Approval Package for:

APPLICATION NUMBER:
NDA 19-943/S-022

Name:	Lupron Depot 3.75 mg leuprolide acetate
Sponsor:	TAP Pharmaceuticals, Inc.
Approval Date:	September 15, 2005

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-943/S-022

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-943/S-022

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDAs 19-732/S-027, S-029
19-010/S-031
19-943/S-022, S-024
20-517/S-018, S-019
20-708/S-020, S-021
20-011/S-029, S-031

TAP Pharmaceutical Products Inc.
Attention: Tonya Haynes, M.P.H.
Regulatory Product Manager
675 North Field Drive
Lake Forest, IL 60045

Dear Ms. Haynes:

Please refer to your supplemental new drug applications as listed below, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act:

NDA	Supplement	Name of Drug	Letter Date	Receipt Date
19-732	SCS-027	Lupron Depot (leuprolide acetate for depot suspension), 7.5mg	May 6, 2005	May 9, 2005
19-732	SLR-029	Lupron Depot (leuprolide acetate for depot suspension), 7.5mg	August 18, 2005	August 19, 2005
20-517	SCS-018	Lupron Depot (leuprolide acetate for depot suspension), 4-month, 30mg	May 6, 2005	May 9, 2005
20-517	SLR-019	Lupron Depot (leuprolide acetate for depot suspension), 4-month, 30mg	August 18, 2005	August 19, 2005
19-010	SLR-031	Lupron Injection (leuprolide acetate	August 18, 2005	August 19, 2005
20-708	SCS-020	Lupron Depot (leuprolide acetate for depot suspension), 3-month	May 6, 2005	May 9, 2005
20-708	SLR-021	Lupron Depot (leuprolide acetate for depot suspension), 3-month	August 18, 2005	August 19, 2005
19-943	SCS-022	Lupron Depot (leuprolide acetate for depot suspension), 3.75 mg	May 6, 2005	May 9, 2005
19-943	SLR-024	Lupron Depot (leuprolide acetate for depot suspension), 3.75 mg	August 18, 2005	August 19, 2005
20-011	SCS-029	Lupron Depot (leuprolide acetate for depot suspension), 3.75mg	May 6, 2005	May 9, 2005
20-011	SLR-031	Lupron Depot (leuprolide acetate for depot suspension), 3.75mg	August 18, 2005	August 19, 2005

The Prior Approval supplemental new drug applications dated August 18, 2005, provide for changes in the package insert to include text regarding pituitary apoplexy.

The "Changes Being Effected" supplemental new drug applications dated May 6, 2005, provide for the addition of an appearance test, and changes in the package insert and mixing instructions regarding the LUPRON recall.

We completed our review of these applications, they are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the submitted labeling (package insert, mixing instructions) on August 18, 2005.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate these submissions "**FPL for approved supplement NDA ##-###/S-YYY, S-ZZZ**", specific to the applications as listed above. Approval of these submissions by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this/these product(s). Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division/ the Division of DIVISION NAME and two copies of both the promotional materials and the package insert(s) directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
Center for Drug Evaluation and Research
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
Food and Drug Administration
Center for Drug Evaluation and Research
5901-B Ammendale Road
Beltsville, MD 20705-1266

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call Nenita Crisostomo, R.N., Regulatory Health Project Manager, at (301) 827-7260.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Director
Division of Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Daniel A. Shames
9/15/2005 12:02:51 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-943/S-022

CHEMISTRY REVIEW(S)

CHEMIST REVIEW
OF **Supplement**

1. **ORGANIZATION: HFD 580**
2. **NDA NUMBER: 19943**
3. **SUPPLEMENT NUMBERS/DATES: SCS-022**
   Letterdate: 06-May-2005
   Stampdate: 09-May-2005
4. **AMENDMENTS/REPORTS/DATES:** None
   Letterdate:
   Stampdate:
5. **RECEIVED BY CHEMIST:** 16-May-2005

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

7. **NAME OF DRUG: Lupron Depot-PED®, Lupron®**

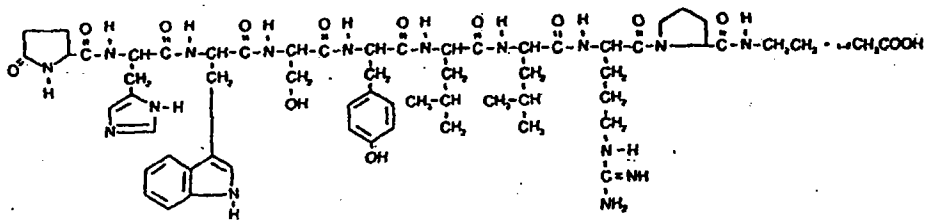
8. **NONPROPRIETARY NAME: Leuprolide Acetate for depot suspension**

   Leuprolide Acetate Injection

9. **CHEMICAL NAME/STRUCTURE:**

   Chemical name: 5-Oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-Tyrosyl-D-leucyl-L-leucyl-L-arginyl-N-ethyl-L-Prolinamide acetate.

   Structural Formula:



10. **DOSAGE FORM(S): Sterile depot suspension for injection**

11. **POTENCY: 3.75 mg**

12. **PHARMACOLOGICAL CATEGORY: LH-RH Agonist/ Prospective management of uterine fibroids**

13. **HOW DISPENSED: Intramuscular Injection**

14. **RECORDS & REPORTS CURRENT: Yes**

15. **RELATED NDAs: 19-732/SCS-028; 20-517/SCS-018; 20-011/SCS-029; 20-708/SCS020; 20-263/SCS-026.**

16. **CHANGES BEING EFFECTED-0 (CBE-0) SUPPLEMENT PROVIDES FOR- the addition of appearance test and to revise the labeling for mixing instructions and package insert for the drug products.**

17. **COMMENTS:** The sponsor has followed the agreements made on previous meetings following Lupron recall (t-con dated 10-March-05 and 23-Mar-05) and has submitted CBE-0 supplements to add appearance test in the specifications for the drug products and updated labeling for the "INSTRUCTIONS ON HOW TO MIX AND ADMINISTER". The application is deemed satisfactory due to following reasons.

- Appearance test will include physical appearance that will confirm the dosage unit contents in the front chamber (leuprolide acetate powder) and it's white appearance. Visual inspection will also include tilting of the syringe to observe the powder flow and will confirm that the leuprolide acetate powder is free-flowing with no visual signs of caking or clumping. Furthermore, if caking or clumping is observed, 100% inspection will be initiated.
- The labeling for the "INSTRUCTIONS ON HOW TO MIX AND ADMINISTER" indicates warning on cake/clump formation of the drug products and is concurred by Medical Officer Dr. M. Hirsch (see labeling review by Nita Crisostomo).

18. **CONCLUSIONS AND RECOMMENDATIONS:**
Based on the information, proposed changes in specification and labeling are satisfactory from CMC perspective.

Issue an 'Approval' Letter

19. REVIEWER NAME	SIGNATURE	DATE COMPLETED
Swapan K. De, Ph.D.		**08-Sept-2005**

cc: Original: NDA #19-943/scs022
HFD-580/Division File
HFD-580/CrisostomoN
HFD-580/RheeM/SDe
R/D INIT by: Moo-Jhong Rhee, Ph.D.

Filename: nda19-943.scs022

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/s/

Swapan De
9/12/2005 10:16:13 AM
CHEMIST

Moo-Jhong Rhee
9/12/2005 10:20:56 AM
CHEMIST
I concur

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-943/S-022

ADMINISTRATIVE

Division of Reproductive and Urologic Products

REGULATORY PROJECT MANAGER REVIEW

Applications: NDA 19-943/S-022, S-024 Lupron Depot 3.75 mg
NDA 20-011/S-029, S-031 Lupron Depot 3.75 mg
NDA 20-708/S-020, S-021 Lupron Depot 3-month 11.25 mg

Applicant: TAP Pharmaceuticals

Submission Date: October 28, 2005

Receipt Dates: October 31, 2005

Materials Reviewed: Final Printed Labeling submitted in this submission and approval letter dated September 15, 2005.

Background and Summary: The sponsor was sent an approval letter dated September 15, 2005 requesting final printed labeling.

Review: The labeling is identical to that in the approval letter.

Recommendation: The sponsor should be sent an acknowledge and retain letter.

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/s/

Jennifer L. Mercier
7/24/2006 10:31:26 AM
CSO

Division of Reproductive and Urologic Drug Products

REGULATORY PROJECT MANAGER REVIEW

Applicant: TAP Pharmaceutical Products, Inc.

Materials Reviewed:

NDA	Supplement	Name of Drug	Letter Date	Receipt Date
19-732	SCS-027	Lupron Depot (leuprolide acetate for depot suspension), 7.5mg	May 6, 2005	May 9, 2005
19-732	SLR-029	Lupron Depot (leuprolide acetate for depot suspension), 7.5mg	August 18, 2005	August 19, 2005
20-517	SCS-018	Lupron Depot (leuprolide acetate for depot suspension), 4-month, 30mg	May 6, 2005	May 9, 2005
20-517	SLR-019	Lupron Depot (leuprolide acetate for depot suspension), 4-month, 30mg	August 18, 2005	August 19, 2005
19-010	SLR-031	Lupron Injection (leuprolide acetate	August 18, 2005	August 19, 2005
20-708	SCS-020	Lupron Depot (leuprolide acetate for depot suspension), 3-month	May 6, 2005	May 9, 2005
20-708	SLR-021	Lupron Depot (leuprolide acetate for depot suspension), 3-month	August 18, 2005	August 19, 2005
19-943	SCS-022	Lupron Depot (leuprolide acetate for depot suspension), 3.75 mg	May 6, 2005	May 9, 2005
19-943	SLR-024	Lupron Depot (leuprolide acetate for depot suspension), 3.75 mg	August 18, 2005	August 19, 2005
20-011	SCS-029	Lupron Depot (leuprolide acetate for depot suspension), 3.75mg	May 6, 2005	May 9, 2005
20-011	SLR-031	Lupron Depot (leuprolide acetate for depot suspension), 3.75mg	August 18, 2005	August 19, 2005

Background and Summary

In January 5, 2005, TAP issued a Dear Healthcare Professional letter and a Voluntary Recall of two particular lots from NDAs 20-517 and 20-708 where complaints of clumping were reported by healthcare professionals to TAP. In addition to TAP's initiation on investigating on the issue, they proposed changes to the labeling as a corrective action to the reported issue. Furthermore, the Sponsor proposes to revise the "Appearance" section of their drug product specification---as a chemistry supplement. These changes affects all of the Lupron Depot drug products with pre-

filled syringes and therefore, the changes are being proposed for all of the NDAs listed above, except for NDA 19-010 (does not have a pre-filled syringe).

In addition, on October 18, 2004, the Office of Drug Safety reviewed the MedWatch reports with significant adverse events of pituitary apoplexy following the administration of GnRH agonists. This review was followed by a Prior Approval supplement request letter dated May 11, 2005, issued by the Division of Reproductive and Urologic Drug Products to all of the sponsors of GnRH agonists, including all of the listed NDAs above, containing the following verbiage:

[redacted]

The above paragraph was further revised by the Division, concluding the final version which was conveyed to the Sponsor on July 15, 2005 prior to submitting the supplement, as follows:

> *Pituitary apoplexy:* During post-marketing surveillance, rare cases of pituitary apoplexy (a clinical syndrome secondary to infarction of the pituitary gland) have been reported after the administration of gonadotropin-releasing hormone agonists. In a majority of these cases, a pituitary adenoma was diagnosed with a majority of pituitary apoplexy cases occurring within 2 weeks of the first dose, and some within the first hour. In these cases, pituitary apoplexy has presented as sudden headache, vomiting, visual changes, ophthalmoplegia, altered mental status, and sometimes cardiovascular collapse. Immediate medical attention has been required.

REVIEW

Of the Lupron Recall changes, the labeling portion of the chemistry supplement was reviewed. See Chemistry review for the changes in the Appearance section of the specification. Listed below are the Sponsor's proposed changes containing the verbiage to the labels:

A. LUPRON RECALL:

1) In the Package Insert, under the DOSAGE AND ADMINISTRATION section, and in the INSTRUCTIONS ON HOW TO MIX AND ADMINISTER pamphlet:

   a. The sponsor proposed to add the following statement as item #1:

   The LUPRON DEPOT powder should be visually inspected and the syringe should NOT BE USED if clumping or caking is evident. A thin layer of powder on the wall of the syringe is considered normal. The diluent should appear clear.

b. The sponsor proposed to add the following statement to add onto item #4:

Keep the syringe UPRIGHT. Gently mix the microspheres ([ ]powder) thoroughly to form a uniform suspension. The suspension will appear milky. If the powder adheres to the stopper or caking/clumping is present, tap the syringe with your finger to disperse. DO NOT USE if any of the powder has not gone into suspension.

B. PITUITARY APOPLEXY: The following text was inserted under the Postmarketing subsection of the Adverse Events section of the Package Insert:

Pituitary apoplexy: During post-marketing surveillance, rare cases of pituitary apoplexy (a clinical syndrome secondary to infarction of the pituitary gland) have been reported after the administration of gonadotropin-releasing hormone agonists. In a majority of these cases, a pituitary adenoma was diagnosed, with a majority of pituitary apoplexy cases occurring within 2 weeks of the first dose, and some within the first hour. In these cases, pituitary apoplexy has presented as sudden headache, vomiting, visual changes, ophthalmoplegia, altered mental status, and sometimes cardiovascular collapse. Immediate medical attention has been required.

A. PACKAGE INSERT: In addition to the changes listed below, all of the NDAs listed

The manufacturing company changed from Takeda Chemical Industries, Ltd. Osaka, Japan 541 to Takeda Pharmaceutical Company Limited Osaka, Japan 540-8645.

NDA	Lupron Recall	Pituitary Apoplexy	Other Changes
	Text inserted is as proposed andn requested for all of the supplements listed below.		
19-732	SCS-027: Acceptable	SLR-029: Acceptable	1. The labeling revision code and date changed from [ ] to TAPDN295-V2; Revised: Month,Year 2. Copyright year changed from [ ] to 1988- Year
20-517, 3 mo	SCS-018: Acceptable	SLR-019: Acceptable	1. The labeling revision code and date changed from [ ] to TAPDN293-V2; Revised: Month,Year 2. Copyright year changed from [ ] to 1995 – Year

20-517, 4 mo	SCS-018 Acceptable	SLR-019 Acceptable	1. The labeling revision code and date changed from [ ] to TAPDN294-V2; Revised: Month,Year 2. Copyright year changed from [ ] to 1997 – Year
20-011	SCS-029 Acceptable	SLR-031 Acceptable	NDA 20-11 & 19-943 share the same label, therefore this portion of the review applies to both applications: 1. Rx only is moved from the end of the label to the beginning—before DESCRIPTION section. 2. The labeling revision code and date changed from [ ] to TAPDN296-V2; Revised: Month,Year 3. Copyright year changed from [ ] to 1990 - Year
19-943	SCS-022 Acceptable	SLR-024 Acceptable	
19-010		SLR 031, Adult & Pediatric Use sections are Acceptable.	1. The labeling revision code and date changed from [ ] to TAPDN299-V2, Rev. Month, Year 2. Copyright year changed from [ ] [ ] to © 1993 – Year
20-708	SCS-020 Acceptable	SLR-021 Acceptable	1. "Rx only" is moved from the end of the label to the beginning 2. The labeling revision code and date changed from [ ] to TAPDN297-V2, Revised: MONTH, YEAR 3. Copyright year changed from [ ] [ ] to © 1993 – YEAR

B. MIXING INSTRUCTIONS: Text inserted in items #1 & #4 are as proposed for all the supplements listed below and are acceptable.

20-708	SCS-020	The following changes are in addition to the changes regarding Lupron Recall and are acceptable: 1. The Sponsor inserted the exact verbiage of the agreed-upon text in all of these supplements on the Mixing Instructions leaflet, as indicated above. 2. In addition, the Sponsor added the following:  REVIEW REVISED MIXING INSTRUCTIONS
19-943	SCS-022	
20-011	SCS-029	
20-517, 3mo & 4mo	SCS-018	
19-732	SCS-027	

Conclusions

Based on this labeling review, these supplemental applications are recommended for approval, as concurred by Chemistry and Clinical.

Nenita Crisostomo, R.N.
Regulatory Health Project Manager

Supervisory Comment/Concurrence:

{see appended electronic signature}

Jennifer Mercier
Chief, Project Management Staff

Drafted: NIC/9.5.05
Revised/Initialed: AGassman9.9.05, MHirsch9.9.05, SDe9.9.05, JMercier
Finalized: DFS/NCrisostomo/9.9.05
Filename: review.SLR.apoplexy.Recall

CSO LABELING REVIEW

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/s/

Nenita Crisostomo
9/9/2005 04:11:28 PM
CSO

Jennifer L. Mercier
9/19/2005 04:48:47 PM
CSO

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-943/S-022

CORRESPONDENCE

Electronic Regulatory Submission for Archive

October 28, 2005

Dr. Daniel Shames, MD, Division Director
Division of Reproductive and Urologic Drug Products, HFD-580
Center for Drug Evaluation and Research
Electronic Document Room
5901-B Ammendale Road
Beltsville, MD 20705

Attn: Nenita Crisostomo, RN, Regulatory Project Manager

RE: Lupron Depot® 3.75 mg (leuprolide acetate for depot suspension)
Uterine Fibroids
NDA 19-943

FPL for Approved Supplements NDA 19-943/S-022, S-024

Dear Dr. Shames:

TAP Pharmaceutical Products Inc. hereby submits the Final Printed Labeling (FPL) per the approval letter dated September 15, 2005 for the above-referenced supplemental New Drug Applications. The FPL is identical to the submitted labeling on August 18, 2005.

The following information is included in this submission:

- Module 1.14.2.2: Final Printed Labeling in PDF format (Commodity Number: 03-5447-R20; Revision Date: October 2005)

- Module 1.14.2.3: Final Labeling Text in MS Word format

This submission is provided in an electronic Common Technical Document (eCTD) format. The only exception from electronic format is signatures, originals of which are provided on paper. Electronic documents are provided in Adobe PDF 1.3 (Adobe 4.05b) format. This submission is approximately 2 megabytes and is provided on one CD-ROM. This submission has been checked for viruses using McAfee Virus Scan Enterprise 7.1.0, and is virus free.

The printed contents of the index-md5.txt file are appended to this letter.

Should you have any questions or comments, please contact me at the information provided below.

Sincerely,

Tonya Haynes
Regulatory Product Manager
TAP Pharmaceutical Products Inc.
675 N. Field Drive
Lake Forest, IL 60045
Tel: (847) 582-2633
Fax: (847) 582-2880

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-732
NDA 20-708
NDA 20-517
NDA 20-011
NDA 20-517
NDA 20-263
NDA 19-943

CBE-30/CBE-0 SUPPLEMENT

TAP Pharmaceutical Products Inc.
Attention: Jessie Y. Lee, Ph.D., R.A.C.
Senior Regulatory Product Manager
675 North Field Drive
Lake Forest, IL 60045

Dear Dr. Lee:

Please refer to our acknowledgment letter to you dated May 23, 2005. This correspondence provides you with a revised version reflecting a change of the assigned supplement number for NDA 19-943 from #000 to #022, as indicated below. Please reflect your records accordingly.

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: LUPRON Depot® (leuprolide acetate for depot suspension)	**NDA Number:**	**Supplement number:**	**Date of supplement:**	**Date of receipt:**
7.5 mg, 1 month	19-732	027	May 6, 2005	May 9, 2005
3.75 mg, 1 month	19-943	022	May 6, 2005	May 9, 2005
30 mg, 4 month & 22.5 mg, 3 month	20-517	018	May 6, 2005	May 9, 2005
3.75 mg,1 month	20-011	029	May 6, 2005	May 9, 2005
11.25 mg, 3 month	20-708	020	May 6, 2005	May 9, 2005
7.5 mg, 11.25 mg, 15 mg	20-263	026	May 6, 2005	May 9, 2005

This supplemental application, submitted as "Supplement - Changes Being Effected" proposes the following changes:

a. Chemistry: addition of appearance test to provide quality control to ensure that the microsphere powder is free-flowing in the final packaged product, and
b. Labeling: add statements to instruct the health care professionals to visually inspect the microsphere powder for caking or clumping prior to mixing and administration of the drug product.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on July 8, 2005, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be November 9, 2005.

Send all electronic or mixed electronic and paper submissions to the Central Document Room at the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room (CDR)
5901-B Ammendale Road
Beltsville, MD 20705-1266

If your submission only contains paper, send it to the following address:

U.S. Postal Service:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Attention: Document Room 8B-45
5600 Fishers Lane
Rockville, Maryland 20857

If you have any question, please call Nenita Crisostomo, R.N., Regulatory Health Project Manager, at (301) 827-7260.

Sincerely,

{See appended electronic signature page}

Nenita Crisostomo, R.N.
Regulatory Health Project Manager
Division of Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Nenita Crisostomo
7/11/05 04:45:58 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 19-732
NDA 20-708
NDA 20-517
NDA 20-011
NDA 20-517
NDA 20-263
NDA 19-943

CBE-30/CBE-0 SUPPLEMENT

TAP Pharmaceutical Products Inc.
Attention: Jessie Y. Lee, Ph.D., R.A.C.
Senior Regulatory Product Manager
675 North Field Drive
Lake Forest, IL 60045

Dear Dr. Lee:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: LUPRON Depot® (leuprolide acetate for depot suspension)	**NDA Number:**	**Supplement number:**	**Date of supplement:**	**Date of receipt:**
7.5 mg, 1 month	19-732	027	May 6, 2005	May 9, 2005
3.75 mg, 1 month	19-943	000	May 6, 2005	May 9, 2005
30 mg, 4 month & 22.5 mg, 3 month	20-517	018	May 6, 2005	May 9, 2005
3.75 mg,1 month	20-011	029	May 6, 2005	May 9, 2005
11.25 mg, 3 month	20-708	020	May 6, 2005	May 9, 2005
7.5 mg, 11.25 mg, 15 mg	20-263	026	May 6, 2005	May 9, 2005

This supplemental application, submitted as "Supplement - Changes Being Effected" proposes the following changes:

a. Chemistry: addition of appearance test to provide quality control to ensure that the microsphere powder is free-flowing in the final packaged product, and
b. Labeling: add statements to instruct the health care professionals to visually inspect the microsphere powder for caking or clumping prior to mixing and administration of the drug product.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on July 8, 2005, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be November 9, 2005.

Send all electronic or mixed electronic and paper submissions to the Central Document Room at the following address:

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Center for Drug Evaluation and Research
Central Document Room (CDR)
5901-B Ammendale Road
Beltsville, MD 20705-1266

If your submission only contains paper, send it to the following address:

U.S. Postal Service:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Attention: Document Room 8B-45
5600 Fishers Lane
Rockville, Maryland 20857

If you have any question, please call Nenita Crisostomo, R.N., Regulatory Health Project Manager, at (301) 827-7260.

Sincerely,

{See appended electronic signature page}

Nenita Crisostomo, R.N.
Regulatory Health Project Manager
Division of Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Nenita Crisostomo
5/23/05 02:16:32 PM

May 6, 2005

Food and Drug Administration
Chicago District Office
550 West Jackson Blvd
Suite 1500
Chicago, IL 60661

ATTENTION: Mr. Scott McIntire
District Director

RE: FIELD COPIES for Supplements of

NDA 19-732	Lupron Depot 7.5 mg (leuprolide acetate for depot suspension)
NDA 19-943	Lupron Depot 3.75 mg (leuprolide acetate for depot suspension)
NDA 20-011	Lupron Depot 3.75 mg (leuprolide acetate for depot suspension)
NDA 20-263	Lupron PED (leuprolide acetate/injection/depot suspension)
NDA 20-517	Lupron Depot - 3 Month 22.5 mg (leuprolide acetate for depot suspension)
	Lupron Depot - 4 Month 30 mg (leuprolide acetate for depot suspension)
NDA 20-708	Lupron Depot - 3 Month 11.25 mg (leuprolide acetate for depot suspension)

Dear Mr. MacIntire:

In accordance with 21 CFR 314.70(a)(5), appended are the Field Copies for the supplemental New Drug Applications for the above-referenced NDAs. TAP Pharmaceutical Products Inc. hereby certifies that these field copies are the true copy of the submissions filed to FDA dated May 6, 2005.

If you have any questions, please feel free to contact me.

Sincerely,

TAP Pharmaceutical Products Inc.

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JYL/jl
Attachments
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