CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40098

CHEMISTRY REVIEW(S)

ANDA APPROVAL SUMMARY

ANDA: 40-098

JG PRODUCT: Acetaminophen and Codeine Phosphate Oral solution USP

FIRM: MOVA Pharmaceutical Corporation

DOSAGE FORM: Oral solution

STRENGTHS: 120 mg/12 mg per 5 mL

CGMP STATEMENT/EIR UPDATE STATUS:

Manufacturer-Finished Dosage Form :

Mova Pharmaceutical Corporation
Calle Zafiro Carretera Num. 1 KM 34.8
Zona Industrial Villa Blanca
Caguas, Puerto Rico 00725.

***Note:** Pre-approval & update EER was requested by L. Tang on 5/2/96.

Manufacturer-Active Ingredients:

NDS for Acetaminophen USP
NDS for Codeine Phosphate, USP

Note: Pre-approval & update EER was requested by L. Tang on 5/2/96.

Contract Laboratories:

None

BIO STUDY:

Bio-waiver was granted on 6-29-94 per reviewers M. Kochhar and M. Park.

VALIDATION -(DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):

Active drug substances and drug dosage form are both compendial items per USP 23.

STABILITY - ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION?:

Stability protocol: Satisfactory

Expiration date: 24 months

24 months expiration date with 3 months challenge data (37°C/75%RH) on lot LJ3451/JL345v for 16 oz bottles (480 cc) and 3 month room temperature data on lot JL3451/JL345v for 16 oz bottles (480 cc).

LABELING:

Satisfactory per A.Vezza reviewed on 4-26-96.

STERILIZATION VALIDATION (IF APPLICABLE):

NA

SIZE OF BIO BATCH (FIRM'S SOURCE OF NDS OK?):

The batch size for lot # JL3451/JL345v is L.

Batch size: L manufactured from the sources of NDS, NDS for Acetaminophen USP and Codeine Phosphate, USP.

DMF was reviewed and found acceptable by L.Tang on 4-29-96.

The updated DMF was reviewed by S. Liu and found acceptable on 12-6-95.

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA THE SAME PROCESS?):

The batches size for the stability batch (lot JL3451/JL345v) is the same as bio-batch and is L

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?:

The proposed production batch is L and has the same manufacturing process as the test batch L).

CHEMIST: Lucia C. Tang /S/ DATE: 5-6-96

SUPERVISOR: John Simmons /S/ DATE: 5-10-96

1. CHEMIST'S REVIEW NO. 1

2. ANDA # 40-098

3. NAME AND ADDRESS OF APPLICANT

MOVA Pharmaceutical Corporation.
P.O. Box 8639
Caguas, Puerto Rico 00762

4. LEGAL BASIS FOR ANDA SUBMISSION

Reference drug product:
Tylenol with Codeine Elixir- McNelab. Inc. (R.W. Johnson)
No patents, AA product

5. SUPPLEMENT(s): N/A

6. PROPRIETARY NAME

7. NONPROPRIETARY NAME

Acetaminophen and Codeine Phosphate Oral solution USP 120 mg/12 mg per 5 mL

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

Firm:

2-25-94: Original submission
3-26-94: NC

FDA:

3-21-94: Acknowledgement

10. PHARMACOLOGICAL CATEGORY

Narcotic Analgesic combination for the relief of mild to moderate pain.

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

DMF
DMF
DMF

DMF
DMF
DMF
DMF

13. DOSAGE FORM

Oral Elixir Solution

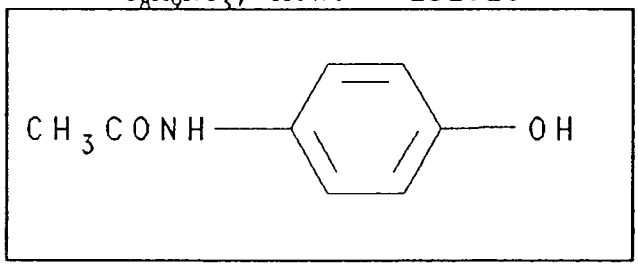
14. POTENCY

120 mg/12 mg per 5 mL

15. CHEMICAL NAME AND STRUCTURE

Acetaminophen USP

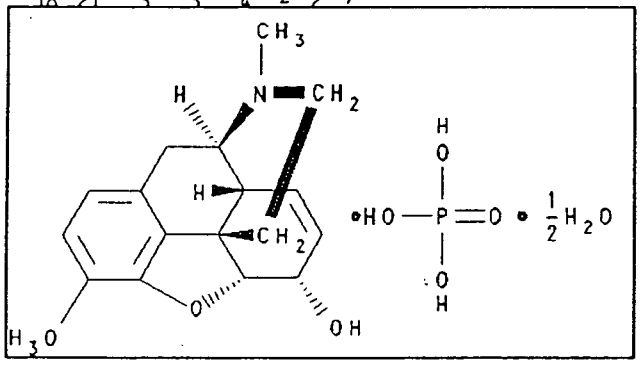
$C_8H_9NO_3$; M.W. = 151.16



4'-Hydroxyacetanilide. CAS [103-90-2]

Codeine Phosphate USP

$C_{18}H_{21}NO_3.H_3PO_4.\frac{1}{2}H_2O$; M.W. = 406.37



7,8-Didehydro-4-5α-epoxy-3-methoxy-17-methylmorphinan-6α-ol phosphate (1:1) (salt) hemihydrate. CAS [41444-62-6]

16. RECORDS AND REPORTS: N/A

17. COMMENTS

Comments:

1. Revise components and composition statement
2. Revise raw materials.
3. Revise fomulation and submit the English batch records.
4. Revise manufacturing process.
5. Revise container/closure system.
6. Revise analytical methodology for finished product and degradation products.
7. Revise stability data and stability protocol.
8. Revise labeling information.

Status:

a. **EER**: Pending

Requested for applicant ,
by Lucia C. Tang on the date for deficiency letter sending out. We need correct addresses for manufacturing sites for the drug substances.

b. MV (method validation):

Methods validation is not required since active ingredients and drug product are monographs in USP.

c. Bio-Review: Pending

Bio-waiver pending. Reviewer, M. Kochhar.

d. Labeling review: Not satisfactory

Not satisfactory per A Vezza reviewed on 6-16-94.

e. DMFs: Satisfactory

DMFs found acceptable by L.Tang, HFD-647 on 6/7/94.

18. CONCLUSIONS AND RECOMMENDATIONS

Not approvable: Major

19. REVIEWER: DATE COMPLETED:

Lucia C. Tang 7-15-94

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Chem. Review #1

1. CHEMIST'S REVIEW NO. 2

2. ANDA # 40-098

3. NAME AND ADDRESS OF APPLICANT

MOVA Pharmaceutical Corporation.
P.O. Box 8639
Caguas, Puerto Rico 00626

4. LEGAL BASIS FOR ANDA SUBMISSION

Reference drug product:
Tylenol with Codeine Elixir- McNelab. Inc. (R.W. Johnson)
No patents, AA product

5. SUPPLEMENT(s): N/A

6. PROPRIETARY NAME

7. NONPROPRIETARY NAME

Acetaminophen and Codeine Phosphate Oral solution USP 120 mg/12 mg per 5 mL

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

Firm:

2-25-94: Original submission
3-26-94: NC
12-5-94: Amendment

FDA:

3-21-94: Acknowledgement
8-10-94: 1st NA letter

10. PHARMACOLOGICAL CATEGORY

Narcotic Analgesic combination for the relief of mild to moderate pain.

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

DMF
DMF
DMF

DMF
DMF
DMF
DMF

13. DOSAGE FORM

Oral Elixir Solution

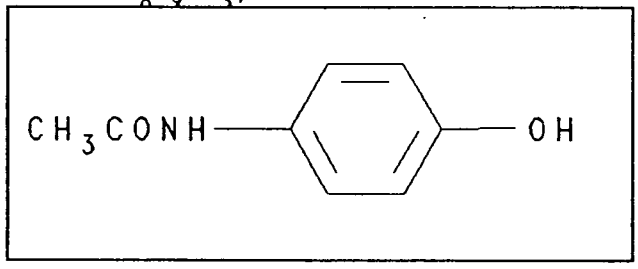
14. POTENCY

120 mg/12 mg per 5 mL

15. CHEMICAL NAME AND STRUCTURE

Acetaminophen USP

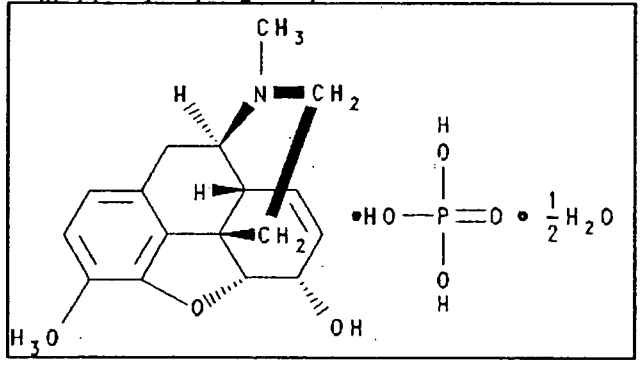
$C_8H_9NO_3$; M.W. = 151.16



4'-Hydroxyacetanilide. CAS [103-90-2]

Codeine Phosphate USP

$C_{18}H_{21}NO_3.H_3PO_4.\frac{1}{2}H_2O$; M.W. = 406.37



7,8-Didehydro-4-5α-epoxy-3-methoxy-17-methylmorphinan-6α-ol phosphate (1:1) (salt) hemihydrate. CAS [41444-62-6]

16. RECORDS AND REPORTS: N/A

17. COMMENTS

Q 1. Regarding components and composition:

Q: a. It is noted that 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.

A: OK (see responses A.1.a. and page 4 of 13 from English version of the 12-5-94 amendment).

Q: b. Please indicate the quantity of used in the composition of the drug product.

A: OK (see composition).

Q: 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.

A: OK (see responses A.1.c. of the 12-5-94 amendment).

Q: 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.

A: OK (see responses A.1.d. of the 12-5-94 amendment).

Q: e. Please include the limits or maximum amounts of Citric Acid, USP used to adjust pH.

A: OK (see responses A.1.e. and Attachment II of the 12-5-94 amendment).

f. Submit the revised and complete components and

composition section for the drug product to include quantities in mg per 5 mL.

A: OK (see responses A.1.f. and Attachment II of the 12-5-94 amendment).

Q 2. Regarding active ingredient:

Q: 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.

A: **The certificates of analysis for Acetaminophen USP from applicant and were 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.**

Q: 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.

A: OK (see responses A.2.b. and Attachment IV of the 12-5-94 amendment).

Q: 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.

A: OK (see responses A.2.c. and Attachment IV of the 12-5-94 amendment).

Q 3. Regarding inactive ingredients:

Q: 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).

A: **Please Cite the appropriate food section of 21 CFR referring to its status [e.g. CFR 172. (Natural flavoring substance and synthetic flavoring substance) and CFR 182 (Substances that are generally recognized as safe)] for artificial cherry flavor**

Q: b. Identify the sources of for injection.

A: **Identify the type of system used for the for injection in the manufacturing process of the subject drug product.**

Q: 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.

A: OK (see responses A.3.c. of the 12-5-94 amendment).

Q: 4. The submission fails to provide a complete formula card and satisfactory batch record. In this regard:

Q: a. The sources of active ingredients and drug product manufacturing site should be included.

A: OK (see responses A.4.a. and Attachment VI of the 12-5-94 amendment).

Q: b. Manufacturing procedure (e.g., pilot or production batch) should be included.

A: OK (see responses A.4.b. of the 12-5-94 amendment).

Q: c. Submit the revised master formula for the drug product based on the above comments and the composition [(1.(a-f)] comments.

A: OK (see responses A.4.c. and Attachment I of the 12-5-94 amendment).

Q: 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.

A: **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 (e.g., line to line certified English translation).**

Q: e. What is the testing protocol for the filter?

A: OK (see responses A.4.e. of the 12-5-94 amendment).

Q: 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.

A. **We note that the types and specification for each 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.**

A: OK (see responses A.4.f. and Attachment VII of the 12-5-94 amendment).

Q: 5. The application fails to include the operation procedures and precautions necessitated by the light sensitivity and control status of the active ingredients.

A: OK (see responses A.5. and Attachment VII of the 12-5-94 amendment).

Q: 6. The application fails to specify any in-process testing. What tests will be conducted and what are the acceptable limits for those tests?

A: OK (see responses A.6. of the 12-5-94 amendment).

Q: 7. Your application fails to contain a complete

description of the container/closure systems. In that regard:

Q: a. Which pigment is used in the resin for bottle and closure ?

A: OK (see responses A.7.a. of the 12-5-94 amendment).

Q: b. Submit the actual test results to demonstrate resin meets the current USP XXII/NFXVII Physicochemical requirements for plastic containers.

A: OK (see responses A.7.b. and Attachment VIII of the 12-5-94 amendment).

Q: c. Please indicate type of resin used for the polypropylene closure and submit USP test results.

A: OK (see responses A.7.c. and Attachment IX of the 12-5-94 amendment).

Q: d. Submit the actual test results of torque required for cap removal.

A: OK (see responses A.7.d. and Attachment X of the 12-5-94 amendment).

Q: e. Identify a DMF # for and submit the authorization letter.

A: OK (see responses A.7.e. and Attachment XI of the 12-5-94 amendment).

Q: 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.

A: OK (see responses A.7.f. of the 12-5-94 amendment).

Q: 8. Regarding finished product:

Q: a. Submit chromatograms to document that the excipients including alcohol do not interfere with Acetaminophen and Codeine Phosphate assays in the finished product.

A: OK (see responses A.8.a. and the Attachment XII of the 12-5-94 amendment).

Q: b. Please provide an adequate stability-indicating assay method. In this regard:

Q: 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.

A: OK (see responses A.8.b.i. and the table 7 in Attachment XII of the 12-5-94 amendment).

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.

A: OK (see responses A.8.b.ii. and Attachment XII of the 12-5-94 amendment).

Q: 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.

A: **We note that specification as presence or absence for in the release product specification is not acceptable. Please provided the potential impurities and degradation products and their limits for the subject drug product in the release product specification and submit the updated certificate analysis of the finished product for lot JL3451.**

Q: 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.

A: OK (see responses A.8.d. and Attachment XII of the 12-5-94 amendment).

Q: 9. Your application fails to contain satisfactory stability protocol and stability data. In this regard:

Q: a. Composition [see comments 1.(a-f)] and batch size of the drug product must be included.

A: Specifications or limits for must be included in the stability data report.

Q: 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.

A: OK (see responses A.9.b. of the 12-5-94 amendment).

Q: 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.

A: OK (see responses A.9.c. of the 12-5-94 amendment).

Q: d. For liquid product, all sizes of the container/closure system should be included in stability studies.

A: OK (see responses A.9.c. and Attachment XIV of the 12-5-94 amendment).

Q: 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.

A: Provide specifications or limits for in the stability data report.

Q: f. Submit the revised stability protocol and stability data based on the above comments.

A: OK (see responses A.9.c. and Attachment XIV of the 12-5-94 amendment).

Comments:

1. Revise raw materials.
2. Submit the English batch records.

3. Revise the specification for degradation products.
4. Revise stability data report.
5. Revise labeling information.

Status:

a. **EER**: Pending

Requested for applicant ,
by Lucia C. Tang on 3-27-95.

b. MV (method validation):

Methods validation is not required since active ingredients and drug product are monographs in USP.

c. Bio-Review: Satisfactory

Bio-waiver was granted on 6-29-94 per reviewers M. Kochhar and M. Park.

d. Labeling review: Not satisfactory

Not satisfactory per A Vezza reviewed on 2-15-95.

e. DMFs: Satisfactory

DMFs found acceptable by L.Tang, HFD-647 on 6/7/94.

18. CONCLUSIONS AND RECOMMENDATIONS

Not approvable: Major

19. REVIEWER: DATE COMPLETED:

Lucia C. Tang 3-28-95

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Chem. Review #2

1. CHEMIST'S REVIEW NO. 3

2. ANDA # 40-098

3. NAME AND ADDRESS OF APPLICANT

MOVA Pharmaceutical Corporation.
P.O. Box 8639
Caguas, Puerto Rico 00626

4. LEGAL BASIS FOR ANDA SUBMISSION

Reference drug product:
Tylenol with Codeine Elixir- McNelab. Inc. (R.W. Johnson)
No patents, AA product

5. SUPPLEMENT(s): N/A

6. PROPRIETARY NAME

7. NONPROPRIETARY NAME

Acetaminophen and Codeine Phosphate Oral solution USP 120 mg/12 mg per 5 mL

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

Firm:

2-25-94: Original submission
3-26-94: NC
12-5-94: Amendment
7-7-95: Amendment

FDA:

3-21-94: Acknowledgement
8-10-94: 1st NA letter
4-24-95: 2ndt NA letter

10. PHARMACOLOGICAL CATEGORY

Narcotic Analgesic combination for the relief of mild to moderate pain.

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

DMF
DMF
DMF

DMF
DMF
DMF
DMF

13. DOSAGE FORM

Oral Elixir Solution

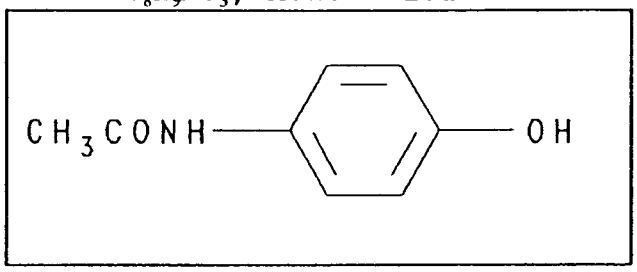
14. POTENCY

120 mg/12 mg per 5 mL

15. CHEMICAL NAME AND STRUCTURE

Acetaminophen USP

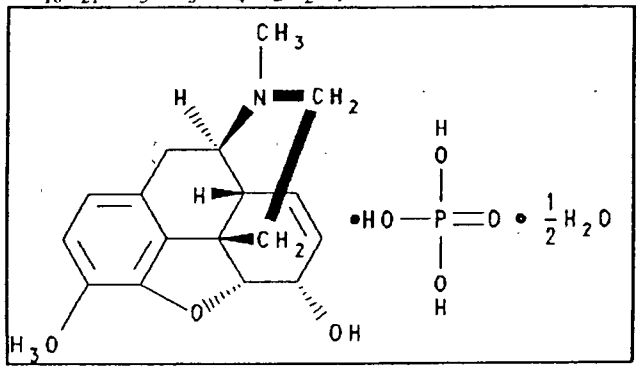
$C_8H_9NO_3$; M.W. = 151.16



4'-Hydroxyacetanilide. CAS [103-90-2]

Codeine Phosphate USP

$C_{18}H_{21}NO_3 . H_3PO_4 . \frac{1}{2}H_2O$; M.W. = 406.37



7,8-Didehydro-4-5α-epoxy-3-methoxy-17-methylmorphinan-6α-ol phosphate (1:1) (salt) hemihydrate. CAS [41444-62-6]

16. RECORDS AND REPORTS: N/A

17. COMMENTS

Comments:

Q: 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.

A: OK (see response 1 and Attachment I of the 7-7-95 amendment).

Q: 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.

A: OK (see response 2 and Attachment II of the 7-7-95 amendment).

Q: 3. Provide a description of the production of the for Injection used for the manufacturing process of the subject drug product.

A: OK (see response 3 and Attachment III of the 7-7-95 amendment).

Q: 4. The submission fails to provide a complete formula card and satisfactory batch record. In this regard:

Q: 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.

A: OK (see response 4a and Attachment IV of the 7-7-95 amendment).

Q:

Q: 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).

A: OK (see response 4b and Attachment V of the 7-7-95 amendment).

Q: 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).

A: OK (see response 5 and Attachment VI of the 7-7-95 amendment).

6. Your application fails to contain satisfactory stability data. In this regard:

Q: a. A component and Composition Statement rather than the formula number must be included in the stability data report.

A: OK (see response 6a and Attachment VI of the 7-7-95 amendment).

b. Please provide specifications or acceptable limits for in the stability data report.

A: OK (see response 6b and Attachment VI of the 7-7-95 amendment).

Status:

a. **EER**: Pending

Requested for applicant ,
by Lucia C. Tang on 4-17-95.

b. MV (method validation):

Methods validation is not required since active ingredients and drug product are monographs in USP.

c. Bio-Review: Satisfactory

Bio-waiver was granted on 6-29-94 per reviewers M. Kochhar and M. Park.

d. Labeling review: Not satisfactory

Not satisfactory per A Vezza reviewed on 2-7-96.

e. DMFs: Satisfactory

DMFs found acceptable by L.Tang, HFD-647 on 6/7/94.

18. CONCLUSIONS AND RECOMMENDATIONS

Not approvable: Major

19. REVIEWER: DATE COMPLETED:

Lucia C. Tang 2-1-96

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Chem Review #3

1. CHEMIST'S REVIEW NO. 4

2. ANDA # 40-098

3. NAME AND ADDRESS OF APPLICANT

MOVA Pharmaceutical Corporation.
P.O. Box 8639
Caguas, Puerto Rico 00626

4. LEGAL BASIS FOR ANDA SUBMISSION

Reference drug product:
Tylenol with Codeine Elixir- McNelab. Inc. (R.W. Johnson)
No patents, AA product

5. SUPPLEMENT(s): N/A

6. PROPRIETARY NAME

7. NONPROPRIETARY NAME

Acetaminophen and Codeine Phosphate Oral solution USP 120 mg/12 mg per 5 mL

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

Firm:

2-25-94: Original submission
3-26-94: NC
12-5-94: Amendment
7-7-95: Amendment
4-22-96: Amendment

FDA:

3-21-94: Acknowledgement
8-10-94: 1st NA letter
4-24-95: 2nd NA letter
3-19-96; Labeling NA letter (3rd NA letter)

10. PHARMACOLOGICAL CATEGORY

Narcotic Analgesic combination for the relief of mild to moderate pain.

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

DMF
DMF
DMF

DMF
DMF
DMF
DMF

13. DOSAGE FORM

Oral Elixir Solution

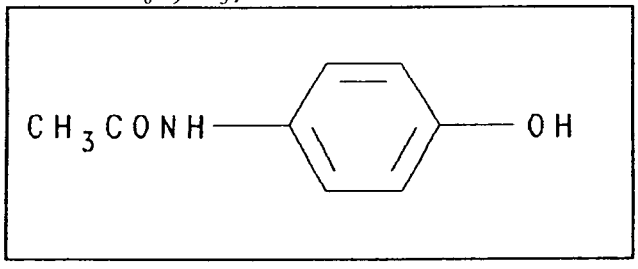
14. POTENCY

120 mg/12 mg per 5 mL

15. CHEMICAL NAME AND STRUCTURE

Acetaminophen USP

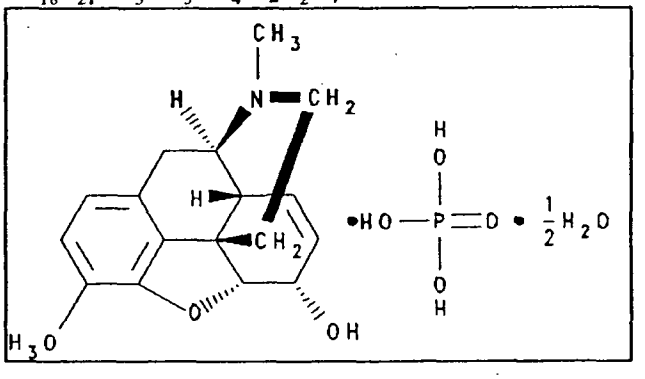
$C_8H_9NO_3$; M.W. = 151.16



4'-Hydroxyacetanilide. CAS [103-90-2]

Codeine Phosphate USP

$C_{18}H_{21}NO_3 . H_3PO_4 . \frac{1}{2}H_2O$; M.W. = 406.37



7,8-Didehydro-4-5α-epoxy-3-methoxy-17-methylmorphinan-6α-ol phosphate (1:1) (salt) hemihydrate. CAS [41444-62-6]

16. RECORDS AND REPORTS

N/A

17. COMMENTS

a. **EER**: Pending

Requested for applicant , by Lucia C. Tang on 4-17-95. Updated and pre-approval EER was requested on 5-2-96 by L. Tang.

b. **MV** (method validation):

Methods validation is not required since active ingredients and drug product are monographs in USP.

c. **Bio-Review**: Satisfactory

Bio-waiver was granted on 6-29-94 per reviewers M. Kochhar and M. Park.

d. **Labeling review: Satisfactory**

Satisfactory per A Vezza reviewed on 4-26-96.

e. DMFs: Satisfactory

DMF was reviewed and found acceptable by L.Tang on 4-29-96.

The updated DMF was reviewed by S. Liu and found acceptable on 12-6-95.

18. CONCLUSIONS AND RECOMMENDATIONS

Approval

19. REVIEWER: DATE COMPLETED:

Lucia C. Tang 5-6-96

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pages of trade

secret and/or

confidential

commercial

information

Chem. Review #4

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
FOOD AND DRUG ADMINISTRATION

ESTABLISHMENT EVALUATION REQUEST

V

EQUEST TYPE *(Check One)*] Original £ FollowUp £ FUR	DATE March 28, 1995	PHONE NO. 301-594-0305	EER ID # 19977
EQUESTORS NAME: Lucia C. Tang/T.Ames	DIVISION: Office of Generic Drugs		MAIL CODE: HFD-647
PPLICATION AND SUPPLEMENT NUMBER: ANDA 40-098			
RAND NAME:	ESTABLISHED NAME: Acetaminophen and Codeine Phosphate Oral solution USP		
OSAGE STRENGTH: 120 mg/12 mg per 5 mL		STERILE £Yes ☒ No	
ROFILE CLASS:: LIQ	PRIORITY CLASSIFICATION *(See SMG CDER-4820.3)*		
PPLICANT'S NAME: MOVA Pharmaceutical Corporation			
PPLICANT'S ADDRESS: Calle Zafiro Carretera Num. 1 KM 34.8, Zona Industrial Villa Blanca, Caguas, Puerto Rico 00762			
OMMENTS :			

ACILITIES TO BE EVALUATED

Name and Complete Address)	RESPONSIBILITY	DMF NUMBER/ PROFILE CODE	FKEY CIRTS ID	HFD-324 USE ONLY ~	
Applicant	Manufacturing and testing facilities	LIQ	19660 MCPC	AC	4/22/94
2.	Manufacturer of NDS (Codeine Phosphate)		MALS	AC	12/13/94
3.	Manufacturer of NDS (Acetaminophen)		19663 RHPL	AC	8/5/94

FOR HFD-324 USE ONLY:	CSO	DATE RECEIVED	APR 18
	CGMP COMPLIANCE STATUS	DATE	8/30/96

RM FDA 3274 (8/92) Distribution: Original and Yellow Copy: HFD-324.
: ANDA 40-098 HFD-647/Div File, HFD-617/JWilson, HFD-617/TAmes, HFD-647/JSimmons HFD-647/LCTang
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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
FOOD AND DRUG ADMINISTRATION

ESTABLISHMENT EVALUATION REQUEST

REQUEST TYPE *(Check One)*	DATE	PHONE NO.	EER ID #
☒ Original £ FollowUp £ FUR	February 5, 1996 4-17-96	301-594-0305	

REQUESTORS NAME: Lucia C. Tang/T.Ames	DIVISION: Office of Generic Drugs	MAIL CODE: HFD-647

APPLICATION AND SUPPLEMENT NUMBER: ANDA 40-098

BRAND NAME:	ESTABLISHED NAME: Acetaminophen and Codeine Phosphate Oral solution USP

DOSAGE STRENGTH: 120 mg/12 mg per 5 mL	STERILE £Yes ☒ No

PROFILE CLASS:: LIQ	PRIORITY CLASSIFICATION *(See SMG CDER-4820.3)*

APPLICANT'S NAME: MOVA Pharmaceutical Corporation

APPLICANT'S ADDRESS: Calle Zafiro Carretera Num. 1 KM 34.8, Zona Industrial Villa Blanca, Caguas, Puerto Rico 00762

COMMENTS : Updated and pre-approval EER

FACILITIES TO BE EVALUATED

Name and Complete Address)

	RESPONSIBILITY	DMF NUMBER/ PROFILE CODE	FKEY CIRTS ID	HFD-324 USE ONLY ~	
1. Applicant	Manufacturing and testing facilities	LIQ			
2.	Manufacturer of NDS (Codeine Phosphate)				
3.	Manufacturer of NDS (Acetaminophen)				

FOR HFD-324 USE ONLY:	CSO	DATE RECEIVED
	CGMP COMPLIANCE STATUS	DATE

FORM FDA 3274 (8/92) Distribution: Original and Yellow Copy: HFD-324.
: ANDA 40-098 HFD-647/Div File, HFD-617/JWilson, HFD-617/TAmes, HFD-647/JSimmons HFD-647/LCTang
:T Disk Approval# 5\eerforms\40098

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
FOOD AND DRUG ADMINISTRATION

ESTABLISHMENT EVALUATION REQUEST

REQUEST TYPE *(Check One)* ☒ Original ☐ FollowUp ☐ FUR	DATE May 2, 1996	PHONE NO. 301-594-0305	EER ID #
REQUESTORS NAME: Lucia C. Tang/T.Ames	DIVISION: Office of Generic Drugs		MAIL CODE: **HFD-647**
APPLICATION AND SUPPLEMENT NUMBER: ANDA 40-098			
BRAND NAME:	ESTABLISHED NAME: Acetaminophen and Codeine Phosphate Oral solution USP		
DOSAGE STRENGTH: 120 mg/12 mg per 5 mL			STERILE ☐Yes ☒ No
PROFILE CLASS:: LIQ	PRIORITY CLASSIFICATION *(See SMG CDER-4820.3)*		
APPLICANT'S NAME: MOVA Pharmaceutical Corporation			
APPLICANT'S ADDRESS: Calle Zafiro Carretera Num. 1 KM 34.8, Zona Industrial Villa Blanca, Caguas, Puerto Rico 00762			
OMMENTS : Updated and pre-approval EER			

FACILITIES TO BE EVALUATED

(Name and Complete Address)

	RESPONSIBILITY	DMF NUMBER/ PROFILE CODE	FKEY CIRTS ID	HFD-324 USE ONLY–	
1. Applicant	Manufacturing and testing facilities	LIQ			
2.	Manufacturer of NDS (Codeine Phosphate)				
3.	Manufacturer of NDS (Acetaminophen)				

FOR HFD-324 USE ONLY:	CSO	DATE RECEIVED
	CGMP COMPLIANCE STATUS	DATE

ORM FDA 3274 (8/92) Distribution: Original and Yellow Copy: HFD-324.
c: ANDA 40-098 HFD-647/Div File, HFD-617/JWilson, HFD-617/TAmes, HFD-647/JSimmons HFD-647/LCTang
CT Disk Approval# 5\eerforms\40098