CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
21-288

Correspondence

TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

July 12, 2000

Susan Allen, MD
Director, Division of Reproductive and Urologic Drug Products
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

ORIG AMENDMENT

13M

RE: NDA 21-288
Trelstar™ LA
(triptorelin pamoate for injectable suspension) 11.25 mg
Request for waiver of the submission of pediatric use information

Dear Dr. Allen:

Reference is made to Debio RP NDA 21-288 submitted to the agency on June 29, 2000. Trelstar™ LA is indicated for the palliative treatment of advanced prostate cancer. In accordance with 21 CFR 314.55 (c)(2)(ii), we are hereby requesting a full waiver for supplying safety and effectiveness information for Trelstar™ LA in a pediatric population. The waiver is being requested since the number of pediatric patients affected with advanced prostate cancer is so small that it would be impossible to study the drug in this population.

Please let me know if you have any questions.

Sincerely,

Robert J McCormack, Ph.D.
Vice President, Regulatory Affairs

REVIEWS COMPLETED

CSO ACTION

☐ LETTER ☐ N.A.L. ☐ MEMO

CSO INITIALS DATE

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DEBIO RECHERCHE PHARMACEUTIQUE S.A.

June 27, 2000

Susan Allen, MD
Acting Director,
Division of Reproductive and
Urologic Drug Products
Food and Drug Administration
5600 Fishers Lane, HFD-580
Rockville MD

RE : Communications regarding Trelstar™ LA
for the palliative treatment of advanced prostate cancer
NDA 21-288

Dear Dr Allen,

We wish to notify the agency of the following :

N. Peter Kostopulos, 1747 Pennsylvania Avenue N.W., Suite 300, Washington, D.C. 20006, telephone (202) 296-4444, remains the registered U.S. agent for Debio. R. P.

Dr Robert J. McCormack, Vice President, Regulatory Affairs, Target Research Associates, 554 Central Avenue, New Providence, NJ 07974, telephone (908) 464 7500, fax (908) 464 7515, is taking care of all scientific and regulatory issues related to NDA 21-288.

Therefore, as part of this NDA submission, we are hereby confirming that all written and telephone communications regarding the above-mentioned NDA be directed to Dr McCormack at the location mentioned above.

Additionally, Debio R.P. confirms that it has authorized Dr McCormack to contact the Agency on its behalf as the need arises related to the above NDA.

Kind regards,

Piero Orsolini, Ph. D.
CEO Debio R.P.

DEBIO R.P. S.A., route du Levant 146, C.P. 368, CH-1920 MARTIGNY – Tél. 027/721 79 00 – Fax 027/721 79 01
Groupe DEBIO, rue des Terreaux 17, C.P., CH-1000 LAUSANNE 9 – Tél. 021/311 21 60 – Fax 021/311 21 69

DEBIO RECHERCHE PHARMACEUTIQUE S.A

Lausanne, 22 June 2001

Susan Allen, MD
Food and Drug Aministration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director Division of Reproductive and
Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600, Fishers Lane
Rockville, Maryland 20857
USA

Ref.: Debio R. P. NDA 21-288 Phase 4 Commitment

Dear Dr Allen,

Based on the teleconference between Debio R. P. and FDA personnel on June 21, 2001, Debio R. P. hereby makes a Phase 4 commitment to collect additional data concerning post-dosing testosterone levels in subjects treated with the 84-day formulation of triptorelin. In order to do this, Debio R. P. will conduct an open-label study in which 15-20 patients will each receive 3 doses Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension). Obtain blood samples for the measurement of serum testosterone at the time of screening, immediately prior to and 48 to 72 hours after the second and the third doses of Trelstar™ LA. Entry criteria should include a screening testosterone level > 5 nmol/l.

Sincerely,

p.a.

Dr. Piero Orsolini
CEO Debio R. P.

Administration: CH-1000 Lausanne 9, rue des Terreaux 17, case postale 211, téléphone +41/21 321 01 11, fax +41/21 321 01 69
Laboratoire: CH-1920 Martigny, route du Levant 146, case postale 348, téléphone +41/27 722 33 83, fax +41/27 722 33 85

TARGET RESEARCH ASSOCIATES

ICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

ORIGINAL

June 29, 2001

BL
NDA ORIG AMENDMENT

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Final Submission of Revised Labeling

Dear Dr. Allen,

.osed is the final revised labeling for Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension). All revisions requested by the agency have been incorporated into this document. Also enclosed is a diskette containing the labeling text in Word 97.

Please let me know if you have any questions.

Sincerely,

Robert McCormack, PhD
Vice President, Regulatory Affairs

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

TARGET
RESEARCH
ASSOCIATES
CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

ORIGINAL

NDA ORIG AMENDMENT
N-BC

June 28, 2001

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Submission of analytical methods validation and injection site information.

Dear Dr. Allen,

Enclosed as requested by the FDA is a copy of the analytical methods validation for determining triptorelin and testosterone levels in study DEB-95-TRI-01 and injection site information from the pharmacokinetic studies conducted with Trelstar LA.

Please let me know if you have any questions.

Sincerely,

for Robert McCormack

Robert McCormack, PhD
Vice President, Regulatory Affairs

REVIEWS COMPLETED
DSD ACTION:
LETTER ☐ N.A.I. ☐ MEMO
INITIALS DATE

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TARGET
RESEARCH
ASSOCIATES
CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

June 27, 2001

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Submission of Revised Labeling

Dear Dr. Allen,

Enclosed is the revised labeling for Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension). All revisions requested by the agency have been incorporated into this document. Also enclosed is a diskette containing the labeling text in Word 97.

The analytical methods validation for triptorelin and testosterone in study DEB-95-TRI-01 and injection site information from the pharmacokinetic studies conducted with Trelstar LA will be sent via FedEx to the agency tomorrow to arrive on Friday, June 29, 2001.

Please let me know if you have any questions.

Sincerely,

Robert McCormack, PhD
Vice President, Regulatory Affairs

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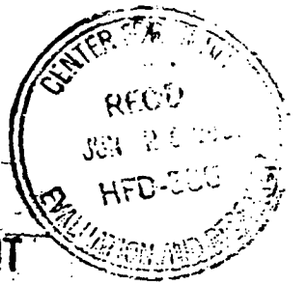
TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

ORIGINAL



June 25, 2001

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

NDA ORIG AMENDMENT

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Phase IV Commitment and CIOMS Report

Dear Dr. Allen,

Enclosed is correspondence from Debio RP which hereby commits them to performing the Phase IV study outlined in their letter.

In addition, as requested by FDA, is the CIOMS Report for patient #330051 listed on page 151 of the Safety Report, dated October 24, 2000.

Please let me know if you have any questions.

Sincerely,

Lloyd J. Baroody
Managing Director

Attachments

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS -- DATE

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TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

NDA ORIG AMENDMENT

June 19, 2001

N-P.C

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Complete Response to Package Insert Revisions request dated June 15, 2001.

Dear Dr. Allen,

This responds to a fax from Jeanine Best to Dr. Robert McCormack dated June 15, 2001 in which NDA 21-288 Package Insert revisions were requested. This provides the revised Package Insert in both hard copy as well as in Word 97.

Sincerely,

Lloyd J. Baroody
Managing Director

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TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

ORIGINAL

NDA ORIG AMENDMENT

NO-BM

June 19, 2001

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Complete Response to Medical Information Questions dated May 25, 2001.

Dear Dr. Allen,

I previously sent you a package dated June 7, 2001 providing a response to medical information questions dated May 25, 2001 regarding the subject NDA. It has been brought to my attention that there were several unintentional omissions to this response due to clerical error. Specifically, (1) we had not signed the Form 356h, (b) a software error caused the first line of each FDA question to be deleted, which was repeated in each Question tab before the response (Note that the response was unaffected), and (c) Appendix 5 to which was referred in Question 7 was missing; this appendix represented the Irish and French SmPCs. Accordingly, we would be most grateful if you would kindly replace the June 7, 2001 package with the enclosed, corrected package. We regret the inconvenience this may have caused you.

Sincerely,

Lloyd J. Baroody
Managing Director

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

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TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

NDA ORIG AMENDMENT

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JUN 0 8 2001
HFD-580

June 7, 2001

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

N - RM

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Complete Response to Medical Information Questions dated May 25, 2001.

Dear Dr. Allen,

Enclosed, in duplicate, we are hereby submitting on behalf of Debio RP a complete response to Medical Information Questions dated May 25, 2001.

Please let me know if you have any questions.

Sincerely,

Lloyd J. Baroody
Managing Director

REVIEWS COMPLETED	
CSO ACTION: ☐ LETTER ☐ N.A.I. ☐ MEMO	
CSO INITIALS	DATE

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TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

NDA ORIG AMENDMENT

June 1, 2001

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Second submission of mock-up container closure labeling.

Dear Dr. Allen,

Reference is made to the above NDA and to the submission dated May 21, 2001 in which mock-up container closure labeling was submitted to the agency. The mock-ups submitted at that time did not contain the color scheme nor were all mock-ups supplied with the dimension specifications. Based on this, we are hereby submitting, in duplicate, on behalf of Debio RP, revised mock-up container closure labeling which shows the color scheme and all dimension specifications. The container closure labeling being submitted is as follows:

- Carton for the vial alone packaging configuration
- Label for vial containing triptorelin pamoate
- Label for pre-filled syringe
- Label for Debioclip ™ blister pack
- Outer carton for single dose vial plus Debioclip ™

These enclosed mock-up container closure labels supercede those provided in the previous submission dated May 21, 2001.

Please let me know if you have any questions.

Sincerely,

Robert McCormack, PhD
Vice President, Regulatory Affairs

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ORIGINAL

TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

June 1, 2001

BC

NDA ORIG AMENDMENT

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Revised Stability Dissolution Specification

Dear Dr. Allen,

As per the discussion during the teleconference with Dr. David Lin and Mrs Jeanine Best on May 30, 2001, Debio RP hereby agrees to modify the in vitro dissolution registration (stability) specifications in the following way :

Parameter		Release specification	Registration (Stability) Specification
		unchanged	new
In vitro dissolution	1 hr	( )%	( )%
	48 hr	( )%	( )%
	72 hr	( )%	( )%

The NDA pages concerned by the modification are pp. 153 and 249, Vol 1.2

Please let me know if you have any questions.

Sincerely,

Robert McCormack, PhD
Vice President, Regulatory Affairs

REVIEWS COMPLETED.

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

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TARGET
RESEARCH
ASSOCIATES
CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

NDA ORIG AMENDMENT

ORIGINAL

May 21, 2001

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Submission of mock up container closure labeling.

Dear Dr. Allen,

In advance of the agency taking an action on NDA-21-288, we are hereby submitting in duplicate on behalf of Debio RP, the following mock up container closure labeling related to the Trelstar ™ 3-month formulation:

- Carton for the vial alone packaging configuration
- Label for vial containing triptorelin pamoate
- Label for pre-filled syringe
- Label for Debioclip ™ blister pack
- Outer carton for single dose vial plus Debioclip ™

Please let me know if you have any questions.

Sincerely,

Robert McCormack, PhD
Vice President, Regulatory Affairs

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

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TARGET RESEARCH ASSOCIATES
CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

May 14, 2001

ORIGINAL

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

NEW CORRESP

N/C

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Electronic submission of figures contained in Human PK and Bioavailability Technical Data Section Summary.

Dear Dr. Allen,

Enclosed as requested by Jeannine Best are two diskettes containing the four figures associated with the Human Pharmacokinetic and Bioavailability Technical Data Section Summary.

Please let me know you have any questions.

Sincerely,

Robert McCormack, PhD
Vice President, Regulatory Affairs

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TARGET RESEARCH ASSOCIATES
CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

ORIG AMENDMENT

May 14, 2001

BI

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Response to question raised by the reviewing Microbiologist.

Dear Dr. Allen,

Listed below, as requested by telephone from reviewing microbiologist, Dr. David Husson, is a brief summary of the sterility testing preformed on the Debioclip™ packaging configuration.

The presentation of Trelstar ™ LA 11.25 mg triptorelin pamoate consists of a Debioclip ™ and a sterilized single use vial. The Debioclip ™ consists of a sterilized pre-filled glass syringe containing 2 mL sterile water for injection, supplied by . The triptorelin pamoate vial is manufactured by Debio RP and is performed by . After sterilization the vials are tested and released by Debio RP according to the testing described in Vol. 1.2 (page 158) of the NDA.

The pre-filled syringes are tested for sterility by according to USP 24 test # <71> using the membrane filtration method. The pre-filled syringes are then shipped to Debiotech (Switzerland) with a certificate of analysis. As outlined in DMF Debiotech tests and releases each incoming lot of pre-filled syringes including performing sterility testing at a contract facility according to USP 24 <71>. The Debioclips are then packaged individually in a blister package, sealed with a cover and sterilized using). After sterilization, representative samples of the Debioclip ™ are sent to for

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sterility testing according to This SOP and validation of the test methods were reviewed and found to be acceptable by FDA during their inspection which took place on April 4 and 5, 2001. Sterility testing is performed by the method as defined in the USP. Briefly, sterility testing is conducted by and removing the Debioclip ™ from the packaging unit. One mL of the water for injection is dispensed from each syringe through the attached needle into sterile media. For each batch 20 samples are evaluated for sterility in media and 20 samples in media. At the same time, duplicate of the media, test sample and recommended test organisms in each media and incubation condition are prepared. Positive controls of media and the test organisms are prepared in and negative controls of media alone are also prepared in .

After testing and release of the sterilized pre-filled syringes, the vials are placed in the empty space of the Debioclip ™ blister.

Please let me know if there are any questions about the enclosed information.

Sincerely,

Robert McCormack, PhD
Vice President, Regulatory Affairs

REVIEWS COMPLETED	
CSO ACTION: ☐ LETTER ☐ N.A.I. ☐ MEMO	
CSO INITIALS	DATE

TARGET RESEARCH ASSOCIATES
CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

April 27, 2001

BM

NDA ORIG AMENDMENT

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Complete response to questions received in a facsimile dated April 3, 2001.

Dear Dr. Allen,

Enclosed is duplicate we are hereby submitting on behalf of Debio RP with a complete response to the questions raised in your facsimile dated April 3, 2001.

We trust that the information provided adequately addresses each of the points raised in the facsimile.

Please do not hesitate to contact me if you have any questions.

Sincerely,

Robert McCormack, PhD
Vice President, Regulatory Affairs

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO
CS[illegible] DATE

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TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

NEW CORRESP

ORIGINAL

April 6, 2001

Susan Allen, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

NC

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Response to medical information request dated April 3, 2001

Dear Dr. Allen,

This letter is to acknowledge receipt of the medical information request dated April 3, 2001 which was faxed to Target Research Associates on the same date.

We plan to provide a complete response to the agency no later than April 30, 2001. Also, due to the amount of data which needs to be submitted, we understand that the secondary user fee date of June 29, 2001 will be used to take an initial action on the application.

Please let me know if you have any questions.

Sincerely,

Robert McCormack, PhD
Vice President, Regulatory Affairs

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

ORIGINAL

March 5, 2001

Susan Allen, MD
Director, Division of Reproductive and Urologic Drug Products (HFD-58
Parklawn Building, Room 17B-45
5600 Fishers Lane
Rockville, MD 20857

ORIG AMENDMENT

B2

Re: NDA 21-288
Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension);
Response to deficiencies regarding Debioclip™ packaging configuration

Dear Dr Allen

This letter in conjunction with the submission dated February 5, 2001 provides a complete response to deficiencies regarding the Debioclip packaging configuration which were cited in Discipline Review Letter from Moo-Jhong Rhee, PhD, received via facsimile on January 11, 200. In addition as requested in the FDA letter dated January 12, 2001 for the Debioclip supplement for NDA 20-715 (Trelstar ™ 3.75 mg), we are also enclosing revised labels with the statement "Sterile Water for Injection, USP" (see point #2 of this letter).

1. ***The integrity test of the Debioclip™ and its blister package with cover have not been documented in the NDA.***

   a. ***Please provide a summary of the methods, acceptance criteria and results that show the integrity of the blister package and its cover.***

   Packaging validation studies for the Debioclip™ blister package were performed by the These studies characterized both the packaging materials and the assembled blister package and included:

   •

   •

REVIEWS COMPLETED	
CSO ACTION: ☐ LETTER ☐ N.A.I. ☐ MEMO	
CSO INITIALS	DATE

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secret and/or

confidential

commercial

information

TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

January 29, 2001

ORIGINAL

Susan Allen, MD
Director, Division of Reproductive and Urologic Drug Products
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

ORIG AMENDMENT
BM

RE: NDA 21-288
Trelstar™ LA 11.25 mg
(triptorelin pamoate for injectable suspension)
Response to FDA Clinical Information Request dated January 8, 2001

Dear Dr. Allen:

Reference is made to Debio RP NDA 21-288 submitted to the agency on June 29, 2000, and to the January 8, 2001 telephone request memorandum of Ms. Jeanine Best for additional clinical information.

On behalf of Debio RP, we are submitting in duplicate, the following responses to the January 8, 2001 request. Listed below are the FDA requests for information (in italics) followed by Debio RP's response:

Request

1. *Please document all protocol deviations involving dosing; specifically all listed in Data Listing 16.2.2 that affected classification or censoring of a patient.*

Response:

Protocol violations involving dosing, in Data Listing 16.2.2, are documented in Table 14.1.1.5 (NDA 21-288 Vol./Page 1.17/108-109) and Table 14.1.1.6. (1.17/110). These tables include classification or censoring of patient. Tables 14.1.1.5 and 14.1.1.6 have been included in this submission as Attachment # 1.

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

Responses to FDA telephone contact of January 08, 2001

Request

2. *Please resolve apparent inconsistencies between data listing 16.2.2 regarding dosing violations and the electronic dosing file and the paper dosing listing (Data Listing, 16.2.5.2). In particular, dosing (cross over violations) for patients 2006, 15025, and 9015 are referred to in listing 16.2.2, but do not appear in listing 16.2.5.2.*

Response:

There are no inconsistencies. Electronic dosing file includes the study drug formulation administered at each visit. The information is in variable , whose codes are Crossover cases are thus identifiable. Details for patient 9015 are in NDA 21-288 Vol./Page 1.17/051 and included in this submission as Attachment #2.

Data Listing 16.2.5.2 does not display the study drug actually administered at each visit, but only the treatment group the patient was allocated to. Study drug administered is provided in response to Question # 3 below, as it is not available in the study report data listings.

Request

3. *Please expand Electronic File to include the injection data (calendar date), the actual study day, and the difference between the actual day and the target day.*

Response:

Requested information has been added in the electronic file " (see Attachment # 3) to contain: injection data calendar date that is in variable name , actual study day in variable difference between the actual day and target day in variable

Please let me know if you have any questions or need additional information.

Sincerely,

Robert J. McCormack, Ph.D.
Vice President, Regulatory Affairs

TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

25th January 2001

Susan Allen, MD
Acting Director
US Food and Drug Administration
Division of Reproductive and Urologic Drug Products
Division Document Room
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
5600 Fishers Lane
Rockville, Maryland 20857

ORIG AMENDMENT

BM

RE: NDA 21-288
Trelstar™ LA 11.25 mg
(triptorelin pamoate for injectable suspension)
Submission of additional information requested by FDA's Medical Officer

Dear Dr. Allen:

On behalf of Debio Recherche Pharmaceutique S.A., we are submitting in duplicate the following information, which we believe constitutes a complete response to the 21st December 2000 request made by FDA's Medical Officer.

Enclosed you will find:

- Form FDA 356h
- Response to FDA letter of December 21, 2000, re: NDA 21-288
- Attachment #1 - One diskette containing the SAS export file ' ', as required.
- Attachment #2 - A paper copy of data listing 16.2.8.2 for . as required.
- Attachment #3 - One diskette containing the SAS export file ' ', as required.
- Attachment #4 - A paper copy of testosterone lab data for SAS export file as required.
- Attachment #5 - One diskette containing the SAS export file ' ', as required.

Note that the file contains data pertinent to both questions #4 and #5; date of sample = visit date, as required in question #5.b).

Thank you for your consideration. We look forward to a favorable response

Respectfully submitted,

Mary Lou Zett, Ph.D., CQE
Senior Director, Regulatory Affairs and Quality Systems
Target Research Associates

REVIEWS COMPLETED	
CSO ACTION: ☐ LETTER ☐ N.A.I. ☐ MEMO	
CSO INITIALS	DATE

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

TARGET
RESEARCH
ASSOCIATES

ORIGINAL

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

December 15, 2000

Susan Allen, MD
Director, Division of Reproductive and Urologic Drug Products
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 21-288
Trelstar™ LA
(triptorelin pamoate for injectable suspension) 11.25 mg
Request for electronic information

Dear Dr. Allen:

Reference is made to Debio RP NDA 21-288 submitted to the agency on June 29, 2000, and to the December 13, 2000 telephone request of Ms. Jeanine Best for additional information on behalf of the medical reviewer.

On behalf of Debio RP, we are submitting in duplicate, the following information in response to the December 13, 2000 request:

- One diskette containing one compressed zipped file (Word 97) of narratives and text tables which appear in NDA 21-288 Volume 26 pages 1-96 and tables 14.2.1.1 to 14.2.1.14 which appear in Volume 29 pages 183-202.

- One diskette containing electronic copies of the Overall Clinical and Statistical Summary and the Integrated Summary of Safety (Word 97).

Please let me know if you have any questions or need additional information.

Sincerely,

Jill A Powers, RAC
Manager, Regulatory Affairs

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

DEBIO RECHERCHE PHARMACEUTIQUE S.A.

October 24, 2000

ORIGINAL

Dr. Susan Allen
Acting Director
Division of Reproductive and Urologic Drug Products (HFD-580)
Office of Drug Evaluation II
Center for Drug Evaluation and Research
U.S. FOOD AND DRUG ADMINISTRATION
5600, Fishers Lane
Rockville, MD 20857

ORIG AMENDMENT

SU

Re: NDA 21-288, Trelstar™ LA 11.25 mg
Triptorelin pamoate, 11.25 mg for injectable suspension

Dear Dr. Allen,

Pursuant to 21 CRF 314.50(d)(5)(vi)(b), Debio R.P. is submitting herewith, in duplicate, the 120 Days Safety Update Report for Trelstar™ LA 11.25 mg, NDA 21-288. This safety report covers the period from September 6, 1999 to September 29, 2000, and includes adverse experiences from clinical studies as well as from post-marketing surveillance. No new animal safety studies have been conducted with Trelstar™, therefore, the enclosed report presents only safety information from humans.

We understand that all information contained therein, otherwise made public by Debio R.P., is CONFIDENTIAL.

If you have any questions about the enclosed information, please do not hesitate to contact:

Target Research Associate Inc.
554, Central Avenue
New Providence, NJ 07974
Phone: (908) 464 75 00
Fax: (908) 464 75 15

REVIEWS COMPLETED	
CSO ACTION: ☐ LETTER ☐ N.A.I. ☐ MEMO	
CSO INITIALS	DATE

Sincerely,

Piero Orsolini
President & CEO, Debio R.P.

Enclosure : ment.

TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

ORIGINAL

October 4, 2000

Susan Allen, MD
Director, Division of Reproductive and Urologic Drug Products
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

ORIG AMENDMENT

Bill

RE: NDA 21-288
Trelstar™ LA
(triptorelin pamoate for injectable suspension) 11.25 mg
Request for testosterone analysis

Dear Dr. Allen:

Reference is made to Debio RP NDA 21-288 submitted to the agency on June 29, 2000, and to the August 16, 2000 telephone request of Ms. Jeanine Best for additional information on behalf of the medical reviewer.

On behalf of Debio RP, we are submitting in duplicate, the following information which we believe constitutes a complete response to the August 16,2000 request:

- A diskette containing one electronic file of testosterone data in : obtained from analysis of frozen serum samples from a subset of patients in Study 96-TRI-01 (first phase). A paper copy of the . is also included in this submission.

- Background information and a brief summary of the analysis results (paper copy only).

- A description and definition of the variables used in the (paper copy only).

Please let me know if you have any questions or need additional information.

Sincerely,

Jill A Powers, RAC
Manager, Regulatory Affairs

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.L. ☐ MEMO

CSO INITIALS DATE

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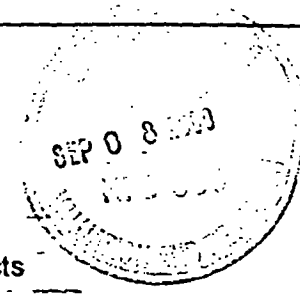
TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

ORIGINAL



September 7, 2000

Susan Allen, MD
Acting Director, Division of Reproductive and Urologic Drug Products
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

NEW CORRESP

N/C

RE: NDA 21-288
Trelstar™ LA
(triptorelin pamoate for injectable suspension) 11.25 mg
Submission of USAN approval

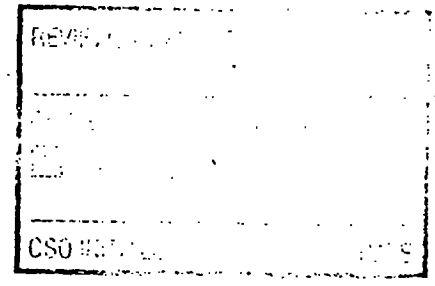
Dear Dr. Allen:

Reference is made to Debio RP NDA 21-288 submitted on June 29, 2000 for Trelstar™ LA in the palliative treatment of advanced prostate cancer. On behalf of Debio RP, we are submitting, in duplicate, the USAN approval notification for triptorelin pamoate as part of the official record for NDA 21-288.

Please contact me if you should have any questions regarding this submission.

Best regards,

Jill A. Powers, RAC
Manager, Regulatory Affairs



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TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

ORIGINAL

September 5, 2000

Susan Allen, MD
Director, Division of Reproductive and Urologic Drug Products
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

ORIG AMENDMENT

BP

RE: NDA 21-288
Trelstar™ LA
(triptorelin pamoate for injectable suspension) 11.25 mg
Request for additional Biopharmaceutics information

Dear Dr. Allen:

Reference is made to Debio RP NDA 21-288 submitted to the agency on June 29, 2000, and to the August 16, 2000 telephone request of Ms. Jeanine Best for additional biopharmaceutics information.

On behalf of Debio RP, we are submitting in duplicate, the following information in response to the August 16, 2000 request.

- One diskette containing electronic files of data in ' from each PK and PD study submitted in NDA 21-288. The files being submitted are for studies 95TRI-01, 96TRI-01 and 99TRI-01 and are named using the applicable study number.
- A printout which describes the for each of the above mentioned electronic files.
- A second diskette containing individual study synopses for the above mentioned studies, and the Human PK and Biopharmaceutics Summary submitted in NDA 21-288.

Please let me know if you have any questions or need additional information.

Sincerely,

JM A Powers, RAC
Manager, Regulatory Affairs

54 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

ORIGINAL

August 23, 2000

Susan Allen, MD
Director, Division of Reproductive and Urologic Drug Products
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

ORIG AMENDMENT
12

RE: NDA 21-288
Trelstar™ LA
(triptorelin pamoate for injectable suspension) 11.25 mg
Request for additional information

Dear Dr. Allen:

Reference is made to Debio RP NDA 21-288 submitted to the agency on June 29, 2000, and to the August 16, 2000 telephone request of Ms. Jeanine Best for additional chemistry, medical and biopharmaceutics information.

On behalf of Debio RP, we are submitting in duplicate, the following partial response to the August 16, 2000 request. Listed below is the FDA request for information (in boldface type) followed by Debio RP's response (in italics).

Chemistry

1. In Volume 1.2 of the NDA, page 278 concerning the Environment Assessment exclusion, there appears to be a typographical error. It is assumed by the agency that the NDA referenced should be 20-715 not .

We confirm that there is a typographical error in Volume 2 on page 278. The NDA reference should be 20-715 not .

2a. In Volume 1.2, pages 275-277, please clarify which method was used to manufacture the clinical, validation, and biopharm batches,

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We confirm that all the batches have been produced with the as mentioned on the top of page 277 (Volume 1.2).

On page 276 (Volume 1.2) the stated used to produce the batches is mistakenly identified in the table by the Debio The following is a clarification: All of the batches have been produced using The batches DLGSD3-95-21, DLGSD3-95-22, DLGSD3-96-24 and DLGSD3-97-25 have been produced with which is the original equipment and is used only . For historical reasons, this is referred to internally by Debio as The batches 4123A9901, D303D67J9, D303D68J9, D303D69K9 and D303D01E0 have been produced with This is referred to internally by Debio as Both have the same components and characteristics.

2b. In addition, on page 132, it appears that a mixture of methods is described, please clarify.

The description of the manufacturing of bulk microgranules on page 132 (Volume 1.2) is correct. There is no discrepancy between the procedure as outlined in NDA and the procedure outlined in NDA 21-288. The ratio of peptide vs. polymer in the one month formulation (NDA 20-715) is roughly while the ratio of peptide vs. polymer in the three month formulation (NDA 20-715) is roughly The intended ratio between each formulation is

3. When will stability be updated?

The next sample points for stability will be as outlined in the table below:

BATCH NUMBER	TIME POINT	DATE
DLGSD3-97-25	Months	Sept 2000
D303D67J9	Months	Sept 2000
D303D68J9	Months	Sept 2000
D303D69J9	Months	Sept 2000
D303D01E0	Months	Sept 2000

Updated stability results will be submitted to the NDA at the end of October 2000.

Clinical/Medical

4. If there is frozen serum remaining from Center No.1, please analyze it for testosterone levels.

Debio will analyze the serum for testosterone levels and submit the results to the agency.

Please be advised that this is a partial response to the August 16 request. The biopharmaceutics information will be sent as soon as it is available.

Please let me know if you have any questions or need additional information.

Sincerely,

Robert J McCormack, Ph.D.
Vice President, Regulatory Affairs

TARGET
RESEARCH
ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

August 17, 2000

ORIGINAL

Susan Allen, MD
Director, Division of Reproductive and Urologic Drug Products
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

(NDA AMENDMENT)

RE: NDA 21-288
Trelstar™ LA
(triptorelin pamoate for injectable suspension) 11.25 mg
Request for additional information

Dear Dr. Allen:

Reference is made to Debio RP NDA 21-288 submitted to the agency on June 29, 2000, and the August 15, 2000 telephone request of Ms. Jeanine Best for an electronic copy of the draft labeling submitted in NDA 21-288. On behalf of Debio RP we are submitting, in duplicate, the above requested draft labeling in Word format.

Please let me know if you have any questions or need additional information.

Sincerely,

Robert J McCormack, Ph.D.
Vice President, Regulatory Affairs

554 Central Avenue • New Providence, NJ 07974 USA • 908/464-7500 • FAX: 908/464-7515

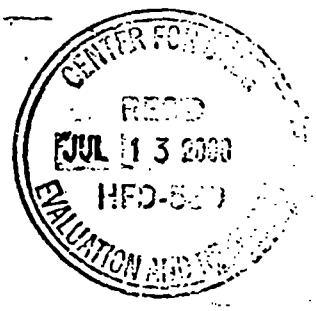
TARGET RESEARCH ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

July 12, 2000

ORIGINAL

Susan Allen, MD
Director, Division of Reproductive and Urologic Drug Products
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
Document Control Room
5600 Fishers Lane
Rockville, MD 20857



RE: NDA 21-288
Trelstar™ LA
(triptorelin pamoate for injectable suspension) 11.25 mg
Request for additional information

NEW CORRESP
NC

Dear Dr. Allen:

Reference is made to Debio RP NDA 21-288 submitted to the agency on June 29, 2000, and the July 6, 2000 telephone request of Ms. Lana Pauls for supplemental information for the Certification of Investigator Financial Interests submitted in NDA 21-288. On behalf of Debio RP we are submitting, in duplicate, the attached information requested by Ms. Pauls.

Please let me know if you have any questions.

Sincerely,

Robert J McCormack, Ph.D.
Vice President, Regulatory Affairs

REVIEWS COMPLETED.
CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS DATE

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TARGET
RESEARCH
ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

July 12, 2000

Susan Allen, MD
Director, Division of Reproductive and Urologic Drug Products
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

ORIG AMENDMENT

13M

RE: NDA 21-288
Trelstar™ LA
(triptorelin pamoate for injectable suspension) 11.25 mg
Request for waiver of the submission of pediatric use information

Dear Dr. Allen:

Reference is made to Debio RP NDA 21-288 submitted to the agency on June 29, 2000. Trelstar™ LA is indicated for the palliative treatment of advanced prostate cancer. In accordance with 21 CFR 314.55 (c)(2)(ii), we are hereby requesting a full waiver for supplying safety and effectiveness information for Trelstar™ LA in a pediatric population. The waiver is being requested since the number of pediatric patients affected with advanced prostate cancer is so small that it would be impossible to study the drug in this population.

Please let me know if you have any questions.

Sincerely,

Robert J McCormack, Ph.D.
Vice President, Regulatory Affairs

REVIEWS COMPLETED

CSO ACTION
☐ LETTER ☐ FAX ☐ MEMO

CSO INITIALS DATE

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TARGET
RESEARCH
ASSOCIATES

CLINICAL RESEARCH, REGULATORY AFFAIRS & BIOSTATISTICS

June 29, 2000

Susan Allen, MD
Acting Director, Division of Reproductive and Urologic Drug Products
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
Document Control Room
5600 Fishers Lane
Rockville, MD 20857

RE: Debio Recherche Pharmaceutique S.A.
NDA 21-288
Trelstar™ LA
(triptorelin pamoate for injectable suspension) 11.25 mg
Indication: Palliative treatment of advanced prostate cancer
Initial filing of NDA 21-288

Dear Dr. Allen:

Persuant to 21 CFR 314.50, we are, on behalf of Debio Recherche Pharmaceutique SA (Debio, R.P.) submitting in duplicate a New Drug Application, NDA 21-288 for Trelstar™ LA (triptorelin pamoate for injectable suspension) 11.25 mg.

Triptorelin pamoate is a synthetic decapeptide agonist analog of naturally occurring luteninizing hormone releasing hormone (LHRH) which acts as potent inhibitor of gonadotropin secretion when given continuously and in therapeutic doses. Trelstar™ LA is a long acting suspension containing a pamoate salt of triptorelin. It is intended as an intramuscular injection to be administered every 84 days as a palliative treatment of advanced prostate cancer. Trelstar™ Depot; a one month formulation of triptorelin pamoate (NDA 20-715) was approved June 15, 2000, also as a palliative treatment of advanced prostate cancer.

This NDA contains a single adequate and well-controlled trial (DEB-96-TRI-01 first phase) which compares the safety and efficacy of the proposed three month formulation (Trelstar™ LA) to the approved one month formulation (Trelstar™ Depot). Reference is made to the June 23, 2000 pre-NDA teleconference between the Agency and Debio, R.P. where it was agreed that study DEB-96-TRI-01 first phase was adequate for filing of the NDA and that information for this submission could, in part, be incorporated by cross-reference to the approved NDA 20-715. This application consists of 60 volumes and contains the required information as per 21 CFR 314.50. We have provided both a complete archival copy and a review copy of

the volumes. We have also included 6 desk copies of volume 1.1 (Application Summary) so that it can be supplied to each reviewer and supervisory personnel as appropriate. All CRFs and case report form tabulations have been supplied on CD-ROM in accordance with FDA guidelines and are located in volumes 1.58 to 1.60 of the archival copy.

- We trust that the information submitted in this NDA is complete for review.

Please let me know if you have any questions regarding this application or need additional information.

Sincerely,

Robert J. McCormack, Ph.D.
Vice President, Regulatory Affairs

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-288

DISCIPLINE REVIEW LETTER

Debio Recherche Pharmaceutique S.A.
c/o Target Research Associates
Attention: Robert J. McCormack, Ph.D.
Vice President, Regulatory Affairs
554 Central Avenue
New Providence, NJ 07974

Dear Dr. McCormack

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Trelstar™ LA 11.25 mg (triptorelin pamoate for injectable suspension).

Our review of the microbiology section of your submission is complete, and we have identified the following deficiencies:

1. The integrity test of the Debioclip™ and its blister package with cover has not been documented in the NDA.

    a. Please provide a summary for the methods, acceptance criteria and results that demonstrate the integrity of the blister package and its cover.

    b. Please discuss any exposed critical parts of the Debioclip™ (for example, the needle), and those barriers to prevent product contamination during use in the clinical setting after the cover has been removed.

2. Please provide the bacteriostasis and fungistasis test methods and results for the sterility test for the new formulation.

3. Please describe the method of selecting samples for sterility and pyrogens testing.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Jeanine Best, M.S.N., R.N., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

1/11/01

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

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-288

JUN 30 2000

Debio Recherche Pharmaceutique S.A.
c/o Target Research Associates
Attention: Robert J. McCormack, Ph.D.
Vice President, Regulatory Affairs
554 Central Avenue
New Providence, NJ 07974

Dear Dr. McCormack:

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

Name of Drug Product: Trelstar™ LA (triptorelin pamoate for injectable suspension) 11.25 mg

Therapeutic Classification: Standard (S)

Date of Application: June 29, 2000

Date of Receipt: June 30, 2000

Our Reference Number: NDA 21-288

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on August 29, 2000 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be April 30, 2000 and the secondary user fee goal date will be June 30, 2000.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will make a determination whether to grant or deny a request for a waiver of pediatric studies during the review of the application. In no case,

however, will the determination be made later than the date action is taken on the application. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA should be addressed as follows:

U.S. Postal/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, call Jeanine Best, M.S.N., R.N., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

/S/

Terri Rumble
Chief, Project Management Staff
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research