

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
40098

CORRESPONDENCE

MAR 21 1994

ANDA 40-098

MOVA Pharmaceutical Corp.
Attention: Dale Kaufman
P.O. Box 8639
Caguas, PR 00726

Dear Madam:

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

NAME OF DRUG: Acetaminophen and Codeine Phosphate Elixir USP,
120 mg/12 mg per 5 mL

DATE OF APPLICATION: February 25, 1994

DATE OF RECEIPT: March 1, 1994

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

Please provide a revised debarment and conviction certification with an original signature as required by the Generic Drug Enforcement Act (GDEA) of 1992 [GDEA Sections 306(k)(1) and (2)].

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

Sincerely yours,

/s/

3/21/94

Robert W. Pollock
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 40-098
DUP/Jacket
Division File
Field Copy
HFD-600/Reading File
HFD-82
HFD-615/MBennett

Endorsements: HFD-615/GJohnston, Chief *Johnston 3/17/94* date
HFD-615/Prickman, CSO *Prickman 3/13/94* date
HFD-615/WRussell, CSO *WRussell 3/15/94* date
HFD-647/Chem Branch *Simonson 3-21-94* date
WP File\russell\40-098
F/T by hrw 3-17-94
ANDA Acknowledgement Letter!



ANDA 40-098

Food and Drug Administration
Rockville MD 20857

MOVA Pharmaceutical Corporation
Attention: Dale Robson
P.O. Box 8639
Caguas, Puerto Rico 00626

MAR 19 1996

Dear Madam:

This is in reference to your abbreviated new drug application dated February 25, 1994, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Acetaminophen and Codeine Phosphate Oral Solution USP, 120 mg/12 mg per 5 mL.

Reference is also made to your amendment dated July 7, 1995 and telephone communications on February 6, 1996 and March 15, 1996.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

Labeling Deficiencies:

INSERT

DESCRIPTION - Revise the molecular weight of acetaminophen to read 151.17 as per USP 23.

Please revise your labeling, as instructed above, and submit final print insert labeling. Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

Please note this request for final printed labeling was made by telephone on February 6, 1996 by Adolph Vezza of our office; and the request was repeated on March 15, 1996. However, as of this date we have not received your response.

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 the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed.

The response to this letter will be considered a **MINOR** amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/s/

3/18/96

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

MOVA Pharmaceutical Corporation
Attention: Dale Kaufman
P.O. Box 8639
Caguas, Puerto Rico 00626

APR 24 1995

Dear Madam:

This is in reference to your abbreviated new drug application dated February 25, 1994, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Acetaminophen and Codeine Phosphate Oral Solution USP, 120 mg/12 mg per 5 mL.

Reference is also made to your amendment dated December 5, 1995.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

A. Chemistry Deficiencies

1. The certificates of analysis for Acetaminophen USP from applicant and are incomplete. The specifications of Organic Volatile Impurities should be numbers or ranges and limits rather than simply "meets the requirements". Please provide the acceptable limits of Organic Volatile Impurities.
2. Please cite the appropriate section of 21 CFR referring to the status of artificial cherry flavor [e.g., CFR 172 (Natural flavoring substance and synthetic flavoring substance) and/or CFR 182 (Substances that are generally recognized as safe)] and certify that it meets the requirements.
3. Provide a description of the production of the for Injection used for the manufacturing process of the subject drug product.
4. The submission fails to provide a complete formula card and satisfactory batch record. In this regard:
 - a. We note that the types and specifications for each piece of the equipment have been identified in the revision of Maximum Batch Size Manufacturing Instructions. Please submit a table comparing equipment and procedures used in the manufacture of the test batch with the Maximum production (intended commercial) batch.

- b. The executed batch record in the original submission and in the Attachment VI of the amendment dated on December 4, 1994 is not acceptable. Please submit the complete executed batch record and packaging records for lot JL345v in English (i.e., a line by line, certified English translation including handwritten notes and footnotes).
5. We note that specification for the presence or absence of _____ in the release product specification is not acceptable. Please provide the potential impurities and degradation products and their limits for the subject drug product in the release product specifications and submit the updated certificate of analysis for the finished product (lot JL3451).
 6. Your application fails to contain satisfactory stability data. In this regard:
 - a. A component and Composition Statement rather than the formula number must be included in the stability data report.
 - b. Please provide specifications or acceptable limits for _____ in the stability data report.

B. Labeling Deficiencies

CONTAINER: 473 mL

Front Panel - Please place the following statement underneath the "WARNING - May be habit forming" statement:

Alcohol ...7%

INSERT:

1. DESCRIPTION
 - a. Third paragraph, line 1
... -ol phosphate...
 - b. "Each 5 mL contains" statement - Delete
 - c. Please include the description of the flavor.
2. PRECAUTIONS

- a. Nursing Mothers, line 4 - Delete the extra space between the words "nursing" and "or".
 - b. Pediatric Use - ... in pediatric patients below the age...
3. DOSAGE AND ADMINISTRATION
- a. Paragraph 1, line 5 -...appreciable...
["appreciable" rather than
 - b. Children (7 to 12 years) - To be consistent with the other dosage statements, indent the "10 mL" so it is in alignment with the "5 mL" from the line below.
4. HOW SUPPLIED

We encourage the inclusion of your storage conditions as seen on the label and the "CAUTION": Federal law..." statement.

Revise your container labels and insert labeling, then prepare and submit final printed container labels and draft insert labeling.

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 the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a MAJOR amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

17

/S/

4/24/95

Frank O. Holcombe, Jr., Ph.D.
Acting Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

MOVA Pharmaceutical Corporation
Attention: Dale Kaufman
P.O. Box 8639
Caguas, Puerto Rico 00726

AUG 10 1994

Dear Madam:

This is in reference to your abbreviated new drug application dated February 25, 1994, submitted pursuant to Section 505(j) of the Food, Drug, and Cosmetic Act for Acetaminophen and Codeine Phosphate Oral Solution USP, 120 mg/12 mg per 5 mL.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

A. Chemistry Deficiencies

1. Regarding components and composition:

- a. It is noted that For Injection, USP were included in the components and composition statement, master formula and manufacturing procedures of the drug product. Please document the amounts of each used and provide any directions for the decision in the batch records.
- b. Please indicate the quantity of For Injection, USP used in the composition of the drug product.
- c. It is noted that FD & C Yellow No. 6 was the only color listed in the composition statement of the finished product and there were no other colors listed in the composition of artificial cherry flavor. However, the description in the HOW SUPPLIED section indicates the finished product has an orange color. Please reconcile.
- d. Alcohol USP, 7% should also be listed in the components and composition section. Please provide the calculations you used to determine the 7.0% v/v absolute alcohol in the composition of the labeled amount.
- e. Please include the limits or maximum amounts of Citric Acid, USP and used to adjust pH.

- f. Submit the revised and complete components and composition section for the drug product to include quantities in mg per 5 mL.
2. Regarding active ingredient:
 - a. The certificates of analysis for Acetaminophen USP and Codeine Phosphate USP from applicant, were incomplete. The specifications for these tests (e.g. Identification, and Organic Volatile Impurities) should be numbers or ranges and limits rather than simply "meets the requirements". Please submit IR & UV spectra, R_f value, and the chromatogram of samples for Identification tests. Please include a chromatogram of the USP reference standard. Please provide the acceptable limits of organic volatile impurities.
 - b. Three manufacturing sites were provided for the Acetaminophen USP in DMF . Which facility actually manufactures the drug substance used for the subject drug product. Please submit the address of the manufacturing site for the drug substance.
 - c. The manufacturing site for the drug substance, Codeine Phosphate USP submitted on page 235 of the original submission is incorrect. Please provide the address of the manufacturing site for the drug substance, Codeine Phosphate USP.
 3. Regarding inactive ingredients:
 - a. Submit the DMF authorization letter for artificial cherry flavor from . Submit the quantitative composition of artificial cherry flavor . Cite the appropriate food section of 21 CFR referring to its status (e.g. GRAS etc).
 - b. Identify the sources of for injection.
 - c. You are advised that microbiological testing should be conducted on each lot of components, prior to use in the manufacture of the drug product, for those components for which the microbial limits test is specified by USP/NF [21 CFR 211.84 (d) (6)]. Please provide a commitment to a 12-month retest period.

4. The submission fails to provide a complete formula card and satisfactory batch record. In this regard:
 - a. The sources of active ingredients and drug product manufacturing site should be included.
 - b. Manufacturing procedure (e.g., pilot or production batch) should be included.
 - c. Submit the revised master formula for the drug product based on the above comments and the composition [(1.(a-f)) comments.
 - d. Submit the complete executed batch record and packaging records on lot JL345v in English. A comprehensive review of manufacturing and processing, and packaging cannot be conducted until the issue of the complete English version of executed batch record is satisfactorily resolved.
 - e. What is the testing protocol for the filter?
 - f. We note the terms suitable mixer and suitable stainless steel holding tank in your application (e.g. the comparative summary of the listing of equipment and batch records). Please identify the types and specifications for each. Please add speed of agitation and time of mixing to the blank batch records.
5. The application fails to include the operation procedures and precautions necessitated by the light sensitivity and control status of the active ingredients.
6. The application fails to specify any in-process testing. What tests will be conducted and what are the acceptable limits for those tests?
7. Your application fails to contain a complete description of the container/closure systems. In that regard:
 - a. Which pigment is used in the resin for bottle and closure ?
 - b. Submit the actual test results to demonstrate resin meets the current USP XXII/NFXVII Physicochemical requirements for plastic containers.

- c. Please indicate type of resin used for the polypropylene closure and submit USP test results.
 - d. Submit the actual test results of torque required for cap removal.
 - e. Identify a DMF # for _____ and submit the authorization letter.
 - f. We note that the reference listed drug is marketed in an amber container. Please provide a justification for the use of a white HDPE bottle and any comparison data available.
8. Regarding finished product:
- a. Submit chromatograms to document that the excipients including alcohol do not interfere with Acetaminophen and Codeine Phosphate assays in the finished product.
 - b. Please provide an adequate stability-indicating assay method. In this regard:
 - i) Present in percentages the assay values of the active ingredients and degradation products under various stress conditions in tabular form. Please submit the chromatograms obtained for each of the conditions tested.
 - ii) Identify the common impurities/degradation products of acetaminophen and codeine phosphate. Label chromatograms and list quantities. You must demonstrate that no degradation products coelute with the acetaminophen and codeine phosphate peaks.
 - c. The certificate of analysis for the finished product is incomplete. Product description, batch size, date of manufacture, the sources of active ingredients, manufacturing procedure (e.g., pilot or production batch), manufacturing site, complete container/closure system and related substance/or impurities should be included.

- d. We note that the lot for the executed batch record in Spanish is JL345v. However, the lot used for the certificate of analysis for the finished product, part of analytical method validation and stability data report is JL3451. Please clarify and submit the COA for lot JL345v. In addition, submit the English translated batch record lot JL3451 used for stability studies.
9. Your application fails to contain satisfactory stability protocol and stability data. In this regard:
- a. Composition [see comments 1.(a-f)] and batch size of the drug product must be included.
 - b. Relative humidity of % is not required for a liquid or elixir in an accelerated stability study. However, the actual relative humidity reading of the 40°C chamber or oven should be recorded.
 - c. For all future studies, room temperature stability testing must be conducted in the 25°C-30°C range. The temperature and humidity conditions are to be monitored and reported in the stability reports.
 - d. For liquid product, all sizes of the container/closure system should be included in stability studies.
 - e. Degradation product or the test results for should be included in the stability studies and stability data report under both room temperature and challenge conditions.
 - f. Submit the revised stability protocol and stability data based on the above comments.

B. Labeling Deficiencies

CONTAINER:

1. FRONT PANEL - The statement "Warning-May be habit forming" should be relocated to appear immediately below "Codeine Phosphate...12 mg" and also should have an asterisk.
2. RIGHT SIDE PANEL - Please include the temperature range. (i.e., 15°-30°C [59°-86°F])
3. Include an asterisk after "CODEINE PHOSPHATE" in the established name.

4. We see no need for the statement "Orange Colored".
You may delete if you wish.

INSERT:

Revise your insert labeling to be in accord with the
Labeling Guidance for Acetaminophen with Codeine
Phosphate Oral Solution, USP (revised December 1993).

Revise your container labels and insert labeling, then
prepare and submit final printed container labels and draft
insert labeling.

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 the deficiencies listed. A partial reply will not
be considered for review, nor will the review clock be
reactivated until all deficiencies have been addressed. The
response to this letter will be considered a **MAJOR** amendment and
should be so designated in your cover letter. If you have
substantial disagreement with our reasons for not approving this
application, you may request an opportunity for a hearing.

Sincerely yours,

^
' /S/ '

Y
8/9/94

C. Greg Guyer, Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

ENCLOSURE: LABELING GUIDANCE



MOVA PHARMACEUTICAL CORPORATION

P. O. Box 8639
Caguas, Puerto Rico 00626
(809) 746 8500

October 7, 1994

Timothy Ames, Consumer Safety Officer
Food & Drug Administration
Office of Generic Drugs
Division of Chemistry II
HFD 625 Room 204
7500 Standish Place
Rockville, MD 20855

BEST POSSIBLE COPY

Dear Mr. Ames:

In reviewing the items in the Major Deficiency Letter ANIDA 40-098 for Acetaminophen and Codeine Phosphate Oral Solution USP, 120 mg/12 mg per 5 mL, dated August 10, 1994, we need to have the following items clarified: *pg 63-64*
82-83

- In item 2(a) please indicate which page reference the item refers to. Is it MOVA's COA or the vendors COA for this issue? *use ref?*

extra not
only marked
above
IR spectra for Acetaminophen, lot #30943, can be found on Pages 89-90 of the ANIDA submission and the USP reference standard on Page 91-92. UV spectra are found on Pages 98-99. chromatogram is on Page 102. *not clearly labeled as use ref + d.*

The IR spectra for the Codeine, lot #31084 can be found on Pages 153-156. Please clarify the request for this information. *pg 153-4 is*

- In item 3(a) of the letter we are asked to submit the quantitative composition of artificial cherry flavor. In section VIII of the original ANIDA submission Pages 296-298, we included a semi quantitative disclosure of this ingredient in which range of percent values of its composition were presented. This report also includes the FEMA-GRAS number requested. A DMF authorization referral letter from the vendor will also be included as part of the response to this item. Is this data sufficient to satisfy this response? *identification of IR is unclear*

- In item 4(a) we are asked to provide a complete formula card and batch record that include the sources of active ingredients and drug product manufacturing site. The information regarding the sources of the active ingredients is included under the title "approved sources" in the ingredient's specification or quality standard. In MOVA's

Make
should be
formula

BEST POSSIBLE COPY

documentation system, the formula card and batch record do not contain this information. It can be traced from the item code number for the individual Raw Material that is assigned for each product. The drug product's manufacturing site, however, is included in the heading of both the formula card (i.e., manufacturing order) and the drug master formula (see Pages 328-334 in Section XI of the ANDA submission). MOVA's manufacturing site for Acetaminophen and Codeine Phosphate Oral Solution USP, 120 mg/12 mg per 5 mL, is Caguas, Puerto Rico. Is this satisfactory in addressing item 4(a)? *we routinely request source on formula card & batch record as a way of*

quickly identifying past or changes *can be attached if records are computer generated*
Item 4(d) requests the submission of the complete executed batch record and packaging records on lot JL345V in English. Section XII of our original ANDA submission contains a copy of the executed manufacturing and packaging batch records in Spanish. The translation of the notes and comments contained in the executed batch records in Spanish are also included. A blank copy of the English translation of the executed manufacturing and packaging batch records are included in this section on Pages 416-431 and 465-477. Please clarify your request for an English executed record (all MOVA manufacturing and packaging records are executed in Spanish).

In item 4(e) we are asked what the testing protocol for the filter is. This filter is a polishing filter and not a sterilization filter (i.e., a new filter is installed for each new production batch). Therefore, a testing protocol is not applicable. What is the reviewer's request in this item? *an explanation is adequate*

Item 7(d) requests the submission of the actual test results of required for cap removal. On page 448 of our original ANDA submission, MOVA has documented the actual readings performed in the packaging process of JL345V (English translation of the form is on page 448). The established range on page 448 calls for a specification of NMT in/pounds and NLT in/pounds. The readings recorded on this page are all within the established range. Does this clarify the reviewer's request? *not obvious translate page does not clarify.*

Regarding the finished product, item 8(a) requests the submission of the chromatograms to document that the excipients, including alcohol, do not interfere with Acetaminophen and Codeine Phosphate assays in the finished product. The individual chromatograms for all the excipients including alcohol were submitted in Section XVI of our original ANDA submission as part of the Method Validation Report #40563-93-003 for Acetaminophen, USP and #004 for Codeine Phosphate, USP (figures 1 to 13). See Pages 885-907 and 920-942.

good

Timothy Ames
October 7, 1994
Page 3

The chromatograms show no evidence of co-elution between an excipient's peak (including alcohol) and the active ingredients. Therefore, we conclude that no interference with the Acetaminophen and Codeine Phosphate occurs.

The method validation package provided on Pages 885-919 for Acetaminophen assay makes the statement on Page 889 that the other substances in the sample (including alcohol) do not interfere with the separation of the Acetaminophen peak. Likewise, in the method validation for Codeine Phosphate on Pages 930-956 the same statement is made on Page 924 for this assay. All chromatograms were included in these reports. Please clarify the reviewer's request for this information.

- In item 9(e) we are requested to include the degradation product or test results for p-aminophenol in the stability studies and stability data report under both room temperature and challenge conditions. Chromatograms in the forced degradation studies (to be included in the response to the deficiency letter) do not show the presence of an impurity related to _____ and this phenomenon could be explained by the fact that the excipients stabilize the active ingredients and no degradation occurs. Therefore, MOVA believes that it is not necessary to perform a test for this degradation product. Can FDA please clarify the reason behind this request and the specific reference to _____

*USP
stability must be
included in stability*

We appreciate the information you can provide us in order to respond promptly and adequately to the items in the deficiency letter.

Sincerely,

Carmen D. Cintrón
Regulatory Affairs Associate

rhc

xc Dale Kaufman

BEST POSSIBLE COPY



MOVA PHARMACEUTICAL CORPORATION
P.O. Box 8639
Caguas, Puerto Rico 00726
(809) 746-8500

*Noted, WAT
CSO
4/8/94*

NEW CORRESP
NC

March 26, 1994

Mr. D. Sporn
Office of Generic Drugs
Center of Drug Evaluation & Research
Food & Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

**RE: ANDA #40-098 Acetaminophen and Codeine Phosphate Oral
Solution, USP 120 mg/12 mg per 5 mL - Amendment**

Dear Mr. Sporn:

In response to the request in your approval to file letter dated March 21, 1994, enclosed you will find a Debarment & Conviction Certification for ANDA #40-098 with an original signature as required by the Generic Drug Enforcement Act (GDEA) of 1992, Sections 306 (k) (1) and (2).

Sincerely yours,

Carmen Delia Cintron
Carmen Delia Cintron
Regulatory Affairs Associate

RECEIVED

APR 4 1994

GENERIC DRUGS

ORIGINAL

*Noted
4/8/94*



*SCS (j) (2) (A)
acceptable for filing
TUC
3/17/94*

*CPH
3/16/94*

*Labeling reviewed & approved
Aliza 5/25/94*

MOVA PHARMACEUTICAL CORPORATION
P.O. Box 8639
Caguas, Puerto Rico 00726
(809) 746-8500

February 25, 1994

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

Ref. Original ANDA for
Acetaminophen and Codeine Phosphate
Oral Solution, USP 120 mg/12 mg per 5 mL

Dear Dr. Williams:

As set forth in 21 U.S.C. 355 (j) and the current Code of Federal Regulations § 314.92 (a)(1), an original Abbreviated New Drug Application (ANDA) is being submitted, herewith, for the drug product Acetaminophen and Codeine Phosphate Oral Solution, USP 120 mg/12 mg per 5 mL. The listed reference drug is TYLENOL with Codeine Elixir, NDA sponsored by McNeil Pharmaceutical, McNeilab Inc. (R. W. Johnson), Spring House, PA 19477-0776.

We are enclosing an archival copy and a review copy, in conformance with the Abbreviated New Drug Application Regulations Final Rule, published in the Federal Register of April 28, 1992. The archival copy (blue jacket) contains all the information required in Volume 1.1 to Volume 1.3. The Technical review copy (red jacket) is contained in Volume 1.1 to Volume 1.3 and contains all items required in an Abbreviated New Drug Application including labeling, chemistry, manufacturing and controls; and a request for waiver of "in vivo" bioavailability data. There is no orange jacket copy enclosed due to the request for waiver of the "in vivo" bioavailability data.

A Field copy (maroon jacket) that contains all items required in conformance with the Abbreviated New Drug Application Regulations Final Rule published in the Federal Register of ~~August 8, 1993~~, has been filed with the San Juan district Food and Drug Administration office.

RECEIVED

MAR 0 1 1994

GENERIC DRUGS

Page 2
Director
Division of Generic Drugs
Ref. Original ANDA
Acetaminophen and Codeine Phosphate
Oral Solution, USP 120 mg/12 mg per 5 mL

Labeling is included as a draft copy. The required four copies of each are included as follows: Four copies in Volume 1.1 of the archival copy and four copies in Volume 1.1 of the review copy.

The information in the attached submission is CONFIDENTIAL because the material in those pages constitute trade secrets or commercial or financial information which is privileged or confidential within the meaning of the Freedom of Information Act (5 USC 552). If for any reason the Food and Drug Administration officials feel that the disclosure of any of the CONFIDENTIAL material should be made available to any member of the public, we expect that because of the importance of maintaining secrecy of this material to MOVA Pharmaceutical Corporation, you will first consult with us on the issue of disclosure.

We look forward to your review and comment.

Sincerely,

A handwritten signature in cursive script that reads "Dale Kaufman" with a horizontal line underneath the name.

Dale Kaufman
Vice President of
Regulatory Affairs &
Corporate Compliance

MOVA Number: 0794



MOVA PHARMACEUTICAL CORPORATION

P. O. Box 8639
Caguas, Puerto Rico 00626
(809) 746-8500

December 5, 1994

Food and Drug Administration
Office of Generic Drugs
Center for Drug Evaluation & Research
Division of Chemistry II
Metro Park North II
7500 Standish Place
Rockville, MD 20857-2773

*Labeling review
completed
A. Vega 1/23/95*

AMENDMENT *FPL*
n/a c

RE: ANDA #40-098 ACETAMINOPHEN AND CODEINE PHOSPHATE ORAL
SOLUTION USP, 120 mg/12 mg per 5 mL

MAJOR AMENDMENT

Dear Sir/Madam:

In response to the deficiency letter dated August 10, 1994, MOVA Pharmaceutical Corporation hereby submits a MAJOR AMENDMENT for the above referenced ANDA.

The following documents are included:

- ✓ A copy of the deficiency letter
- ✓ Responses to each of the chemistry deficiencies
- ✓ Attachments I - XIV which consist of documents that support MOVA's responses to the deficiencies
- ✓ Attachment XV which consist of twelve (12) final printed container labels and four (4) copies of the revised draft insert with the changes requested.

If you have any question regarding this amendment submission, please contact me at (809) 746-8500, extension 234.

Cordially,

Carmen Delia Cintron

Carmen Delia Cintron
Regulatory Affairs Associate

rhc

RECEIVED

DEC 9 1994

GENERIC DRUGS



MOVA PHARMACEUTICAL CORPORATION

P. O. Box 8639
Caguas, Puerto Rico 00626
(809) 746-8500

May 15, 1995.

Timothy Ames
Consumer Safety Officer
Office of Generic Drugs
Division of Chemistry II
HFD 625, Room 204
7500 Standish Place
Rockville, MD 20855

Dear Mr. Ames:

In reviewing the chemistry deficiencies in your letter dated 4/24/95 for ANDA #40-098, Acetaminophen and Codeine Phosphate Oral Solution USP, 120mg/12mg per 5 mL., we need to clarify the following items:

- Item A.1. states that the certification of analysis for Acetaminophen USP from MOVA and [redacted] are incomplete since the specifications provided for OVI were submitted as, "meets the requirements" and not as numbers or ranges. MOVA believes we responded to this item in our previous amendment submission (12/5/94). (Please refer to statement #2.a. and Attachment III of the response). At that time we stated that based on USP <467> testing is not required if the vendor can certify that OVIs are not produced during the manufacturing, handling or storage of the material. A copy of this certification (from [redacted]) was included in Attachment III of our response along with copies of the material's CoAs and raw data. Please note that for OVI in MOVA's CoA, we reference the vendor's CoA which states that per USP, the material "meets all requirements", including OVI. Why is this response incomplete?

- In item #4.b. we are requested to submit in English the complete executed batch record and packaging records for lot JL345V. This item was addressed previously in our response dated 12/5/94. (Please refer to item #4.d. and Attachment VI). Copies of the executed batch record and its corresponding packaging record were resubmitted along with a certification of translations and written translations in English directly adjacent to all notes/comments. The only items not translated are numbers and signatures which do not require translation. Originally, translations and a blank English copy of records were also included in the ANDA, pages 415-431 and 460-477. Can you please be more specific as to why the information we have provided is not sufficient?

● Item 6.a. states that a component and composition statement must be included in the Stability Data Report. The stability reports we previously submitted in our response describe the active ingredient(s) and the container/closure system used in the product. Do you want a list of all the excipients used to be included in this stability report?

● In the previous deficiency you requested a specific assay for . Now you are requesting specific limits of the other impurities as well. MOVA has not observed any of the other impurities in our stability program to date. Please explain the purpose of now requesting this information, as we have shown from our method validation that they can be qualitatively detected using our active ingredient assay.

We appreciate the information you can provide us in order to respond promptly and adequately to the Chemistry deficiencies. I will contact you tomorrow Tuesday, May 15, 1995 to confirm the fax transmittal and if possible, to clarify the deficiency items above.

Sincerely,



Carmen Delia Cintron
Regulatory Affairs Associate



MOVA PHARMACEUTICAL CORPORATION
P.O. Box 8639
Caguas, Puerto Rico 00726
(809) 746-8500

July 7, 1995

FPL/Oral
AMENDMENT
N/A/C

Food and Drug Administration
Office of Generic Drugs
Center for Drug Evaluation & Research
Division of Chemistry II
Metro Park North II
7500 Standish Place
Rockville, MD 20857-2773

RE: ANDA #40-098 ACETAMINOPHEN AND CODEINE PHOSPHATE ORAL SOLUTION USP, 120 mg/12 mg per 5 mL

MAJOR AMENDMENT

Dear Sir/Madam:

In response to the deficiency letter dated April 24, 1995, MOVA Pharmaceutical Corporation hereby submits a MAJOR AMENDMENT for the above referenced ANDA.

The following documents are included:

- A copy of the deficiency letter
- Responses to each of the chemistry deficiencies cited in the letter
- Attachments I - VI which consist of documents that support MOVA's responses to the deficiencies
- Attachment VII which consist of twelve (12) final printed container labels and four (4) copies of the revised draft insert with the changes requested.

If you have any question regarding this amendment submission, please contact me at (809) 746-8500, extension 234.

Cordially,

Carmen Delia Cintron
Carmen Delia Cintron
Regulatory Affairs Associate

RECEIVED

JUL 10 1995

GENERIC DRUGS

Madeline



MOVA PHARMACEUTICAL CORPORATION
P.O. Box 8639
Caguas, Puerto Rico 00726
(809) 746-8500

*Labeling minor change
App. 02/02 submitted
model Lab Control NDA ORIG AMENDMENT
4/25/96*

FPL
SM
RECEIVED

April 22, 1996

Dr. Charles Ganley
FDA Office of Generic Drugs
Document Control Room MNPII - 150
75 Standish Place
Rockville, MD 20855-2773

APR 23 1996

GENERIC DRUGS

RE: ANDA 40-098 ACETAMINOPHEN AND CODEINE PHOSPHATE ORAL
SOLUTION USP, 120 MG/12 MG PER 5 ML
MINOR AMENDMENT (LABELING)

Dear Sir:

In response to the FDA's letter dated March 19, 1996, MOVA Pharmaceutical hereby submits an amendment to the above referenced ANDA.

The following information is provided:

1. A copy of the deficiency letter
2. Twelve (12) copies of final printed insert labeling.

As this minor amendment only relates to labeling issues, it is MOVA's understanding that as per Policy and Procedure Guide #21-90, the first in - first reviewed policy does not apply to this amendment.

If you have any questions regarding this amendment, please contact me at (787) 746-8500, ext. 234.

Sincerely,

Olga M. Batista
Regulatory Affairs Associate

Enclosure