Clinical

1. Based on the preliminary results provided, does the Division agree that the results from studies DEB-96-TRI-01, DEB-96-TRI-02, and DEB-98-TRI-01 are sufficient to satisfy the clinical deficiencies in the non-approvable letter?
2. Will the Division please clarify the format and content of the ISE?
3. Will the Division please clarify the format and content of the ISS?
4. Will the Division please clarify electronic submission requirements, if any?

APPEARS THIS WAY
ON ORIGINAL

Biopharmaceutics

1. Does the Division agree that the information provided in the February 19, 1999 submission are sufficient to satisfy the Biopharmaceutics requirements for NDA approval?

2. Since the same Biopharmaceutics information applies to the triptorelin NDAs for both prostate cancer (NDA 20-715) and [redacted] (NDA [redacted]), will the Division agree to harmonize the review of Biopharmaceutics information for the two NDAs?

APPEARS THIS WAY
ON ORIGINAL

Manufacturing/Quality Control

1. Debio would like to have the option of marketing three different packaging configurations:
   (i) Decapeptyl® vial alone
   (ii) Decapeptyl® vial plus Debioclip®
   (iii) Decapeptyl® Debioject® single dose delivery system

   Does the Division agree that Debio may add the two additional packaging configurations as part of the current review process for NDA 20-715?

2. Does the Division agree that the information provided in the February 19, 1999 submission are sufficient to satisfy the Manufacturing/Quality Control requirements for NDA approval?

3. Does the Division agree that either the [redacted] may be used for manufacturing of triptorelin pamoate microgranules?

4. On April 12, 1999, Debio notified the Division in writing of its intent to add a second manufacturer for the pre-filled syringe containing 2 mL Sterile Water for Injection and the Debioclip/Debioject. Does the Division agree that Debio may switch to Debioclip/Debioject units manufactured at the new site after submitting three months comparative accelerated and available long-term stability data on one to three batches of pre-filled syringes and Debioclip/Debiojects manufactured at the new site, along with a commitment to conduct [redacted] stability studies on the first three production batches of pre-filled syringes and Debioclip/Debiojects manufactured at the new site and annual batches thereafter, performed in accordance with the submitted protocol?

5. In order to meet projected volumes for its marketing partner, Debio is establishing a new drug product manufacturing facility on the same campus as the current manufacturing facility it Martigny, Switzerland. In the new facility, Debio will use the process, same components, same equipment [redacted] and the same SOPs, environmental conditions, and controls as used in the current facility. Does the Division agree that following satisfactory completion of [redacted] Debio may start using the new manufacturing facility after submitting three months comparative accelerated and available long-term stability data on one to three batches of drug product manufactured at the new facility, along with a commitment to conduct three-year room temperature stability studies on the first three production batches manufactured in the new facility and annual batches thereafter?

6. Since the same Manufacturing/Quality Control information applies to the triptorelin NDAs for both prostate cancer (NDA 20-715) and [redacted] (NDA [redacted]) will the Division agree to harmonize the review of Manufacturing/Quality Control information for the two NDAs?

Microbiology

1. Does the Division agree that the information provided in the February 19, 1999 submission and the additional information provided in the pre-meeting information package submitted on May 10, 1999 are sufficient to satisfy the Microbiology requirements for NDA approval of the packaging configurations consisting of the Decapeptyl vial alone and the Decapeptyl vial plus Debioclip?

2. Since the same Microbiology information applies to the triptorelin NDAs for both prostate cancer (NDA 20-715) and [redacted] (NDA [redacted]), will the Division agree to harmonize the review of Microbiology information for the two NDAs?

APPEARS THIS WAY
ON ORIGINAL

Decapeptyl 3-Month Formulation

1. Although Debio originally had intended to file the 3-month formulation as a supplement to the approved 1-month formulation, will the Division accept for review a separate NDA for the 3-month formulation which is filed within a few months after submitting information to resolve the deficiencies in the NDA for the 1-month formulation?

APPEARS THIS WAY
ON ORIGINAL

Teleconference Minutes

Date: April 1, 1999 **Location:** Parklawn, 17B-45 (my office)

NDA 20-715 **Drug:** Decapeptyl Depot, 2.75 mg **Indication:** prostate cancer

Sponsor: Debio Recherche Pharmaceutique SA

Type of Meeting: Information Request

FDA Attendee:
Kim Colangelo, BS, Regulatory Project Manager, Division of Reproductive and Urologic Drug Products (DRUDP ;HFD-580)

/S/

External Attendee:
Robert J. McCormack, Vice President, Regulatory Affairs, Target Research Associates

Meeting Objective: To request information pertaining to — sterilization of the Debiojects at the request of the Review Microbiologist, Dr. Brenda Uratani.

Discussion:
The following information was requested:

- whether the residual — data in Appendix K are derived from the WFI or from WFI plus the Debioject device
- an outline of the procedures of how samples from the Debioject Delivery System are prepared for — determination
- the calculation to convert the — levels from mg/device (as shown in the Griffith report on page 240) to ppm

Decisions made:
None
Unresolved decisions:
None
Action Items:

- Mr. McCormack will request the information from the sponsor and submit it to the application for review

cc:
Original NDA 20-715
HFD-580/DivFile
HFD-580/Colangelo/Rumble/Rarick/Mann/Shames/Marks/Lin/Rhee/Madani/Parekh
HFD-805/Uratani

drafted: Colangelo, 04.08.99
concurrence: Rumble, 04.09.99
final: Colangelo, 04.09.99
TELECONFERENCE MINUTES

MEETING MINUTES

Date: February 4, 1997 **Time:** 2:00 - 3:00 P.M. **Location:** Parklawn; Room 17B-43

NDA: 20-715 **Drug Name:** Decapeptyl (triptorelin pamoate)

External Participant: Debio Recherche Pharmaceutique, S.A.

Type of Meeting: Industry (Face-to-Face)

Meeting Chair: Lisa Rarick, M.D. **External Participant Lead:** Neil L. Brown, Msc, Ph.D.

Meeting Recorder: Alvis Dunson, B.S.

FDA Attendees:

Lisa Rarick, M.D., Director, Division of Reproductive and Urologic Drug Products (DRUDP; HFD-580)
Heidi Jolson, M.D., M.P.H. - Deputy Director, (DRUDP; HFD-580)
Theresa van der Vlugt, M.D., M.P.H. - Medical Officer, DRUDP (HFD-580)
Daniel Shames, M.D. - Medical Officer, DRUDP (HFD-580)
Moo-Jhong Rhee, Ph.D. - Chemistry Team Leader, Division of New Drug Chemistry II (DNDC) at Division of Reproductive and Urologic Drug Products (DRUDP; HFD-580)
Baldeo Taneja, Ph.D. - Statistician, Division of Biometrics II (DBII) @ DRUDP (HFD-580)
Mark Askine, R.Ph - Regulatory Review Officer, Division of Drug Marketing, Advertising and Communications (DDMAC; HFD-40)
Lana L. Pauls, M.P.H. - Chief, Project Management Staff, DRUDP (HFD-580)
Alvis Dunson, B.S. - Consumer Safety Officer, DRUDP (HFD-580)

External Constituents:

Neil L. Brown, M.Sc., Ph.D. - Executive Director
Pierre Grosgurin, M.Sc. - Manager, Clinical Research, Biostatistics & Clinical Data
Dan Mannix - Regulatory Affairs
Herve'C. Porchet, M.D. - Director, Clinical Pharmacology
Robert McCormack, Ph.D. (Oxford Research)

Meeting Objectives:

To discuss questions concerning the NDA for Decapeptyl in the treatment of prostate cancer.

Discussion Points:

- the Division letter dated January 29, 1997, outlining deficiencies in application was discussed (see Attachment)
- data from the three European studies and study problems such as lack of randomization
- loss-to-follow-up data (for reasons other than death) is extensive
- use of drug vials labeled 4.2 mg in UK study and its equivalence to vials labeled 3.75 mg for US commercial use needs to be evaluated
- [redacted]
- lack of adequate documentation for electronic data files is of concern

Decisions reached:

- sponsor will submit a written response to January 29, 1997 letter including laboratory data for testosterone levels in the three clinical trials
- sponsor must submit information clarifying ranges and the randomization procedures used in each study; the palmar study should be considered non-randomized
- sponsor must submit information on how Decapeptyl was administered according to different schedules during the first study month to some or to all patients and why they don't believe it affects the efficacy results
- sponsor must submit letter clarifying how patients randomized to the orchiectomy group were not informed that they were participating in a clinical trial, nor about the existence of an investigative treatment and that this was common practice at that time in Belgium
- sponsor must provide complete documentation (i.e., a code) for the SAS datasets previously submitted, that explains the variables (demographic, efficacy and safety) for the three individual studies; data on each study should be submitted separately

Unresolved Issues: None

Action Items:

Item:	Responsible Person:	Due Date:
◆ submission of complete written response to Jan 29, 1997 letter	Debio RP	?

- Submission of SAS datasets and complete documentation — Debio RP — ?

/S/ 4/24/97
Signature, minutes preparer

/S/ 4-25-97
Concurrence, Chair

drafted: ADunson/2.7.97/n20715im2

cc:
NDA Arch:
HFD-580
HFD-580/JMercier/Attendees
HFD-580/ADunson/2.7.97

Concurrences:
DShames2.7.97/MAskine, van der Vlugt, HJolson2.10.97/LRarick2.11.97/LPauls2.18.97

Concurrences not recieved:
BTaneja, MRhee

MEETING MINUTES

Date: September 9, 1997 **Time:** 9:00 AM - 10:30 AM **Location:** Parklawn; C/R "L"

NDA: 20-715 **Drug Name:** Decapeptyl (triptorelin pamoate)

External Participant: Debio Recherche Pharmaceutique, S.A.

Type of Meeting: Industry meeting

Meeting Chair: Lisa Rarick, M.D. **External Participant Lead:** J. Kay Noel, Ph.D.

Meeting Recorder: Alvis Dunson

FDA Attendees:

Lisa Rarick, M.D., Director, Division of Reproductive and Urologic Drug Products (DRUDP; HFD-580)
Heidi Jolson, M.D., M.P.H. - Deputy Director, DRUDP (HFD-580)
Daniel Shames, M.D. - Medical Officer, DRUDP (HFD-580)
Moo-Jhong Rhee, Ph.D. - Chemistry Team Leader, Division of New Drug Chemistry II (DNDC) @ DRUDP(HFD-580)
Gary Barnette, Ph.D. - Pharmacokineticist, Division of Pharmaceutical Evaluation II (DPEII; HFD-870) @ DRUDP(HFD-580)
Lisa Kammerman, Ph.D. - Statistical Team Leader, Division of Biometrics II (DBII) @ DRUDP (HFD-580)
Baldeo Taneja, Ph.D. - Statistician, Division of Biometrics II (DBII) @ DRUDP (HFD-580)
Lana L. Pauls, M.P.H. - Chief, Project Management Staff, DRUDP (HFD-580)
Alvis Dunson, B.S. - Consumer Safety Officer, DRUDP (HFD-580)

External Constituents:

Piero Orsolini, Ph.D. - President & CEO, Debio R.P.
Herve` C. Porchet, M.D. - Director, Clinical Pharmacology
Pierre Grosgurin, M.Sc. - Manager, Clinical Research, Biostatistics & Clinical Data
[ ]
Daniel G. Mannix, Ph.D. - Director, Regulatory Affairs, (Pharmacia & Upjohn)
[Robert McCormack, Ph.D. (Oxford Research)]

Meeting Objectives:

To discuss sponsor proposals relevant to the resolution of deficiencies listed in the Not Approval letter issued on June 26, 1997.

Discussion Points:

Q1. Will the data from studies DEB-96-TRI-01 and DEB-96-TRI-02 be sufficient to resolve the clinical deficiencies in the NDA file?

A1. No, in the absence of an active control, it will not be possible to determine whether this drug works as well as currently available drugs for this indication or how its safety compares. A third control arm could be added to study DEB-96-TRI-01 or a new study could be initiated to compare Decapeptyl 1-month depot with an approved control (or surgical castration).

The sponsor was informed that a control was required in order to ensure that the clinical endpoint data could be interpreted. Only one adequate and well-controlled study will be required. The sponsor was also reminded that the 1-month depot would have to be approved prior to approving the 3-month depot on the basis of its comparability to the 1-month depot on the pharmacodynamic endpoint.

Q2. Will the data from these two studies be sufficient to resolve the deficiency in the bioequivalence study in the NDA file?

A2. Yes, if the to-be-marketed formulation is used. Sponsor should submit the study report for review.

Q3. Will the Division agree to accept the *in vitro* dissolution test method originally proposed by Debio?

A3. The sponsor has attempted to reduce the dissolution method paddle speed from 200 rpm. However, the sponsor believes their method is acceptable. Further review of the *in vitro* and IVIVC data is needed to determine the adequacy of the proposed method.

Q4. Will the Division accept dissolution specification ranges based on the ranges demonstrated by the bio/clinical lots?

A4. Yes, sponsor should submit specification ranges on clinically-tested products.

Q5. Does the Division agree that the release specification for the major degradation product may be changed to [redacted]%?

A5. No, the high rate of deamidation reaction has not been seen with other peptides. The sponsor needs to explain and support their proposal that the [redacted] process causes the deamidation product.

Unresolved Issues: None

Action Items:

	Item:	Responsible Person:	Due Date:
♦	submission of amended protocol or new protocol for review prior to initiation of study	Debio	?
♦	submission of data from the two studies that demonstrate the absence of stimulation of LH and FSH following the second, fourth, and seventh injections	Debio	?
♦	resubmission of *in vitro* and IVIVC data	Debio	?
♦	submission of specification ranges for the clinically tested products	Debio	?
♦	submission of data to resolve the degradation product issue	Debio	?

/S/ 9/26/97
Signature, minutes preparer

/S/ 9/26/97
Concurrence, Chair

drafted: ADunson/9.15.97/n20715im3

cc:
NDA Arch:
HFD-580
HFD-580/JMercier/Attendees
HFD-580/ADunson/9.15.97

Concurrences:
LPauls, DShames,GBarnette, BTaneja, HJolson9.16.97/LRarick9.17.97
LKammerman9.18.97/MRhee9.22.97

TELECONFERENCE MINUTES

Date: January 17, 1997 **Time:** 11:00 - 11:30 a.m. **Location:** Parklawn; Room 17B-43

NDA: 20-715 **Drug Name:** Decapeptyl (triptorelin pamoate)

External Participant: Robert J. McCormick, Ph.D., Vice President, Regulatory Affairs, Oxford Research International Corporation

Type of Meeting: Internal Medical Officer/Statistician meeting to discuss clinical trial issues of NDA

Meeting Chair: Heidi Jolson, M.D., M.P.H.

Meeting Recorder: Alvis Dunson, B.S.

FDA Attendees:

Heidi Jolson, M.D., M.P.H. - Deputy Director, Division of Reproductive and Urologic Drug Products (DRUDP; HFD-580)
Daniel Shames, M.D. - Medical Officer, DRUDP (HFD-580)
Lisa Kammerman, Ph.D. - Statistical Team Leader, Division of Biometrics II (DBII) @ DRUDP (HFD-580)
Baldeo Taneja, Ph.D. - Statistician, DBII @ DRUDP (HFD-580)
Alvis Dunson, B.S. - Consumer Safety Officer, DRUDP (HFD-580)

Meeting Objectives:

To discuss questions concerning the three clinical trials submitted in the NDA.

Discussion Points:

- relationship between Bob McCormack and Debio RP should be clarified
- [redacted]
- failure rate of decapeptyl versus orchiectomy should be clarified and on what value is this rate determined
- adequate documentation for clinical trial datasets has not been provided

Decisions reached:

- sponsor must submit documentation explaining SAS data sets and include a code book for variables

♦ Modify meeting agenda to reflect change in length of time	Alvis Dunson	January 17, 1997

/S/

Signature, minutes preparer

/S/

Concurrence, Chair

Post Meeting Note:

- ♦ sponsor submitted letter outlining responsibilities of the companies involved in the submission of this application on 1/24/97
- ♦ a list of deficiencies was communicated to Oxford Research via teleconference on 1/24/97 and fax on 1/29/97
- ♦ Baldeo Taneja and Mark Askine have been invited to the 2:00 P.M., 2/5/97 meeting
- ♦ agenda has been modified to reflect change in length of each meetings

drafted: ADunson/1.17.97/n20715tcon

cc:
NDA Arch:
HFD-580
HFD-580/JProchnow/Attendees
HFD-580/ADunson/1.17.97

Concurrences:
HJolson1.21.97/DShames, LPauls1.22.97/LKammerman1.23.97

Concurrence not recieved:
BTaneja

MEETING MINUTES

Date: December 20, 1996 **Time:** 10:30 - 11:30 a.m. **Location:** Parklawn; Room 17B-43

NDA: 20-715 **Drug Name:** Decapeptyl (triptorelin pamoate)

External Participant: none

Type of Meeting: Internal Medical Officer/Statistician meeting to discuss clinical trial issues of NDA

Meeting Chair: Heidi Jolson, M.D., M.P.H.

Meeting Recorder: Alvis Dunson, B.S.

FDA Attendees:

Heidi Jolson, M.D., M.P.H. - Acting Deputy Director, Division of Reproductive and Urologic Drug Products (DRUDP; HFD-580)
Daniel Shames, M.D. - Medical Officer, DRUDP (HFD-580)
Baldeo Taneja, Ph.D. - Statistician, Division of Biometrics II (DBII) @ DRUDP (HFD-580)
Lisa Kammerman, Ph.D. - Statistician, DBII @ DRUDP (HFD-580)
Alvis Dunson, B.S. - Consumer Safety Officer, DRUDP (HFD-580)

Meeting Objectives:

To discuss questions concerning the three clinical trials submitted in the NDA.

Discussion Points:

- how should data analysis be approached
- can meta-analysis be used as an option to demonstrate efficacy
- are the studies well-randomized
- what is the failure rate of decapeptyl versus orchiectomy and on what value is this determined

Decisions reached:

- sponsor needs to submit a diskette version of demographic and efficacy data for the three pivotal studies; diskette should be in ASCII or SAS data format
- graphical displays of failure rates would be helpful

- sponsor needs to submit a copy of the protocol appendix (Appendix H) for their "pivotal" bioequivolence study comparing the 1- month to 3- month depots
- data should be sent by COB December 23, 1996
- schedule another MED/STAT meeting for mid-January, 1997

Unresolved Issues: None

Action Items:

Item:	Responsible Person:	Due Date:
♦ Submission of efficacy data	Debio	December 23, 1996
♦ Submission of protocol appendix	Debio	December 23, 1996
♦ Schedule MED/STAT meeting	Alvis Dunson	mid-January, 1997

/S/
Signature, minutes preparer

/S/ w.d.
Concurrence, Chair

drafted: ADunson/1.6.97/medstat1

cc:
NDA Arch:
HFD-580
HFD-580/JProchnow/Attendees
HFD-580/ADunson/1.6.97

Concurrences:
LPauls12.24.96/DShames12.26.96/LKammerman12.31.96/BTaneja1.2.97/HJolson1.3.97

MEETING MINUTES

Date: November 5, 1996 **Time:** 9:00 - 9:30 AM **Location:** Parklawn; Room 17B-43

NDA: 20-715 **Drug Name:** Decapeptyl (triptorelin pamoate for injection)

Type of Meeting: Internal Status Meeting

Meeting Chair: Lana L. Pauls, M.P.H.

Meeting Recorder: Lana L. Pauls, M.P.H.

FDA Attendees:

Heidi Jolson, M.D., M.P.H. - Acting Deputy Director, Division of Reproductive and Urologic Drug Products (DRUDP; HFD-580)
Lana L. Pauls, M.P.H. - Chief, Project Management Staff, DRUDP (HFD-580)
Daniel Shames, M.D. - Medical Officer, DRUDP (HFD-580)
Jean Fourcroy, M.D., Ph.D. - Medical Officer, DRUDP (HFD-580)
Moo-Jhong Rhee, Ph.D. - Acting Chemistry Team Leader, Division of New Drug Chemistry II (DNDC II) @ DRUDP (HFD-580)
Krishan Raheja, Ph.D., D.V.M. - Pharmacologist, DRUDP (HFD-580)
Lisa Kammerman, Ph.D. - Team Leader, Division of Biometrics II (DBII) @ DRUDP (HFD-580)
Baldeo Taneja, Ph.D. - Mathematical Statistician, DBII @ DRUDP (HFD-580)

Meeting Objectives:

To obtain the review status of this application from each reviewer.

Discussion Points:

- Clinical - although studies are poor, the application will most likely be approvable; no estimated completion date was provided
- Chemistry - review will be started week of November 10, 1996; expected completion date (ECD) 12/15/96
- Pharmacology - review completed
- Biopharmaceutics - ECD 01/30/97
- Statistics - review will be started week of November 10, 1996; expected completion date (ECD) 01/15/97
- all reviewers would like scientific rounds (currently scheduled for December 18, 1996), to be rescheduled for sometime in January '97

Action Items:

	Item:	Responsible Person:	Due Date:
♦	reschedule scientific rounds?	Heidi Jolson	next week

/S/

Signature, minutes preparer

/S/ 12/19/96

Concurrence, Chair

cc:
NDA Arch:
HFD-580
HFD-580/JProchnow/Attendees/ADunson
HFD-580/LPauls/11.12.96

Concurrences:

KRaheja 11.14.96/HJolson 11.15.96/LKammerman 11.18.96/MRhee 11.19.96

Response not Received from:

DShames, JFourcroy, BTaneja

MEETING MINUTES

Date: September 3, 1996 **Time:** 9:00 - 9:40 AM **Location:** Parklawn; Room 14-56

NDA: 20-715 **Drug Name:** Decapeptyl (triptorelin pamoate)

External Participant: none

Type of Meeting: Internal Status Meeting

Meeting Chair: Lana L. Pauls, M.P.H. **External Participant Lead:** none

Meeting Recorder: Lana L. Pauls, M.P.H.

FDA Attendees:

Heidi Jolson, M.D., M.P.H. - Acting Deputy Director, Division of Reproductive and Urologic Drug Products (DRUDP;HFD-580)
Daniel Shames, M.D. - Medical Officer, DRUDP (HFD-580)
Lana L. Pauls, M.P.H. - Chief, Project Management Staff, DRUDP (HFD-580)
Moo-Jhong Rhee, Ph.D. - Chemist, DRUDP (HFD-580)
Krishan Raheja, Ph.D., D.V.M. - Pharmacologist, DRUDP (HFD-580)
Tien-Mien Chen, Ph.D. - Pharmacokinetic Reviewer, Division of Pharmaceutical Evaluation II (DPE II; HFD-870)
Baldeo Taneja, Ph.D. - Mathematical Statistician, Division of Biometrics II (HFD-715)

Not in Attendance:

Peter Cooney, Ph.D. - Director, Division of Microbiology, Office of New Drug Chemistry II (ONDC; HFD-805)
Brenda Uratani, Ph.D. - Microbiologist, ONDC (HFD-805)

External Constituents: none

Meeting Objectives:

To determine the status of the review process for the application. Decapeptyl is proposed for use as a palliative treatment for prostate cancer.

Discussion Points:

- Clinical (Dr. Shames)
  - product is similar to others approved for this indication
  - the adverse events seen are expected with this class of drug
  - review will be completed by the end of March 1997
- Chemistry (Dr. Rhee)
  - review not started; estimated completion November 1996

- two sites to be inspected on EER (both Swiss); requested response from Compliance by December 1996

♦ Biopharmaceutics
- review not started; estimated completion March 1997

♦ Statistics
- review not started; estimated completion March 1997

♦ Pharmacology
- review not started; estimated completion November 1996

♦
-
-

Decisions reached:

♦ all reviews should be completed by the end of March 1997

Unresolved Issues: none

Action Items:

	Item:	Responsible Person:	Due Date:
♦	Status of microbiology review	Lana Pauls	1 week (09/10/96)

/S/
Signature, minutes preparer

/S/ MD
Concurrence, Chair

Post-meeting Note:

cc:

NDA Arch:
HFD-580
HFD-580/JProchnow/Attendees (incl stat)
HFD-510/DMarticello
HFD-805/BUratani/PCooney
HFD-870/AChen/ADorantes
HFD-580/LPauls/09.04.96

Concurrences:
KRaheja, MRhee, TChen 09.04.96/BTaneja 09.05.96/DShames, HJolson 09.08.96

MEETING MINUTES

JUL 3 1 1996

Date: July 25, 1996 **Time:** 8:30 - 8:50 AM **Location:** Parklawn; Room 14-56

NDA: 20-715 **Drug Name:** Decapeptyl (triptorelin pamoate)

External Participant: none

Type of Meeting: Internal Filing Meeting

Meeting Chair: Lana L. Pauls, M.P.H. **External Participant Lead:** none

Meeting Recorder: Lana L. Pauls, M.P.H.

FDA Attendees:

Lisa Rarick, M.D. - Acting Director, Division of Reproductive and Urologic Drug Products (DRUDP;HFD-580)
Heidi Jolson, M.D., M.P.H. - Acting Deputy Director, DRUDP (HFD-580)
Jean Fourcroy, M.D., Ph.D. - Medical Officer, DRUDP (HFD-580)
Lana L. Pauls, M.P.H. - Project Manager, DRUDP (HFD-580)
Helen Davies, Ph.D. - Chemistry Team Leader, Division of New Drug Chemistry II (DNDC II) @ DRUDP (HFD-580)
Moo-Jhong Rhee, Ph.D. - Chemist, DRUDP (HFD-580)
Krishan Raheja, Ph.D., D.V.M. - Pharmacologist, DRUDP (HFD-580)
Tien-mien Chen, Ph.D. - Pharmacokinetic Reviewer, Division of Pharmaceutical Evaluation II (DPE II; HFD-870)
Peter Cooney, Ph.D. - Director, Division of Microbiology, Office of New Drug Chemistry II (ONDC; HFD-805)
Brenda Uratani, Ph.D. - Microbiologist, ONDC (HFD-805)

Not in Attendance:

Baldeo Taneja, Ph.D. - Mathematical Statistician, Division of Biometrics II (HFD-715)

External Constituents: none

Meeting Objectives:

To determine whether the application is acceptable for filing. Decapeptyl is proposed for use as a palliative treatment for prostate cancer.

Discussion Points: see below

Decisions reached:

- Medical - Acceptable for filing (AF); three pivotal trials, primary endpoint = testosterone suppression. Data in Excel should be requested from the firm. The application will be co-reviewed by Drs. Fourcroy and Shames (expected mid-August).
- Chemistry - AF; Environmental Assessment (EA) sent to Nancy Sager for review.
- Pharmacology - AF
- Biopharmaceutics - AF
- Statistics - Not in attendance, see action items.
- Microbiology - AF; many deficiencies. A product sample of the container-closure system should be requested from the firm.
- DSI - Dr. Fourcroy will identify the sites (2) and will notify Ms. Pauls.
- Status meetings will be held on an every other month basis; team leaders should be notified, but their calendars need not be cleared.
-
- UF Goal Date = June 26, 1997; however given the above AC date, it was determined that all reviews would be completed by mid-February 1997 to allow ample time for preparation as well as sign-off at the Office level as this product is a new molecular entity (NME).

Unresolved Issues: none

Action Items:

Item:	Responsible Person:	Due Date:
The following will be requested from the sponsor: ♦ Product samples/container closure samples ♦ Data on excel ♦ The number of patients at each clinical trial site	Lana Pauls	July 25, 1996
Fileability decision from statistics	Baldeo Taneja	ASAP

Signature, minutes preparer

/S/
Concurrence, Chair

Post-meeting Note:

- Ms. Pauls requested the information indicated above in a telephone conversation to Kostopolus and Associates on July 25, 1996
- Dr. Taneja determined that the application was fileable from a statistical standpoint

cc:

NDA Arch:
HFD-580
HFD-580/JProchnow/Attendees (incl stat)/AJordan
HFD-510/DMarticello
HFD-870/AChen/ADorantes
HFD-580/LPauls/07.24.96

Concurrences:
JFourcroy, HDavies, MRhee, KRaheja, TChen, PCooney, BUratani 07.25.96/HJolson, LRarick 07.26.96

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

IND [redacted]
Decapeptyl® (triptorelin pamoate)
Debio, R.A.

January 18, 1995

MEMORANDUM OF PRE-NDA MEETING

Representatives from Debio, R.A.:

Jean F. Pyrus, M.D. - Exec. Vice President & Director, Regulatory Affairs, Debio R.A., Inc.
Peter Kostopolus - Regulatory Affairs Associate, Debio R.A., Inc.
R.-Y. Mauvernay, Ph.D. - C.E.O., Debio Group
Piero Orsolini, Ph.D. - President, Debio R.P. Switzerland
Myriam Weiner, Ph.D. - Project Coordinator, Debiopharm SA Switzerland
[redacted] - Consultant,
[redacted] Consultant,
[redacted] consultant
[redacted] consultant

FDA Staff:

Dr. Sobel	Dr. Niu	Dr. Fossler (HFD-426)
Dr. Fourcroy	Ms. Pauls	Mr. Marticello (HFD-713)
Dr. Chiu	Mr. Hunt (HFD-426)	

Purpose:

Debio requested the meeting to discuss the requirements for a new NDA for the use of triptorelin pamoate in the treatment of advanced prostatic carcinoma.

Discussion and Conclusions:

Dr. Pyrus began with a brief introduction of the participants, and then continued by presenting the two questions requiring input from the FDA. The first question was presented as follows (paraphrased from the pre-meeting package material dated December 23, 1994):

> **The safety and efficacy of triptorelin as an alternative to orchiectomy for the palliative treatment of advanced prostate cancer have been demonstrated in three European clinical trials. Additional supportive data has been demonstrated in the medical literature. Does the Division agree that these data are sufficient to support an NDA for triptorelin for the palliative treatment of advanced prostate cancer?**

Mr. Marticello responded by asking about the poolability of the data (Table 2). Debio indicated that the data was not ideal, but it was the only data available. Mr. Marticello then asked about the confidence intervals (CIs) to be used in the meta-analysis. Debio referred him to Table 3.

Dr. Fourcroy asked whether the data would be available for audit. Debio indicated that some, but not all would be available.

Dr. Sobel indicated that he could see no apparent problems with the acceptability of the data (as presented thus far) as long as the data could be validated (by the FDA Division of Scientific Investigations). Debio then indicated that all data would be provided. Dr. Fourcroy asked that it be submitted in an electronic format.

Dr. [redacted] then continued with the second question (paraphrased) as follows:

> The clinical studies were performed using a controlled release formulation of triptorelin acetate. However the lyophilized pamoate formulation has many advantages compared to the acetate formulation. A series of bioavailability and pharmacodynamic studies have shown the two formulations to be equivalent. Does the Division agree that the data on pharmacodynamics of serum testosterone are sufficient to support an NDA?

Mr. Hunt responded by asking whether the lyophilized product was used in any clinical studies. Debio answered negatively. Mr. Hunt indicated that the data comparison was similar to comparing product A to product B, and product B to product C, and asking the Division to make a decision by comparing A to C ("a leap of faith"). He then asked exactly what was being compared between the two forms. Debio indicated that it was the peptide moiety.

Mr. Hunt indicated that a head-to-head comparison between the acetate and pamoate should be performed. Debio agreed, however, asked for input regarding the study design. Dr. Fourcroy indicated that from an ethical standpoint, the use of normal volunteers for this type of study was very questionable. Debio indicated that normal volunteers were used in Europe (approved through an IRB). Debio asked for confirmation from the Division regarding the use of normal volunteers. Mr. Hunt deferred the answer to Dr. Fourcroy. Dr. Fourcroy went on the record by stating that she would prefer that normal volunteers not be used, however, she would accept the data generated from such a study. Dr. Fourcroy further indicated that such a study would necessarily be performed in Europe as it would not pass a U.S. IRB.

Dr. Chiu asked whether the dose was based on peptide or salt. Debio indicated that it was based on the peptide.

Dr. [redacted] summarized by indicating tht the existing clinical data is sufficient, however a head-to-head study must be performed. Ms. Pauls confirmed her concern regarding the preclinical data by indicating that it was sufficient for an NDA submission.

Ms. Pauls then indicated that the issues regarding the endometriosis indications would be discussed at a later time.

Dr. [redacted] indicated that the comparative trial would most likely be completed within four months, and therefore, the NDA submission would be forthcoming within approximately six months (June 1995).

The meeting concluded with the representative of Debio thanking the Division members for their time and input in regard to their drug development plans.

S

Lana L. Pauls, M.P.H.
Consumer Safety Officer

cc:
IND Arch.
HFD-510
HFD-426/JHunt/AChen
HFD-510/EGalliers/AFleming/Attendees
HFD-713/DMarticello/ENevius
HFD-511/LPauls/01.18.95/Debiomtg.002

IND ( )/Pre-NDA
Decapeptyl (triptorelin pamoate) Injection
Debio R.A.

June 16, 1994

Memorandum of Pre-NDA Meeting

DeBio Representatives:

Jean F. Pyrus, M.D. - Debio R.A., Vice President and Director, Regulatory Affairs
[Consultant]
Piero Orsolini, Ph.D. - Debio R.P., President
[ ]
Harry Dugger - Debio R.P., Consultant, CMC Section
[ ]
N. Peter Kostopolus - Debio R.A., Regulatory Affairs Associate

FDA Staff:

Dr. Sobel	Dr. Rarick	Dr. Bey
Dr. Corfman	Dr. Niu	Ms. Pauls
Dr. A. Chen (HFD-427)	Dr. Nevius (HFD-713)	

Purpose:

DeBio requested the meeting to discuss their proposed plans for an NDA submission.

Discussion and Conclusions:

Dr. Simon began the meeting with a brief description of the information to be discussed along with a brief history of the company structure and the IND correspondence to date. No formal introductory presentation was made by DeBio; the meeting continued with a "round table: discussion.

Dr. Rarick then indicated that the issue of structural similarity between the DeBio product and other similar products (approved GnRH agonists) would not be sufficient to support approval (as suggested in the pre-meeting package by Debio).

Dr. Nevius indicated that the data from the three foreign trials presented in the pre-meeting package should be updated to include both statistical tests, and confidence intervals (CIs) in comparison to the active controls. He also indicated that the CIs should be relatively narrow so that the active control studies could be used as supportive data. He stated that the meta-analysis could be used as supportive data as well.

Dr. Chen raised concern regarding the increasing plasma profile levels depicted over time with the microgranular formation. He stated that it was unclear from the data whether this increase may cause toxicity over time( ) [The firm has requested approval for a

Dr. Rarick indicated that a firm connection between the to-be-marketed formulation (lyophilized microgranular pamoate salt) and the foreign studies that were performed with the alternate product (microspherical acetate salt) would be needed to be established . In addition, data on blood levels, etc. would be required. Dr. Chen concurred. Dr [redacted] asked if a bioequivalence study could be performed in men [redacted]. Dr. Corfman indicated that an internal meeting would be held to discuss this issue.

Dr. Sobel then confirmed the previous discussion regarding the lack of significance regarding the structural similarity between the DeBio's product and other GnRH agonists, and addressed the issue of bioequivalence.

Dr. Corfman asked why DeBio was switching formulations. The firm indicated that it was primarily to reduce the use of solvents in the manufacturing process. (Europe has banned the use of freon).

Dr. Bey asked how DeBio arrived at the dose that was administered in the clinical trials. DeBio stated that it was based on in vitro data along with data from the literature on other LHRH agonists. Dr. Bey also asked if the methodology to measure bone density had been standardized between all centers.

Dr. [redacted] asked for clarification regarding the issue of bone mineral density. Dr. Rarick indicated that the degree of bone loss has been examined as a primary safety issue in the approval of all LHRH agonists to date. Dr. Rarick asked Dr. Sobel his opinion regarding the firms lack of bone loss data. Dr. Sobel responded by stating that, in his opinion, it was important to maintain consistency regarding approval of all similar products, and therefore, at a minimum, some supportive literature would be required.

Dr. Orsolini then discussed the difference between the pamoate and the acetate. He reiterated that freon had been banned in Europe, and indicated that in addition, DeBio wished to develop a product that could be stored at room temperature.

Dr. Niu raised questions of whether any adduct [redacted] could be formed during the process of [redacted] Dr. Orsolini responded by stating that during the [redacted] process, the mixture containing the peptide and co-polymer is [redacted] However, he did not know whether any adduct was formed, and indicated that they would investigate the matter.

Dr. [redacted] asked again about the bone mineral density data required fr the application. Dr. Rarick indicated that long term data (if available) regarding bone mineral density should be included in the application.

The meeting then turned back to CMC issues. Dr. Niu asked about the purity before and after the [redacted] radiation. Dr. Orsolini stated that the purity profile is checked before and

after [redacted] radiation and there is a slight increase in impurities. Dr. Niu asked the firm to identify the impurities in thei submission.
Ms. Pauls then indicated that an internal meeting would be held to address the following issues:

1. bioequivalence between the pamoate and acetate products;
2. bone mineral density information required;
3. the number of patients studied in clinical trials, and the confidence intervals required to demonstrate comparability to currently marketed products; and
4. the answers to the six questions posed by DeBio (attached).

She stated that the Division would respond within two weeks (week of July 3).

DeBio then thanked the Division for their time and input in regard to their drug development plans.

Lana L. Pauls, M.P.H.
Consumer Safety Officer

cc:
IND Arch
HFD-510
HFD-510/gonadotropins
HFD-510/EGalliers/Attendees
HFD-427/AChen/JHunt
HFD-713/ENevius
HFD-510/LPauls/06.21.94/DEBIO.MTG

Concurrences:
LRarick, ABey, PCorfman 06.21.94/CNiu, ENevius (per e-mail) 06.22.94/AChen 06.27.94/SSobel 06.28.94

NDA 20-715
Trelstar® Depot (triptorelin pamoate for injectable suspension)
Debio Recherche Pharmaceutique S.A.

This Application was not the subject of an Advisory Committee Meeting.

APPEARS THIS WAY
ON ORIGINAL

NDA 20715
Decapeptyl™ (triptorelin pamoate)

Advisory Committee Meeting Minutes

This application was not the subject of an Advisory Committee Meeting.

APPEARS THIS WAY
ON ORIGINAL

NDA 20-715
Trelstar® Depot (triptorelin pamoate for injectable suspension)
Debio Recherche Pharmaceutique S.A.

Financial Disclosure Information

APPEARS THIS WAY
ON ORIGINAL

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: March 9, 2000 LLP 3/9/00

From: Lana L. Pauls, M.P.H.
Associate Director, Division of Reproductive and Urologic Drug Products (HFD-580)

Subject: Review of Financial Disclosure documents

To: The file (NDA 20-715)

I have reviewed the financial disclosure information submitted by Target Research Associates on behalf of Debio Recherche Pharmaceutique SA in support of their NDA, NDA 20-715.

This NDA was issued a non-approval letter on June 26, 1997. The applicant was required to perform an additional clinical trial in order to respond to the deficiencies cited in the letter. The study outlined below was conducted to support the safety and efficacy for Trelstar (triptorlin acetate) for injection for use in the treatment of advanced prostate cancer.

Study No.	Study Status	Financial Disclosure Documentation
DEB-96-TRI-01	Ongoing as of February 2, 1999 (completed February 11, 1999)	Appropriate documentation; no financial arrangements or proprietary interest

Conclusion:

Adequate documentation has been provided to ensure that the sponsor is in compliance with 21 CFR 54.

APPEARS THIS WAY
ON ORIGINAL

Food and Drug Administration

Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

(1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	list attached	

(2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

(3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Orsolini Piero	CEO
FIRM/ORGANIZATION	
Debio Recherche Pharmaceutique S.A.	
SIGNATURE	**DATE**
	11-2-99

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

Created by Electronic Document

Redacted 1

pages of trade

secret and/or

confidential

commercial

information

MAY 17 2000

CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED: 2/4/00	DUE DATE: 4/10/00	OPDRA CONSULT #: 00-0041

TO: **Susan Allen, M.D.**
Acting Director, Division of Reproductive and Urologic Drug Products
HFD-580

THROUGH: **Jeanine Best, Project Manager, DRUDP**
HFD-580

PRODUCT NAME: Trelstar® Depot 3.75 mg (triptorelin pamoate for injectable suspension) NDA #: 20-715	**MANUFACTURER:** Debio Recherche Pharmaceutique (Target Research Associates)
Safety Evaluator: Peter Tam, RPh.	

OPDRA RECOMMENDATION:
OPDRA has no objections to the use of the proprietary name Trelstar®. See the checked box below.

For NDA/ANDA WITH ACTION DATE BEYOND 90 DAYS OF THIS REVIEW
This name must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary names/NDA's from the signature date of this document. A re-review request of the name should be submitted via e-mail to "OPDRA-REQUST" with the NDA number, the proprietary name, and the goal date. OPDRA will respond back via e-mail with the final recommendation.

✓ FOR NDA/ANDA WITH ACTION DATE WITHIN 90 DAYS OF THIS REVIEW
OPDRA considers this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary names/NDA's from this date forward.

FOR PRIORITY 6 MONTH REVIEWS
OPDRA will monitor this name until approximately 30 days before the approval of the NDA. The reviewing division need not submit a second consult for name review. OPDRA will notify the reviewing division of any changes in our recommendation of the name based upon the approvals of other proprietary names/NDA's from this date forward.

S 5/18/2000

Jerry Phillips, RPh.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment
Phone: (301) 827-3242
Fax: (301) 480-8173

S 5/18/00

Peter Honig, MD
Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm 15B03
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

Date of Review: 4/3/00

NDA#: 20-715

Name of Drug: **Trelstar®** Depot 3.75 mg
(triptorelin pamoate for injectable suspension)

NDA Holder: Debio Recherche Pharmaceutique
(Target Research Associates)

I. INTRODUCTION

This consult was written in response to a request from the Division of Reproductive and Urologic Drug Products (HFD-580) on February 4th, 2000, to review the proposed proprietary drug name, Trelstar® in regard to potential name confusion with existing proprietary/generic drug names.

The Labeling and Nomenclature Committee (LNC) had reviewed the first submitted proprietary name, [redacted] on 1/19/99. LNC found the name was acceptable but the NDA not approved. A second proposed name, Trelstar was subsequently submitted to LNC for review. LNC found the proposed name, Trelstar, is acceptable on 6/7/99. Since this NDA is a resubmission, there is a 6 month timeline for action.

PRODUCT FORMATION

Trelstar® Depot 3.75 mg is a synthetic decapeptide agonist analog of luteinizing Harmone-releasing hormone (LHRH or GnRH) with greater potency than naturally occurring LHRH. It is a sterile, lyophilized biodegradable microgranule formulation supplied as a single-dose containing triptorelin pamoate (3.75 mg as the peptide base). Triptorelin is a potent inhibitor of gonadotropin secretion when given continuously and in therapeutic doses.

The metabolism of Trelstar® in humans is unknown, but is unlikely to involve hepatic microsomal enzymes (cytochrome P-450). It is mainly eliminated by both the liver and the kidneys.

Trelstar® Depot 3.75 mg is indicated in the palliative treatment of advanced prostate cancer. It offers an alternative treatment for prostate cancer when orchiectomy or estrogen administration are either not indicted or unacceptable to the patient. The recommended dose of Trelstar® Depot is 3.75 mg and the lyophilized microgranules are to be reconstituted and administered monthly as single intramuscular injection under the supervision of a physician.

Trelstar® Depot 3.75 mg will be supplied in a single-dose vial with a flip-off seal.

II. RISK ASSESSMENT

In order to determine the potential for medication errors and to find out the degree of confusion of the proposed proprietary name, Trelstar® with other drug names, the medication error staff of OPDRA searched Micromedex online, PDR (1999 Edition), American Drug Index (43rd Edition), Drug Facts and Comparisons (update monthly), the Electronic Orange Book, and US Patent and Trademark Office online database. In addition, OPDRA also searched several FDA databases for potential sound-alike and look-alike names to approved/unapproved drug products through DPR, Medline, Decision Support System (DSS), Establishment Evaluation System, and LNC database. An expert panel discussion was conducted to review all the findings from the searches. OPDRA also conducted studies of written and verbal analysis of the proposed proprietary name employing healthcare practitioners within FDA to evaluate potential errors in handwriting and verbal communication of the name. This exercise was conducted to simulate the prescription order process.

A. EXPERT PANEL DISCUSSION:

The expert panel consists of members of OPDRA medication error safety evaluator staff and a representative from the Division of Drug Marketing, Advertising and Communication.

1. The panel discussed the following look-alike drug name:

Product name	Generic name: Strength	Usual Dose	Observation
Trelstar	Triptorelin pamoate for injectable suspension	3.75 mg IM monthly	
Trental	Pentoxifylline, tablets	400mg tid	*L/A

*Look-alike

According to the expert panel, the proposed proprietary name, Trelstar, looks-alike Trental. However, Trental is a tablet dosage form and is indicated for intermittent claudication on the basis of chronic occlusive arterial disease of the limbs. Trelstar is an injection and is used for the palliative treatment of advanced prostate cancer. In addition, there is no overlapping dosing intervals between these two products. The panel, therefore, concluded that the above listed drug and Trelstar pose no significant safety risk and hence, the proprietary name, Trelstar, is not objectionable.

2. DDMAC- no objections

B. STUDY CONDUCTED BY OPDRA

Methodology:

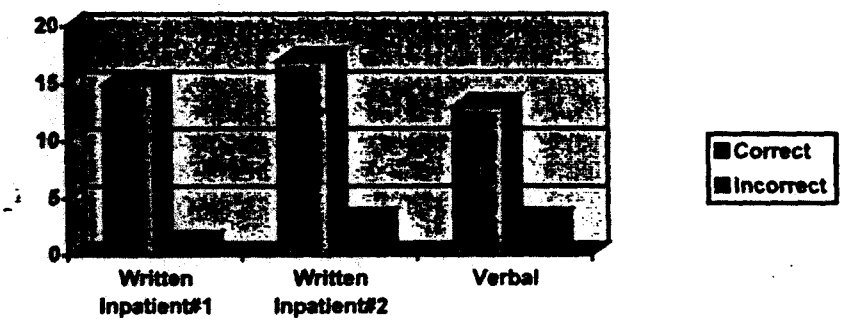
This study involved 94 health professionals consisting of physicians, nurses and pharmacists within FDA to determine the degree of confusion of [redacted] with other drug names due to the similarity in handwriting and verbal pronunciation of the name. Written prescriptions, consisting of (known/unknown) drug products and a prescription for Trelstar were scanned into a computer and were then delivered to a random sample of the participating health professionals via e-mail. In addition, verbal orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff. We conducted two inpatient written studies to see if a poorly written script (which is often seen in actual prescription) can result in dramatically different results. We did not conduct the outpatient written study since this drug would not normally be prescribed in that setting.

APPEARS THIS WAY
ON ORIGINAL

The results are summarized in Table I.

Table I

Study	# of Samples	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted
Written Inpatient#1	32	16 (50%)	15	1
Written Inpatient#2	31	20 (65%)	17	3
Verbal	31	16 (52%)	13	3
Total	94	52 (55%)	45 (87%)	7 (13%)



Eighty-seven percent of the participants responded with the correct name Trelstar®. The incorrect written and verbal responses are as follows in Table II.

Table II

	Incorrectly Interpret
Written Inpatient#1	Trekstar
Written Inpatient#2	Trelstin
	Trelater (2)
	Phonetic Response Variables
Verbal	Trosta
	Tropstar
	Trovstar

C. SAFETY EVALUATOR RISK ASSESSMENT

Trental was identified to have potential for confusion with Trelstar due to its look-alike name. However, Trelstar is available as an injectable formulation and its usual dosage is 3.75 mg IM once monthly for the palliative treatment of advanced prostate cancer. Trental is available as a tablet dosage and is indicated for chronic occlusive arterial disease of the limbs. There is no overlapping administration dosing schedule and strength between Trelstar and Trental. Considering all the circumstances under which Trelstar will be used, it is unlikely that Trental would be confused and result in potential medication errors.

The results of the verbal prescription study indicate that thirteen (out of sixteen) participants interpreted Trelstar correctly. In the first written study, fifteen (out of sixteen) interpreted Trelstar correctly while the second written study has seventeen (out of 20) participants answer the name correctly. We conducted two inpatient written studies to see if a poorly written prescription can produce different result. In this case, the results were similar.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container label, carton and insert labeling of Trelstar, OPDRA has attempted to focus on safety issues relating to possible medication errors. OPDRA has reviewed the current package insert and has identified several areas of possible improvement, which might minimize potential user error.

A. CONTAINER LABEL AND CARTON LABELING:

Neither container label nor carton labeling was submitted for review. However, see comments below.

B. INSERT LABELING:

General Comments:

Current USP nomenclature standards, under General Notices, recommend that both the active moiety and drug substance names and their equivalent amounts are provided in the labeling.

In this case, we believe it is more accurate and less confusing if the pamoate salt is not included in the established name.

Trelstar Depot
(triptorelin for injectable suspension)
3.75 mg

Revise the Description Section as follows:

Draft

III. RECOMMENDATIONS

OPDRA has no objections to the use of the proprietary name Trelstar®.

Should you have any questions concerning this review, please contact Peter Tam at 301-827-3241.

/S/ 5/18/00

Peter Tam, RPh.
Safety Evaluator
Office of Post-Marketing Drug Risk Assessment

Concur

/S/ 5/18/00

Jerry Phillips, RPh.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment

C.C.

NDA 20-715
Office File
HFD-580; DivFiles; Jeanine Best, Project Manager, DRUDP
HFD-580; Susan Allen, M.D., Acting Division Director, DRUDP
HFD-440; Denise Toyer, Safety Evaluator, DDRE II, OPDRA
HFD-42; Patricia Staub, Regulatory Review Officer, DDMAC (electronic copy)
HFD-400; Jerry Phillips, Associate Director, OPDRA
HFD-400; Peter Honig, Director, OPDRA (electronic copy)
HFD-002; Murray Lumpkin, Deputy Center Director for Review Management (electronic copy)

REQUEST FOR TRADEMARK REVIEW

To: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair (HFD-530), 9201 Corporate Blvd, Room N461

From: **Division of** Reproductive and Urologic Drug Products	**HFD-580**
Attention: David T. Lin, Ph.D.	**Phone: (301)827-4230**
Date: April 5, 2000	
Subject: Request for Assessment of a Trademark for a Proposed New Drug Product	
Proposed Trademark: Trelstar Depot	**NDA 20-715**
Established name, including dosage form: triptorelin pamoate for injectable suspension	
Other trademarks by the same firm for companion products: Decapeptyl	
Indications for Use (may be a summary if proposed statement is lengthy): Palliative treatment for advanced prostate cancer.	
Initial Comments from the submitter (concerns, observations, etc.): The sponsor had originally requested review of the trademark [redacted] This trademark was considered to be acceptable by the LNC (consult #1109). The sponsor has proposed the above new trademark to replaced [redacted]	

Note: Meetings of the Committee are scheduled for the 4th Tuesday of the month. Please submit this form at least one week ahead of the meeting. Responses will be as timely as possible.

Rev. December 95

REQUEST FOR TRADEMARK REVIEW

To: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair (HFD-530), 9201 Corporate Blvd, Room N461

From: Division of Reproductive and Urologic Drug Products	HFD-580
Attention: David T. Lin, Ph.D.	**Phone: (301)827-4230**
Date: January 27, 2000	
Subject: Request for Assessment of a Trademark for a Proposed New Drug Product	
Proposed Trademark: Trelstar	**NDA 20-715**
Established name, including dosage form: triptorelin pamoate for depot suspension	
Other trademarks by the same firm for companion products: Decapeptyl	
Indications for Use (may be a summary if proposed statement is lengthy): Palliative treatment for advanced prostate cancer.	
Initial Comments from the submitter (concerns, observations, etc.): The sponsor had originally requested review of the trademark [redacted] This trademark was considered to be acceptable by the LNC (consult #1109). The sponsor has proposed the above new trademark to replaced [redacted]	

Note: Meetings of the Committee are scheduled for the 4th Tuesday of the month. Please submit this form at least one week ahead of the meeting. Responses will be as timely as possible.

Rev. December 95

CDER LABELING AND NOMENCLATURE COMMITTEE

CONSULT # 1182	HFD# 580	PROPOSED PROPRIETARY NAME:	PROPOSED ESTABLISHED NAME:
ATTENTION: David T. Lin		Trelstar	triptorelin pamoate for depot suspension

A. Look-alike/Sound-alike

	Potential for confusion:
VALSTAR	XXX Low ____ Medium ____ High
VELSAR	XXX Low ____ Medium ____ High
NEOSAR	XXX Low ____ Medium ____ High
	____ Low ____ Medium ____ High
	____ Low ____ Medium ____ High

B. Misleading Aspects:

C. Other Concerns:

D. Established Name

____ Satisfactory

XXX Unsatisfactory/Reason

Recommended Established Name

triptorelin for injectable suspension

E. Proprietary Name Recommendations:

XXX ACCEPTABLE ____ UNACCEPTABLE

F. Signature of Chair/Date /S/ 6/7/99

CDER LABELING AND NOMENCLATURE COMMITTEE

CONSULT #	HFD#	PROPOSED PROPRIETARY NAME:	PROPOSED ESTABLISHED NAME:
1109	580		triptorelin pamoate depot

ATTENTION: Moo-Jhong Rhee

A. Look-alike/Sound-alike

	Potential for confusion:		
TRENDAR	XXX Low	____ Medium	____ High
TELOPAR	XXX Low	____ Medium	____ High
TRILAFON	XXX Low	____ Medium	____ High
TRILASATE	XXX Low	____ Medium	____ High
	____ Low	____ Medium	____ High

B. Misleading Aspects:

C. Other Concerns:

D. Established Name

XXX Satisfactory

____ Unsatisfactory/Reason

Recommended Established Name

E. Proprietary Name Recommendations:

XXX ACCEPTABLE ____ UNACCEPTABLE

F. Signature of Chair/Date /S/ 1/19/99

MEMORANDUM

Date: June 2, 1997

To: NDA 20-715, Decapeptyl (triptorelin pamoate), Debio Recherche Pharmaceutique SA

From: Moo-Jhong Rhee, Ph.D. Chemistry Team Leader, HFD-820 @HFD-58[illegible] ~6/2/97

Subject: Tradename

/S/

On May 2, 1997, the firm submitted an amendment proposing a new tradename, [redacted]. Since it appears that this NDA is not going to be approved, the consult review of this new tradename has not been initiated in order to avoid unnecessary work for the the Labeling and Nomenclature Committee. It will be done, however, when the firm resubmits the NDA in the future.

cc:
Origianl NDA 20-715
HFD-580/Division File
HFD-580/ADunson
HFD-580/MRhee
n20715.#2-