CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 20-517/S-006

Name:	Lupron Depot-3 Month 22.5 mg & Lupron Depot-4 Month 30 mg (leuprolide acetate for depot suspension)
Sponsor:	TAP Pharmaceuticals, Inc.
Approval Date:	August 13, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-517/S-006

CONTENTS

Reviews / Information Included in this Review	
Approval Letter	X
Approvable Letter(s)	X
Final Printed Labeling	
Medical Review(s)	
Chemistry Review(s)	X
EA/FONSI	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	X
Clinical Pharmacology/Biopharmaceutics Review(s)	
Administrative Document(s)	
Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-517/S-006

APPROVAL LETTER

NDA 19-732/S-016
NDA 19-943/S-010
NDA 20-011/S-016
NDA 20-263/S-012
NDA 20-517/S-006
NDA 20-708/S-006

AUG 13 1999

TAP Holdings, Inc.
Attention: Aruna Dabholkar, M.D.
Associate Director, Regulatory Affairs
2355 Waukegan Road
Deerfield, IL 60015

Dear Dr Dabholkar:

Please refer to your supplemental new drug applications dated December 23, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lupron Depot® (leuprolide acetate depot suspension).

We acknowledge receipt of your submissions dated June 21, 1999 and July 9, 1999.

These supplemental new drug applications provide for a new manufacturing site for the prefilled dual chamber syringe.

We have completed the review of these supplemental applications and they are approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Jennifer Mercier, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

8/13/99

Moo-Jhong Rhee, Ph.D.
Chemistry Team Leader, for the
Division of Reproductive and Urologic Drug Products,
(HFD-580)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:
Archival NDAs 19-732, 19-943, 20-011, 20-263, 20-517, 20-708
HFD-580/Div. Files
HFD-580/J.Mercier
HFD-580/Raraick/Mann/Rhee/De
HFD-160/Cooney/Vincent
HFD-094/DDMS (with labeling)
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: JM/August 13, 1999
Initialed by: Rhee8.13.99/De8.13.99
final: August 13, 1999

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-517/S-006

APPROVABLE LETTER

21-1

NDA 20-011/S-016
NDA 19-732/S-016
NDA 19-943/S-010
NDA 20-263/S-012
NDA 20-517/S-006
NDA 20-708/S-006

TAP Holdings, Inc.
Attention: Aruna Dabholkar, M.D.
Associate Director, Regulatory Affairs
2355 Waukegan Road
Deerfield, IL 60015

JUN 25 1999

Dear Dr. Dabholkar:

Please refer to your supplemental new drug applications dated December 23, 1998, received December 28, 1998, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Lupron Depot® (leuprolide acetate for depot suspension).

We acknowledge receipt of your faxed submission dated June 21, 1999.

These supplements propose a new manufacturing site for manufacturing the prefilled dual chamber syringe.

We have completed the review of these applications, as amended, and they are approvable. Before these applications may be approved, however, it will be necessary for you to address the following:

1.

2.

3.

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information from

Approvable Letter
(5-006)

NDA 20-011/S-016
NDA 19-732/S-016
NDA 19-943/S-010
NDA 20-263/S-012
NDA 20-517/S-006
NDA 20-708/S-006

8. [redacted]

Within 10 days after the date of this letter, you are required to amend the supplemental applications, notify us of your intent to file amendments, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the applications. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

These products may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if they are marketed with these changes prior to approval of these supplemental applications.

If you have any questions, contact Jennifer Mercier, Project Manager, at (301) 827-4260.

Sincerely,

Marianne Mann, M.D. (for LRarick)
Deputy Dir 6/25/99

Lisa Rarick, M.D.
Director
Division of Reproductive and Urologic Drug Products,
(HFD-580)
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Archival NDAs 20-011, 19-732, 19-943, 20-263, 20-517, 20-708
HFD-580/Div. Files
HFD-580/J.Mercier/Rumble
HFD-580/Rarick/Mann/Rhee/De
HFD-95/DDMS
DISTRICT OFFICE

Drafted by: JM/June 25, 1999
Initialed by: Rumble 6.24.99/Rhee6.24.99/De6.25.99/Rarick6.25.99/Mann6.25.99
final: June 25, 1999
filename:

APPROVABLE (AE)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-517/S-006

CHEMISTRY REVIEW(S)

JUN 16 1999

~~JUN 15 1999~~

CHEMIST REVIEW
OF **Supplement**

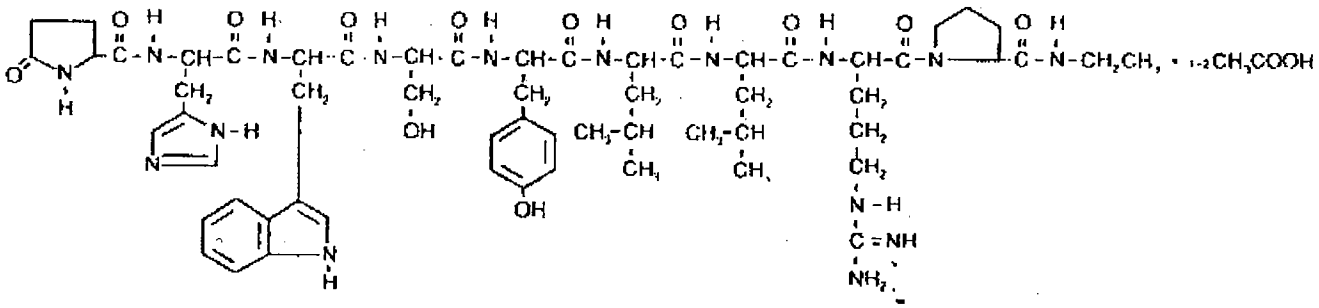
1. **ORGANIZATION:** HFD 580
2. **NDA NUMBER:** 20-517
3. **SUPPLEMENT NUMBERS/DATES:** SCM-006
   Letterdate: 12-23-98
   Stampdate: 12-28-98
4. **AMENDMENTS/REPORTS/DATES:** None
   Letterdate:
   Stampdate:
5. **RECEIVED BY CHEMIST:** 1-3-99

6. APPLICANT NAME AND ADDRESS:
TAP Pharmaceuticals Inc.
2355 Waukegan Road
Deerfield, IL-60015

7. NAME OF DRUG: Lupron Depot^{R} 3 Month 22.5 mg.
Lupron Depot^{R} 4 Month 30 mg

8. NONPROPRIETARY NAME: leuprolide acetate for depot suspension

9. CHEMICAL NAME/STRUCTURE:
5-Oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-leucyl-L-leucyl-L-arginyl-N-ethyl-L-prolinamide acetate



10. **DOSAGE FORM(S):** Sterile Depot Suspension for Injection

11. POTENCY: 3 Month 22.5 mg.
4 Month 30 mg

12. PHARMACOLOGICAL CATEGORY: Palliative treatment of advanced prostatic cancer

13. HOW DISPENSED: Intramuscular Injection

14. RECORDS & REPORTS CURRENT: Yes

15. **RELATED IND/NDA/DMF:** This is part of a bundled supplements. Related applications include the following:

NDA 19732-scm016
NDA 19943-scm010
NDA 20263 -scm012
NDA 20001-scm016
NDA 20708-scm006

16. **PRIOR APPROVAL SUPPLEMENT PROVIDES FOR: New manufacturing site for manufacturing the prefilled dual chamber syringe**

17. **COMMENTS:**

The prefilled dual chamber syringe was approved as a new container closure system in December 1996 (NDA 20-517/S001) and in July 1998 (NDA 20-517, S005 and NDA 20-708, S004). The manufacturing was approved at Osaka plant in Japan. The manufacturer, Takeda Chemical Industries submitted this supplement to add an additional site for filling the syringes at Hikari plant. The diluent used to fill in these syringes will be manufactured at the Hikari plant. The active drug, [redacted] will be manufactured at the previously approved sites (Shanan plant and Osaka plant). The syringe components, manufacturing method and the final product specifications and testing methods are the same as approved before. The new plant and the manufacturing process are validated. Three months of accelerated and RT stability has been included in the application for one production lot of each of Lupron Depot –3 month 11.25 mg, 22.5 mg and 4-Month 30 mg and the results are satisfactory. Quality of the product manufactured at Hikari plant was compared with the corresponding one manufactured at the approved site, Osaka plant and no significant changes have been observed.

The new facility (Hikari plant) should be inspected according to CFR 314.70 and a request had been forwarded through EES on 28-December-1998. Overall recommendation is found 'acceptable' on 6/15/99 based on an inspection performed on 5-19-99.

Since the diluent will be manufactured at the Hikari plant and it needs to be sterile, the application was also reviewed by a microbiologist (Dr. Carol K. Vincent, HFD-805) and it was found deficient.

18. **CONCLUSIONS AND RECOMMENDATIONS:**

This application is 'approvable' pending satisfactory resolution of the microbiologist's concerned issues as delineated in the draft letter.

Issue "Approvable" letter

19. REVIEWER NAME	SIGNATURE	DATE COMPLETED
Swapan K. De, Ph.D.	Swapan De 6/15/99	**5/6/99**

cc:
Orig. NDA #20-517
HFD-580/Division File
HFD-580/Mercierj
HFD-580/MRhee/SDe

R/D Init by: MJ Rhee, Ph.D. MJRhee 6/16/99
filename: nda20517.scm006

ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application: NDA 20517/006
Stamp: 28-DEC-1998
Regulatory Due: 28-APR-1999
Applicant: TAP HOLDINGS
2255 WAUKEEGAN RD
DEERFIELD, IL 60015
Priority: 3S
Org Code: 580

Action Goal:
District Goal: 24-MAR-1999
Brand Name: LUPRON DEPOT-4 MONTH 30 MG
Estab. Name:
Generic Name: LEUPROLIDE ACETATE FOR DEPOT SUSPENSION

Dosage Form: (INJECTION)
Strength: 3 MON 22.5MG/4 MON 30MG

Application Comment: SUPPLEMENT PROVIDES FOR NEW MANUFACTURING SITE FOR MANUFACTURING THE PREFILLED DUAL CHAMBER SYRINGE. SAME CHANGES WILL BE APPLICABLE TO NDA20708-SCM006. (on 28-JAN-1999 by S. DE (HFD-580) 301-827-7516)

FDA Contacts: S. DE (HFD-580) 301-827-7516 , Review Chemist

Overall Recommendation: ACCEPTABLE on 15-JUN-1999 by M. EGAS (HFD-322) 301-594-0095

Establishment: 9610307
TAKEDA CHEMICAL INDUSTRIES LTD
4720 TAKEDA MITSUI
HIKARI, YAMAGUCHI, JA

DMF No:
AADA:
Responsibilities: FINISHED DOSAGE MANUFACTURER
Profile: SVS
OAI Status: NONE

Estab. Comment: THE PREFILLED DUAL CHAMBER SYRINGE WAS APPROVED AT OSAKA PLANT IN JAPAN. THE MANUFACTURER TAKEDA CHEMICAL INDUSTRIES HAS NOW COMPLETED AN ADDITIONAL SITE FOR FILLING THE SYRINGES AT HIKARI PLANT. THE ACTIVE DRUG, [redacted] WILL BE MANUFACTURED AT THE PREVIOUSLY APPROVED SITE. THE SYRINGE COMPONENTS, MANUFACTURING METHOD AND THE FINAL PRODUCT SPECIFICATIONS AND TESTING METHODS ARE SAME AS APPROVED BEFORE. THE NEW PLANT AND THE MANUFACTURING PROCESS ARE VALIDATED. BATCH INSTRUCTIONS AND BATCH RECORD FOR ONE LOT ARE SUBMITTED. THREE MONTHS OF ACCELERATED AND RT STABILITY DATA ARE SUBMITTED FOR ONE PRODUCTION LOT EACH OF LUPRON DEPOT-3 MONTH 11.25 MG, 22.5 MG AND 4-MONTH 30 MG. (on 29-JAN-1999 by S. DE (HFD-580) 301-827-7516)

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	28-JAN-1999				DES
SUBMITTED TO DO	29-JAN-1999	GMP			FERGUSONS
ASSIGNED INSPECTION '	02-FEB-1999	PS			EGASM
ASSIGNED INSPECTION '	02-FEB-1999	PS			RKIMMEL
INSPECTION SCHEDULED	15-APR-1999		19-MAY-1999.		IRIVERA
INSPECTION PERFORMED	24-MAY-1999		19-MAY-1999		EGASM
DO RECOMMENDATION	15-JUN-1999			ACCEPTABLE	EGASM
OC RECOMMENDATION	15-JUN-1999			INSPECTION ACCEPTABLE DISTRICT RECOMMENDATION	EGASM

JUN 24 1999

CHEMIST REVIEW
OF **Supplement**
CHEMISTRY REVIEW #2

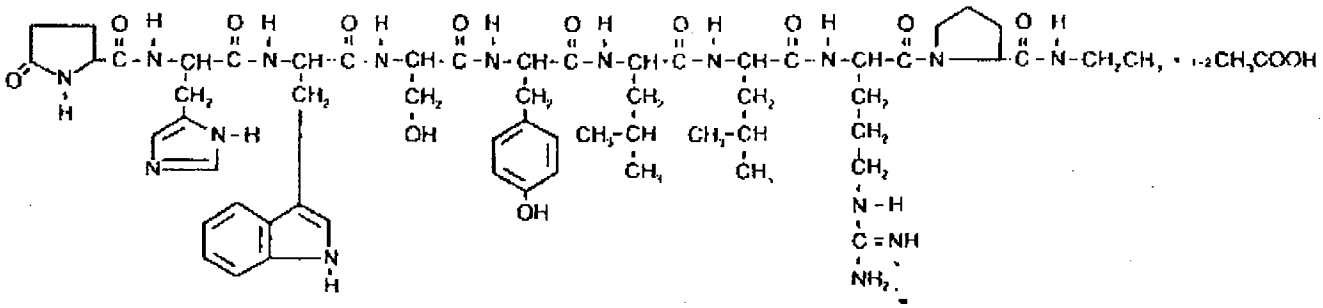
1. **ORGANIZATION:** HFD 580
2. **NDA NUMBER:** 20-517
3. **SUPPLEMENT NUMBERS/DATES:** SCM-006
   Letterdate: 12-23-98
   Stampdate: 12-28-98
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate: 6-21-99 [fax]
   Stampdate:
5. **RECEIVED BY CHEMIST:** 1-3-99/6-21-99

6. APPLICANT NAME AND ADDRESS:
TAP Pharmaceuticals Inc.
2355 Waukegan Road
Deerfield, IL-60015

7. NAME OF DRUG: Lupron Depot[R] 3 Month 22.5 mg.
Lupron Depot[R] 4 Month 30 mg

8. NONPROPRIETARY NAME: leuprolide acetate for depot suspension

9. CHEMICAL NAME/STRUCTURE:
5-Oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-leucyl-L-leucyl-L-arginyl-N-ethyl-L-prolinamide acetate



10. **DOSAGE FORM(S):** Sterile Depot Suspension for Injection

11. POTENCY: 3 Month 22.5 mg.
4 Month 30 mg

12. PHARMACOLOGICAL CATEGORY: Palliative treatment of advanced prostatic cancer

13. HOW DISPENSED: Intramuscular Injection

14. RECORDS & REPORTS CURRENT: Yes

15. **RELATED IND/NDA/DMF:** This is part of a bundled supplements. Related applications include the following:

NDA 19732-scm016
NDA 19943-scm010
NDA 20263 -scm012
NDA 20001-scm016
NDA 20708-scm006

16. **PRIOR APPROVAL SUPPLEMENT PROVIDES FOR: New manufacturing site for manufacturing the prefilled dual chamber syringe**

17. **COMMENTS:**
The amendment sent by the sponsor on 21-June-1999 was the response of the microbiologist's comments (send to the sponsor on 18 June-1999). The response, as reviewed by the microbiologist (Dr. Carol K. Vincent, HFD-805) is still found to be deficient.

18. **CONCLUSIONS AND RECOMMENDATIONS:**
This application is 'approvable' pending satisfactory resolution of the microbiologist's concerned issues as delineated in the draft letter of the microbiologist's review.

Issue "Approvable" letter

19. **REVIEWER NAME** **SIGNATURE** **DATE COMPLETED**
Swapan K. De, Ph.D. 6/24/99 **6/24/99**

cc:
Orig. NDA #20-517
HFD-580/Division File
HFD-580/Mercierj
HFD-580/MRhee/SDe

R/D Init by: MJ Rhee, Ph.D. 6/24/99
filename: nda20517.scm006

AUG 1 3 1999

CHEMIST REVIEW
OF **Supplement**
CHEMISTRY REVIEW #2

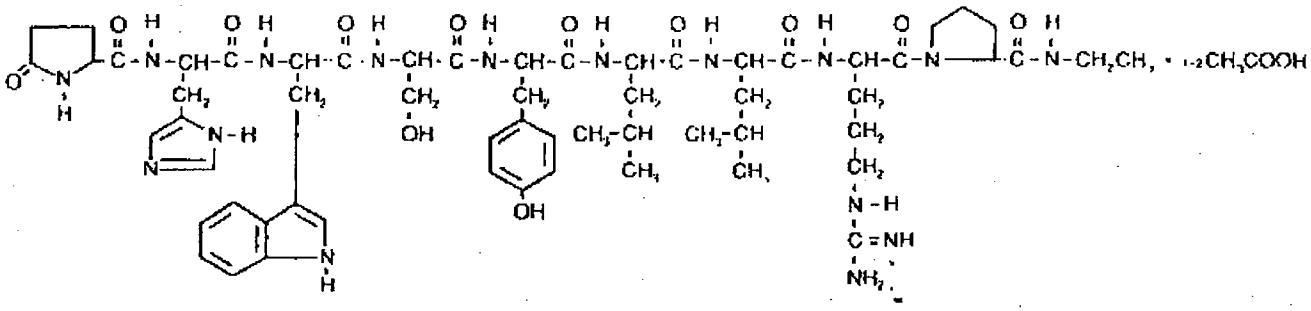
1. **ORGANIZATION:** HFD 580
2. **NDA NUMBER:** 20-517
3. **SUPPLEMENT NUMBERS/DATES:** SCM-006
   Letterdate: 12-23-98
   Stampdate: 12-28-98
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate: 6-21-99 [fax]; 7/9/99
   Stampdate: 7-12-99
5. **RECEIVED BY CHEMIST:** 1-3-99/6-21-99/7-14-99

6. APPLICANT NAME AND ADDRESS:
TAP Pharmaceuticals Inc.
2355 Waukegan Road
Deerfield, IL-60015

7. NAME OF DRUG: Lupron Depot^{R} 3 Month 22.5 mg.
Lupron Depot^{R} 4 Month 30 mg

8. NONPROPRIETARY NAME: leuprolide acetate for depot suspension

9. CHEMICAL NAME/STRUCTURE:
5-Oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-leucyl-L-leucyl-L-arginyl-N-ethyl-L-prolinamide acetate



10. **DOSAGE FORM(S):** Sterile Depot Suspension for Injection

11. POTENCY: 3 Month 22.5 mg.
4 Month 30 mg

12. PHARMACOLOGICAL CATEGORY: Palliative treatment of advanced prostatic cancer

13. HOW DISPENSED: Intramuscular Injection

14. RECORDS & REPORTS CURRENT: Yes

15. **RELATED IND/NDA/DMF:** This is part of a bundled supplements. Related applications include the following:

NDA 19732-scm016
NDA 19943-scm010
NDA 20263 -scm012
NDA 20001-scm016
NDA 20708-scm006

16. **PRIOR APPROVAL SUPPLEMENT PROVIDES FOR: New manufacturing site for manufacturing the prefilled dual chamber syringe**

17. **COMMENTS:**
The amendment sent by the sponsor on 07-July-1999 was the response of the "approvable" letter from the Agency (send to the sponsor on 25 June-1999). The response is found satisfactory (see attached review) as reviewed by the microbiologist (Dr. Carol K. Vincent, HFD-805).

18. **CONCLUSIONS AND RECOMMENDATIONS:**
Based on the information provided by the firm and the microbiologist's recommendation, this supplement may be approved.

Issue "Approval" letter

19. REVIEWER NAME	SIGNATURE	DATE COMPLETED
Swapan K. De, Ph.D.	Swapan De 8/13/99	**8/12/99**

cc:
Orig. NDA #20-517
HFD-580/Division File
HFD-580/Mercierj
HFD-580/MRhee/SDe

R/D Init by: MJ Rhee, Ph.D. 8/13/99
filename: nda20517.scm006a2

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Chemistry Review #2 (8/13/99)
(S-006)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-517/S-006

MICROBIOLOGY REVIEW(S)

FEB 2 3 1999

MICROBIOLOGIST'S REVIEW OF SUPPLEMENT FOR
DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS, HFD-580
OFFICE OF NEW DRUG CHEMISTRY, MICROBIOLOGY STAFF, HFD-805
FEBRUARY 11, 1999

Reviewing Microbiologist: Carol K. Vincent, HFD-805

NDA / Supplement Number: NDA 19-732 / SCM-016
NDA 20-517 / SCM-006
NB: These supplements are reviewed in tandem.

Drug Product:
NDA 19-732 / SCM-016 — Lupron Depot® 7.5mg [leuprolide acetate depot suspension]
NDA 20-517 / SCM-006 — Lupron Depot® -3 month 22.5mg and -4 month 30mg [leuprolide acetate depot suspension]

Received for Review: January 4, 1999

COMIS User Fee Goal Date: April 28, 1999

COMIS User Fee Due Date: June 26, 1999

Applicant:
TAP Pharmaceuticals Inc.
Bannockburn Lake Office Plaza
2355 Waukegan Road
Deerfield, IL 60015

Manufacturer and Site:
Takeda Chemical Industries
4720 Mitsui Aza Takeda
Hikari, Yamaguchi 743-8502
Japan

Supplement Provides For: New manufacturing site in Hikari, Japan for the manufacture of the prefilled dual chamber syringe.

Dosage Form / Route of Administration: Pre-filled syringe; for injection. Sterile diluent to be mixed with dry drug product powder at point of use.

Conclusions and Recommendations: We **do not** recommend approval of the supplements because inadequate sterilization process validation information for a new manufacturing location has been provided.

See **Review Notes**, below.

cc:
NDA 19-732 / SCM-016
NDA 20-517 / SCM-006
HFD-580/CKish / SDe
HFD-160/Consult file/CKVincent [HFD-805]
Drafted by: CKVincent/01-29-99 C:\CKV97\NDA20517.006

Carol K. Vincent, HFD-805
2-11-99
Pdc 2/23/99

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information from

Microbiology Review #1
(S-006)

JUN 28 1999

MICROBIOLOGIST'S REVIEW NO. 2 OF SUPPLEMENT FOR
DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS, HFD-580
OFFICE OF NEW DRUG CHEMISTRY, MICROBIOLOGY STAFF, HFD-805

JUNE 23, 1999

Reviewing Microbiologist: Carol K. Vincent, HFD-805

NDA / Supplement Number:
NDA 19-732 / SCM-016
NDA 19-943 / SCM-010
NDA 20-011 / SCM-016
NDA 20-263 / SCM-012
NDA 20-517 / SCM-006
NDA 20-708 / SCM-006

Drug Product: Lupron Depot® [leuprolide acetate depot suspension]

Document Date: December 23, 1998

Amendment: June 21, 1999 [fax]

Amendment received for review: June 21, 1999

COMIS User Fee Due Date: June 26, 1999 **COMIS User Fee Goal Date:** April 28, 1999

Name and Address of Applicant:	**Name and Address of Manufacturer:**
TAP Pharmaceuticals, Inc. Bannockburn Lake Office Plaza 2355 Waukegan Road Deerfield, IL 60015	Takeda Chemical Industries 4720 Mitsui Aza Takeda Hikari, Yamaguchi 743-8502 Japan

Supplement Provides For: New manufacturing site in Hakari, Japan for the manufacture of the prefilled dual chamber syringe.

Dosage Form: Pre-filled syringe for injection. Sterile diluent to be mixed with dry drug product powder at point of use.

Conclusions and Recommendations: The subject supplements are **approvable** pending satisfactory review of sterilization process validation information requested herein. See **E: Review Notes:** below.

cc:
NDA 19-732 / SCM-016
NDA 19-943 / SCM-010
NDA 20-011 / SCM-016
NDA 20-263 / SCM-012
NDA 20-517 / SCM-006
NDA 20-708 / SCM-006
HFD-580/Rarick/MRhee/SDe/LPauls/JMercier
HFD-160/Consult file/CKVincent [HFD-805]
Drafted by: CKVincent/06-22-99

C:\CKV99\NDA19732.016

Carol K. Vincent

Carol K. Vincent, HFD-805

06-23-99

PAC 6/24/99 JUN 28 1999

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Microbiology Review #2
(S-006)

AUG 12 1999

MICROBIOLOGIST'S REVIEW NO. 3 OF SUPPLEMENT FOR
DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS, HFD-580
OFFICE OF NEW DRUG CHEMISTRY, MICROBIOLOGY STAFF, HFD-805

AUGUST 11, 1999

Reviewing Microbiologist: Carol K. Vincent, HFD-805

NDA / Supplement Number:
NDA 19-732 / SCM-016
NDA 19-943 / SCM-010
NDA 20-011 / SCM-016
NDA 20-263 / SCM-012
NDA 20-517 / SCM-006
NDA 20-708 / SCM-006

Drug Product: Lupron Depot® [leuprolide acetate depot suspension]

Document Date: July 9, 1999

Received for review: June July 16, 1999

COMIS User Fee Due Date: August 25, 26, 1999

Name and Address of Applicant:	**Name and Address of Manufacturer:**
TAP Pharmaceuticals, Inc. Bannockburn Lake Office Plaza 2355 Waukegan Road Deerfield, IL 60015	Takeda Chemical Industries 4720 Mitsui Aza Takeda Hikari, Yamaguchi 743-8502 Japan

Supplement Provides For: New manufacturing site in Hakari, Japan for the manufacture of the prefilled dual chamber syringe.

Dosage Form: Pre-filled syringe for injection. Sterile diluent to be mixed with dry drug product powder at point of use.

Conclusions and Recommendations: We recommend **approval** for the subject supplements.

See **E: Review Notes:** below.

cc:
NDA 19-732 / SCM-016
NDA 19-943 / SCM-010
NDA 20-011 / SCM-016
NDA 20-263 / SCM-012
NDA 20-517 / SCM-006
NDA 20-708 / SCM-006
HFD-580/Rarick/MRhee/SDe/LPauls/JMercier
HFD-160/Consult file/CKVincent [HFD-805]
Drafted by: CKVincent/08-03-99

C:\CKV99\19732106.3RD

Carol K. Vincent

Carol K. Vincent, HFD-805 8-11-99

AC 8/12/99

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information from

Microbiology Review #3

(S-006)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-517/S-006

CORRESPONDENCE

TAP HOLDINGS INC.
parent of TAP Pharmaceuticals Inc.

Lannockburn Lake Office Plaza
355 Waukegan Rd
Deerfield IL 60015

file

July 9, 1999

NDA 20-011/S-016
NDA 19-732/S-016
NDA 19-943/S-010
NDA 20-263/S-012
NDA 20-517/S-006
NDA 20-708/S-006

Mary Kay Rybicki
August 17, 1999

Lisa M. Rarick, MD
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Attn: Central Document Room 17 B-20
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 19-732/S-016
Lupron Depot ®7.5 mg
(leuprolide acetate for depot suspension)
Amendment to Supplemental Application for New Manufacturing Site (Hikari Plant) for Pre-Filled Dual Chamber Syringe

Dear Dr Rarick:

TAP Holdings Inc, in accordance with 21CFR314.110(1), amends the supplemental application for a new manufacturing site for the pre-filled dual chamber syringe in response to the approvable letter dated June 25, 1999 for NDA 20-011/S-016, NDA 19-732/S-016, NDA 19-943/S-010, NDA 20263/S-012, NDA 20-517/S-006, and NDA 20-708/S-006.

The field copy of this amendment is being submitted to the Division. In accordance with 21 CFR 314.5(K)(3), TAP Holdings Inc. certifies that the field copy is a true copy of the information submitted in this amendment to the supplemental application.

Following are the comments from the approvable letter and the responses of TAP Holdings Inc to those comments:

1 [redacted]

Redacted 3 page(s)

of trade secret and/or

confidential commercial

information from

Correspondence (Amendment to Suppl. Application)
S-006

[redacted]

8.

[redacted]

Please do not hesitate to contact me at **847-317-5780** if you have any questions.

Sincerely,

Dean Sundberg
Director, Regulatory Affairs

TAP HOLDINGS INC.
parent of TAP Pharmaceuticals Inc.

Bannockburn Lake Office Plaza
55 Waukegan Rd.
erfield, IL 60015

ORIGINAL

SUPPL NEW CORRESP

SNC 006

July 1, 1999

Division of Reproductive and Urologic Products, HFD-580
Document Control Room 17B-20
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

NDA 20-011/S-016
19-732/S-016
19-943/S-010
20-263/S-012
20-517/S-006
20-708/S-006

RE: Lupron Depot/Hikari Plant SNDAs

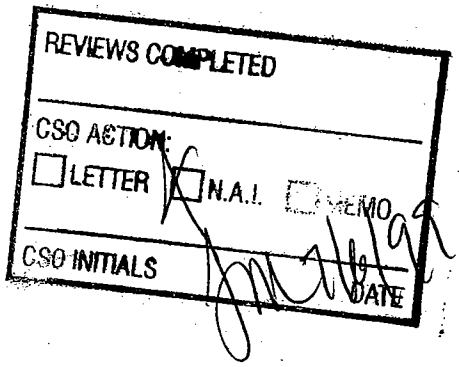
Dear Dr. Rarick,

This is to notify that the sponsor TAP Holdings Inc. intends to file amendments to these supplemental applications as requested in the approvable letter dated June 25, 1999.

Sincerely,

for Aruna Dabholkar, M.D.
Associate Director, Regulatory Affairs

AD/mea



TAP HOLDINGS INC.
parent of TAP Pharmaceuticals inc.

Innockburn Lake Office Plaza
55 Waukegan Rd.
Deerfield, IL 60015

file

NDA 20-011/S-016
NDA 19-732/S-016
NDA 19-943/S-010
NDA 20-263/S-012
NDA 20-517/S-006
NDA 20-708/S-006

June 21, 1999

Division of Reproductive and Urologic Drug Products, HFD-580
Document Control Room 17B-20
Center for Drug Evaluation & Research
Food and Drug Administration
5800 Fishers Lane
Rockville, MD 20857

Mary Kay Leybicke
TAP Regulatory Affairs
August 17, 1999

RE: Lupron Depot®7.5mg (leuprolide acetate depot suspension)

NDA 19-732, S-016
Amendment No. 001

Dear Dr. Rarick,

The sponsor, TAP Holdings Inc., submits this Amendment to the supplemental Application under the provisions of Section 505(I) of the Federal Food, Drug and Cosmetic Act and 21 CFR 314.60 (a).

This amendment includes the data requested by the microbiology reviewer, communicated to the sponsor via a draft letter on June 16, 1999.

Attached is the information required for this amendment.

Sincerely,

Aruna Dabholkar, M.D.
Associate Director, Regulatory Affairs
(847) 317-4893 phone
(847) 317-5795 fax

AD/mea

Attachments

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-517/S-006

Tap Holdings, Inc.
2355 Waukegan Road
Deerfeild, IL 60015

DEC 30 1998

Attention: Aruna Dabholkar, M.D.
Associate Director, Regulatory Affairs

Dear Dr. Dabholkar:

We acknowledge receipt of your supplemental application for the following:

Name of Drug:	Lupron Depot® -3 Month 22.5mg and 4-Month 30mg (leuprolide acetate for depot suspension)
NDA Number:	20-517
Supplement Number:	S-006
Date of Supplement:	December 23, 1998
Date of Receipt:	December 28, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on February 26, 1999, in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation II
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

Lana Pauls
Chief, Project Management Staff
Division of Reproductive and Urologic
Drug Products, HFD-580
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 20-517/S-006
HFD-580/Div. Files
HFD-580/CSO/C. Kish

SUPPLEMENT ACKNOWLEDGEMENT

TAP HOLDINGS INC.
parent of TAP Pharmaceuticals Inc.

ORIGINAL

NDA NO. 20517 REF. NO. 006
NDA SUPPL FOR SCM

Bannockburn Lake Office Plaza
2355 Waukegan Rd
Deerfield, IL 60015

December 23, 1998

Division of Reproductive and Urologic Products, HFD-580
Document Control Room 17B-20
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

RE: Lupron Depot®-3 Month 22.5mg and 4-Month 30mg (leuprolide acetate for depot suspension)

NDA 20-517
Supplemental Application for new manufacturing site for manufacturing the prefilled dual chamber syringe

Dear Dr. Rarick,

The sponsor, TAP Pharmaceuticals Inc., Submits this supplemental Application under the provisions of Section 505(I) of the Federal Food, Drug and Cosmetic Act and 21 CFR 314.70 (b) (2) (vi) and (viii).

This supplement requests for approval of a new manufacturing site for the manufacturing of the prefilled dual chamber syringe.

This supplement consists of 2 volumes labeled as Volume 1.1 and 1.2. The volume 1.1 contains required manufacturing and controls information. Volume 1.2 contains information for Facilities and [ ] Process Validations. Three copies of each Volume 1.1 and 1.2 are submitted.

Since the new site is in Japan, the field copy of this application is also submitted to the Division. Pursuant to 21CFR 314.5 (K) (3) we certify that the field copy is the true copy of the manufacturing and controls information submitted in this supplemental application.

Attached is the information required for this supplement.

Sincerely,

Aruna Dabholkar, M.D.
Associate Director, Regulatory Affairs
(847) 317-4893 phone
(847) 317-5795 fax

AD/mea
Attachment

Reviewed 5/6/99

REVIEWS COMPLETED
CSO ACTION:
[X] LETTER [ ] N.A.I. [ ] MEMO
CSO INITIALS DATE 8/12/99

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
DEC 2 8 1998
HFD-580