ML GASTROCROM AZUR PHARMA
074706 AT No CROMOLYN SODIUM SOLUTION/DROPS; OPHTHALMIC 4% CROMOLYN SODIUM AKORN
075282 AT No CROMOLYN SODIUM SOLUTION/DROPS; OPHTHALMIC 4% CROMOLYN SODIUM ALCON
018155 AT Yes CROMOLYN SODIUM SOLUTION/DROPS; OPHTHALMIC 4% OPTICROM ALLERGAN
074443 AT No CROMOLYN SODIUM SOLUTION/DROPS; OPHTHALMIC 4% CROLOM BAUSCH AND LOMB
075615 AT No CROMOLYN SODIUM SOLUTION/DROPS; OPHTHALMIC 4% CROMOLYN SODIUM NOVEX
075087 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM ACTAVIS MID ATLANTIC
075585 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM BAUSCH AND LOMB
074209 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM DEY
075271 AN Yes CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM IVAX PHARMS
075346 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM MORTON GROVE
075333 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM NOVEX
075437 AN No CROMOLYN SODIUM SOLUTION; INHALATION 10MG/ML CROMOLYN SODIUM PHARMASCIENCE INC
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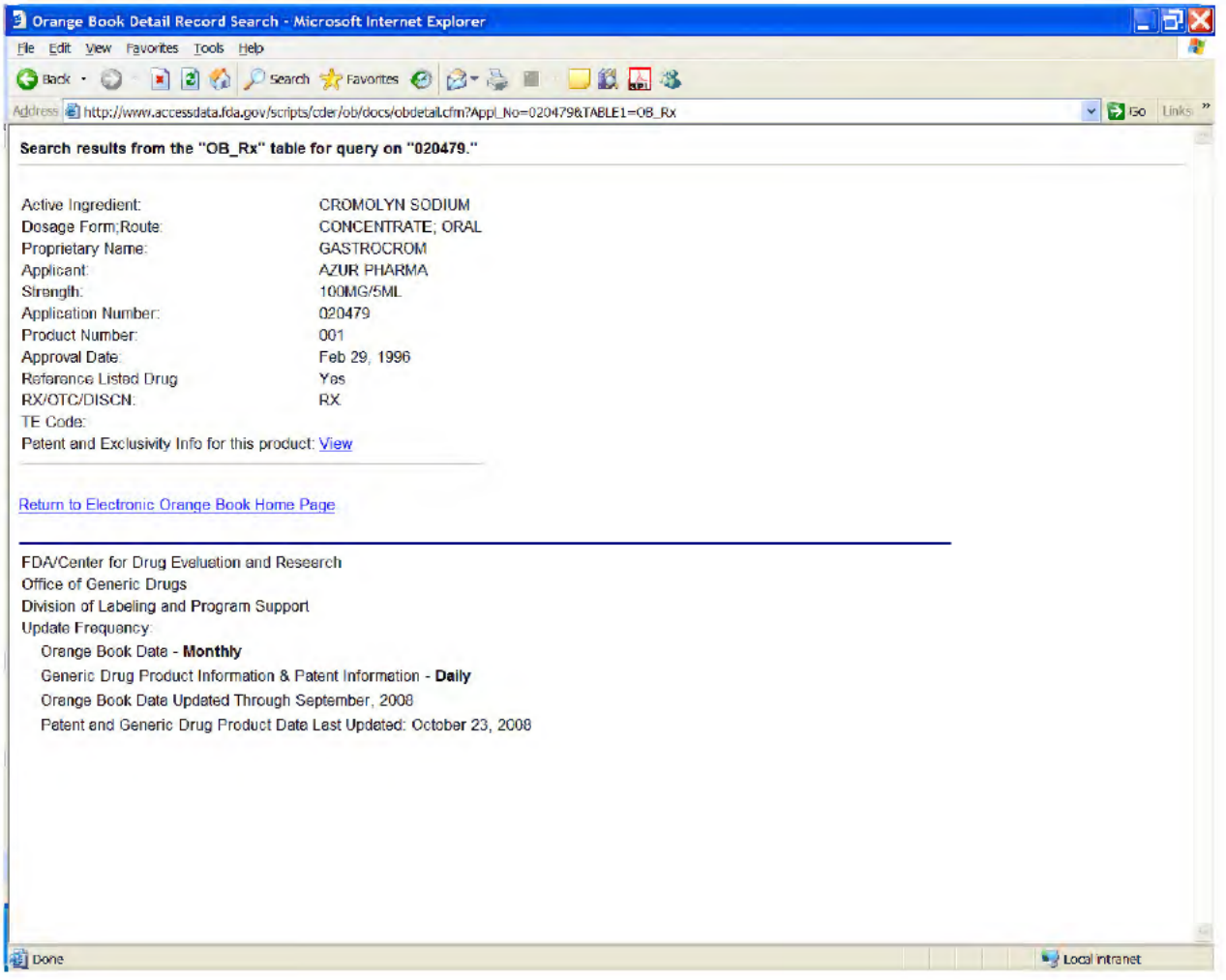
Local intranet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Applicant: AZUR PHARMA
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Application Number: 020479
Product Number: 001
Approval Date: Feb 29, 1996
Reference Listed Drug Yes
RX/OTC/DISCN: RX
TE Code:
Patent and Exclusivity Info for this product: View
Return to Electronic Orange Book Home Page
FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Date - Monthly
Generic Drug Product Information & Patent Information - Daily
Orange Book Date Updated Through September, 2008
Patent and Generic Drug Product Date Last Updated: October 23, 2008
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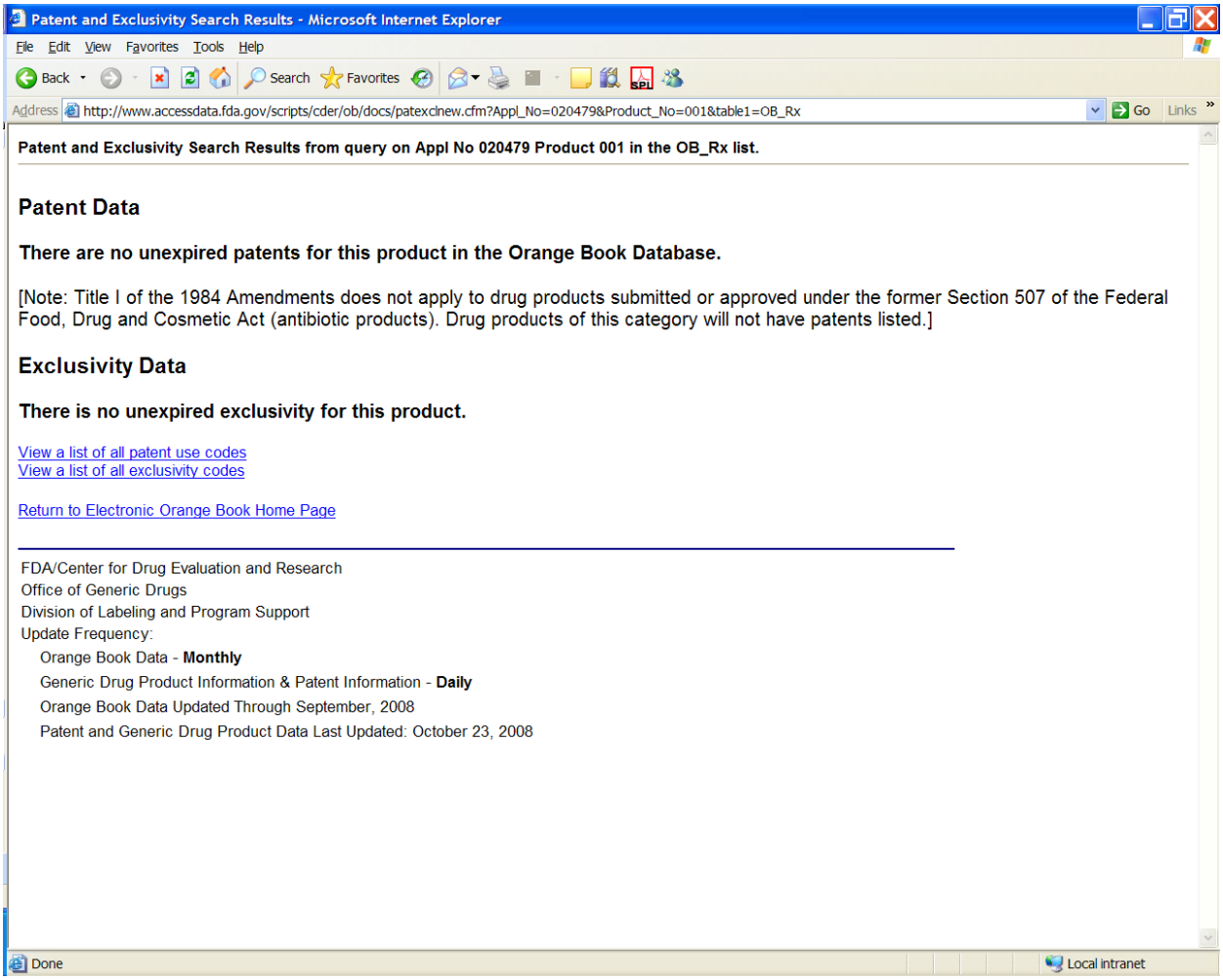
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Go Links
Patent and Exclusivity Search Results from query on Appl No 020479 Product 001 in the OB_Rx list.
Patent Data
There are no unexpired patents for this product in the Orange Book Database.
[Note: Title I of the 1984 Amendments does not apply to drug products submitted or approved under the former Section 507 of the Federal Food, Drug and Cosmetic Act (antibiotic products). Drug products of this category will not have patents listed.]
Exclusivity Data
There is no unexpired exclusivity for this product.
View a list of all patent use codes
View a list of all exclusivity codes
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FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - Monthly
Generic Drug Product Information & Patent Information - Daily
Orange Book Data Updated Through September, 2008
Patent and Generic Drug Product Data Last Updated: October 23, 2008
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DESCRIPTION AND COMPOSITION OF THE DRUG PRODUCT

What are the components and composition of the final product? What is the function(s) of each excipient?

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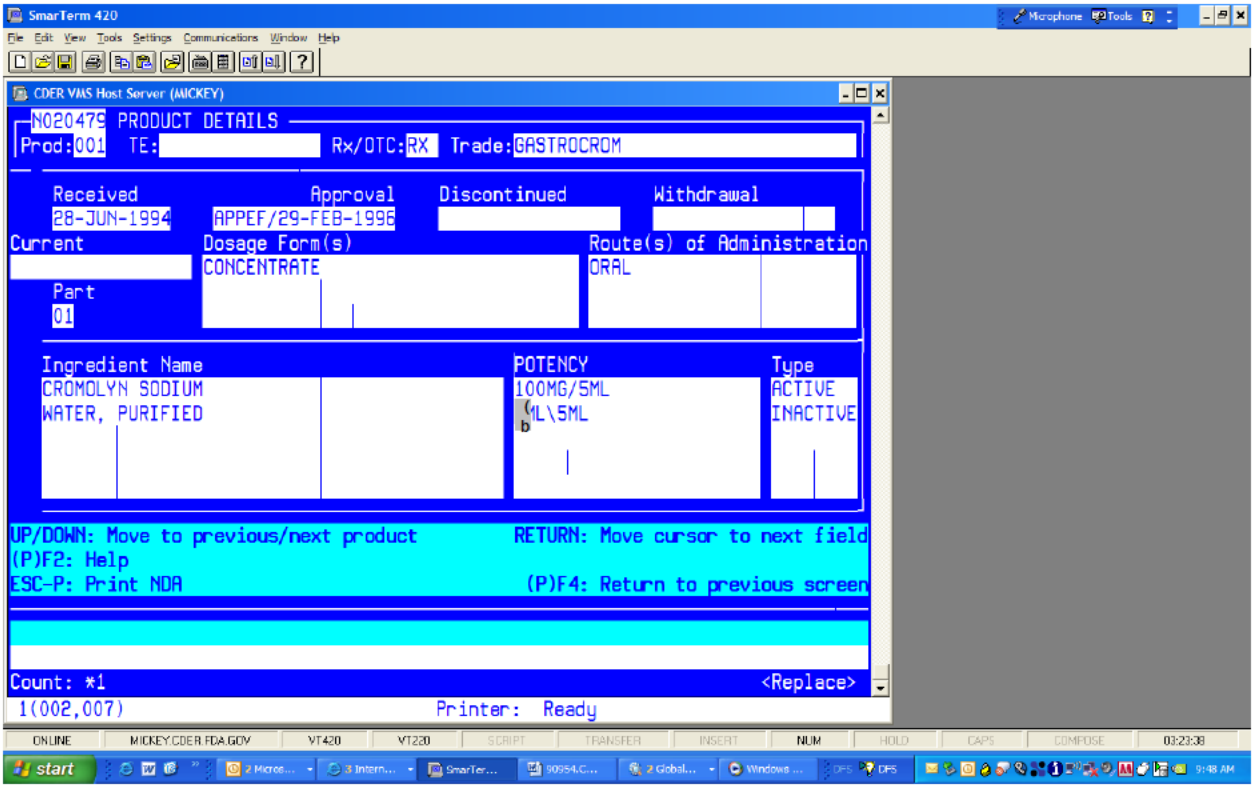
Component	Quality Standard	Function	Cromolyn Sodium Oral Concentrate 100 mg/ 5 mL
Cromolyn Sodium	USP	Drug Substance	(b) (4) mg/mL1
Water for Injection	USP	(b) (4)	
Total Volume		5.0 mL	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CDER VMS Host Server (MICKEY)
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Approval
APPEF/29-FEB-1996
Discontinued
Withdrawal
Current
Part
01
Dosage Form(s)
CONCENTRATE
Route(s) of Administration
ORAL
Ingredient Name
CROMOLYN SODIUM
WATER, PURIFIED
POTENCY
100MG/5ML
5ML\5ML
Type
ACTIVE
INACTIVE
UP/DOWN: Move to previous/next product
RETURN: Move cursor to next field
(P)F2: Help
ESC-P: Print NDA
(P)F4: Return to previous screen
Count: *1
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Printer: Ready
ONLINE
MICKEY.CDER.FDA.GOV
VT420
VT220
SCRIPT
TRANSFER
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HOLD
CAPS
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/s/

Martin Shimer

10/28/2008 06:56:49 AM